

Society of Anesthesia and Sleep Medicine (SASM)

SASM



3rd Annual Meeting
October 10-11, 2013
Le Méridien San Francisco



Opioids, Respiratory Depression and Sleep-Disordered Breathing (SDB): Perioperative Implications

Program Chair:
Babak Mokhlesi, MD, MSc
University of Chicago

Program Co-Chair:
Frances Chung, MBBS
University of Toronto
SASM President-Elect

Syllabus

Invited Faculty

Dennis Auckley, MD
MetroHealth Medical Center
Case Western Reserve University

Norman Bolden, MD
SASM Secretary
MetroHealth Medical Center
Case Western Reserve University

Jolie Chang, MD
University of California,
San Francisco

Frances Chung, MBBS
SASM President-Elect
Program Co-Chair
University of Toronto

Tom Cloward, MD
Intermountain Healthcare
University of Utah

Anthony Doufas, MD
Stanford University

Matthias Eikermann, MD
Massachusetts General Hospital
Harvard University

Robert Farney, MD
Intermountain Healthcare
University of Utah

Jane C.K. Fitch, MD
Incoming ASA President
University of Oklahoma Health
Sciences Center

Peter Gay, MD
SASM Treasurer
Mayo Clinic

David Hillman, MD
SASM President
Sir Charles Gairdner Hospital
University of Western Australia
at Perth

Richard Horner, PhD
University of Toronto

Shahrokh Javaheri, MD
Sleepcare Diagnostics
Professor Emeritus, University of
Cincinnati

Roop Kaw, MD
SASM Board Member
Cleveland Clinic

Jacqueline Leung, MD, MPH
University of California,
San Francisco

Ralph Lydic, PhD
University of Michigan

Atul Malhotra, MD
University of California,
San Diego

Mervyn Maze, MB, ChB
University of California, San
Francisco

Babak Mokhlesi, MD, MSc
SASM Board Member
Program Chair
University of Chicago

Kimmo Murto, MD
Children's Hospital of Eastern
Ontario
University of Toronto

Mark Opp, PhD
University of Washington

Sairam Parthasarathy, MD
University of Arizona

Michael Pilla, MD
Vanderbilt University School of
Medicine

Satya Krishna Ramachandran, MD
University of Michigan

Roman Schumann, MD
Tufts Medical Center
Tufts University Health Center

Edwin Seet, MD
Alexandra Health Private Limited

Ken Solt, MD
Massachusetts General Hospital
Harvard University

Andreas Taenzer, MD
Dartmouth College
Geisel School of Medicine,
Dartmouth

Meeting Accreditation Information

Learning Objectives

1. Understand the mechanism of ventilatory control and the relationship between anesthesia and sleep medicine
2. Recognize risk factors for the development of central sleep apnea due to opioids as well as the perioperative impact of sedatives/narcotics in both adults and children;
3. Interpret the perioperative complications of sleep-disordered breathing;
4. Develop practice pathways to screen, diagnose, monitor/manage sleep-disordered breathing in the perioperative period.

Practice Gaps

The overall goal of SASM is to advance standards of care for clinical problems shared by anesthesiology and sleep medicine, including perioperative management of Sleep-Disordered Breathing (SDB), and to promote interdisciplinary communication, education and research in matters common to anesthesia and sleep.

- Explore the relationship between opioids, respiratory depression and Sleep-Disordered Breathing in the postoperative setting.
- Understand the growing evidence linking opioids to central sleep apnea.
- Understand the adverse impact of SDB on postoperative outcomes.
- Best practices in protocol development for the perioperative management of patients with SDB.
- Explore various methods of perioperative management of SDB, including both PAP and non-PAP modalities

Target Audience

This conference is designed for anesthesiologists, critical care physicians, residents, fellows-in-training, general medicine physicians, pulmonary physicians, sleep medicine physicians, surgeons, scientists and allied health care professionals.

Accreditation Statement

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of the Institute for the Advancement of Human Behavior (IAHB) and the Society of Anesthesia and Sleep Medicine (SASM). The IAHB is accredited by the ACCME to provide continuing medical education for physicians.

Credit Designation Statement

The IAHB designates this live activity for a maximum of **11.5 AMA PRA Category 1 Credit(s)[™]**. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Program Objective

The objective of this meeting is to provide a forum for discussions pertaining to the common grounds between sleep and anesthesia. The goal is to promote excellence in medical care, research and education in anesthesia, sleep medicine and perioperative medicine.

Meeting Accreditation Information

Planning Committee Disclosures

Babak Mokhlesi, MD, MSc
2013 Program Chair

Frances Chung, MBBS
2013 Program Co-Chair

Statement of Disclosure: All faculty/speakers, planners, abstract reviewers, moderators, authors, co-authors and administrative staff participating in the continuing medical education programs jointly sponsored by IAHB are expected to disclose to the program audience any/all relevant financial relationships related to the content of their presentation(s). All faculty/speakers, planners, abstract reviewers, moderators, authors, co-authors and administrative staff indicated with asterisks (*) stated they had no such relevant financial relationships to disclose.

Speaker Disclosures

*No Disclosures

Dennis Auckley, MD
ResMed, Research Grant Site Principal Investigator

***Norman Bolden, MD**

***Jolie Chang, MD**

***Frances Chung, MBBS**

***Tom Cloward, MD**

***Anthony Doufas, MD**

Matthias Eikermann, MD
ResMed, Research Grant Site Principal Investigator

***Robert Farney, MD**

***Peter Gay, MD**

***David Hillman, MD**

***Richard Horner, MD**
Shahrokh Javaheri, MD
Philips-Repironics, Speaker

***Roop Kaw, MD**

***Jacqueline Leung, MD, MPH**

***Ralph Lydic, PhD**

***Atul Malhotra, MD**

***Mervyn Maze, MB, ChB**

Babak Mokhlesi, MD, MSc
Philips-Repironics, Consultant and Site Principal Investigator

Kimmo Murto, MD

Janssen Pharmaceuticals, Inc, Research Grant Site Principal Investigator

***Mark Opp, PhD**

Sairam Parthasarathy, MD
Philips-Respironics, Inc, Research Grant Site Principal Investigator

Niveus Medical, Inc, Research Grant Site Principal Investigator

***Michael Pilla, MD**

***Satya Krishna Ramachandran, MD**

***Roman Schumann, MD**

***Edwin Seet, MD**

***Ken Solt, MD**

***Andreas Taenzer, MD**

Conflict Resolution: All conflicts of interest have been resolved. Speakers were limited to data and results of research. All other faculty/speakers, planners, abstract reviewers, moderators, authors, co-authors and administrative staff indicated they had no such relevant financial relationships to disclose.



Meeting Agenda

Thursday, October 10, 2013

| | | |
|--------------------|---|-------------------------|
| 2:00-3:00pm | Basic Science Special Interest Group | |
| 3:00-3:05pm | Introduction to Workshops | Babak Mokhlesi, MD, MSc |
| 3:05-6:00pm | Moderators: Peter Gay, MD and Roop Kaw, MD | |
| 3:05-6:00pm | Workshop 1: Protocol Development for the Perioperative Management of Patients with SDB <ul style="list-style-type: none"> Review Challenges in Implementing a Perioperative OSA Program (Intermountain Experience: Tom Cloward, MD; Toronto & Singapore Experience: Edwin Seet, MD, Vanderbilt Experience: Michael Pilla, MD) Discussion/Q&A How to do PAP Therapy (MetroHealth Experience: Dennis Auckley, MD) Clinical Trial Design and Outcomes to be Measured (David Hillman, MD) Discussion/Q&A | |
| 3:05-6:00pm | Moderators: Mervyn Maze, MB, ChB, Mark Opp, PhD, Richard Horner, PhD | |
| 3:05-6:00pm | Workshop 2: Basic Science of Sleep <ul style="list-style-type: none"> Upper Airway Tone and Patency in the Postoperative Period (Atul Malhotra, MD) Interactive Effects of Anesthesia, Opioids and Sleep on Breathing and Arousal in the Perioperative Period (Matthias Eikermann, MD) Sleep as an Immune System Regulator During the Perioperative Period (Mark Opp, PhD) Discussion/Q&A Sedation and Natural Sleep (Mervyn Maze, MB, ChB) Reanimation from General Anesthesia: The Role of Dopamine (Ken Solt, MD) Discussion/Q&A | |
| 6:00-6:45pm | Welcome Reception | |
| 6:45-9:30pm | Dinner with Invited Speakers (Additional Fee Required) | |
| | Introduction of the Incoming ASA President: Jane C.K. Fitch, MD | David Hillman, MD |
| | Shared Circuits of Anesthesia and Sleep: Basic Mechanisms and Clinical Relevance | Ralph Lydic, PhD |

Friday, October 11, 2013

| | | |
|------------------------|--|--------------------------------|
| 7:15-7:55am | Annual General Meeting | |
| 7:00-7:55am | Registration and Continental Breakfast | |
| 7:55-8:00am | Introduction | David Hillman, MD |
| 8:00-10:45am | Moderator: Babak Mokhlesi, MD, MSc | |
| 8:00-8:50am | Keynote: Neural Mechanisms of Sleep and Sedation-Induced Respiratory Depression | Richard Horner, PhD |
| 8:50-9:30am | Keynote: Opioids and Central Sleep Apnea | Shahrokh Javaheri, MD |
| 9:30-10:00am | Delirium in Hospitalized Patients, Role of Sleep Disruption, Opioids and Pain | Jacqueline Leung, MD, MPH |
| 10:00-10:15am | Discussion/Q&A | |
| 10:15-10:45am | Refreshment Break and Poster Viewing | |
| 10:45am-12:15pm | Moderator: Frances Chung, MBBS | |
| 10:45-11:10am | Should All Postoperative Patients be Monitored on the Wards? Pro | Andreas Taenzer, MD |
| 11:10-11:35am | Should All Postoperative Patients be Monitored on the Wards? Con | Satya Krishna Ramachandran, MD |
| 11:35am-12:00pm | Sedation and Anesthesia as a Surrogate for Sleep in Clinical Investigation of the Upper Airway | Jolie Chang, MD |

Meeting Agenda

| | | |
|----------------------|---|--------------------------|
| 12:00-12:15pm | Discussion/Q&A | |
| 12:15-1:15pm | Lunch Break and Poster Viewing | |
| 1:15-1:35pm | Awards to Scientific Abstract Winners | Frances Chung, MBBS |
| 1:15-1:20pm | Research Award Presented (Frances Chung, MBBS and Roop Kaw, MD) | |
| 1:20-1:25pm | Abstract Awards Presented (Frances Chung, MBBS and Yandong Jiang, MD) | |
| 1:25-1:30pm | Basic Research First Place Winner Presentation | |
| 1:30-1:35pm | Clinical Research First Place Winner Presentation | |
| 1:40-3:15pm | Moderator: Roop Kaw, MD | |
| 1:40-2:10pm | Non-PAP and PAP Treatment of OSA Postoperatively | Sairam Parthasarathy, MD |
| 2:10-2:35pm | Impact of SDB on Postoperative Outcomes | Babak Mokhlesi, MD, MSc |
| 2:35-2:50pm | Discussion/Q&A | |
| 2:50-3:15pm | Refreshment Break and Poster Viewing | |
| 3:15-5:00pm | Moderator: Norman Bolden, MD | |
| 3:15-3:40pm | Anesthesia, SDB and Bariatric Surgery | Roman Schumann, MD |
| 3:40-4:05pm | Suboxone (Buprenorphine/Naloxone) and Sleep-Disordered Breathing, or Look Out for that Low Ceiling! | Robert Farney, MD |
| 4:05-4:25pm | Pain Management with Opioids in the Postoperative Period and Impact on SDB | Anthony Doufas, MD |
| 4:25-4:45pm | Analgesic Management in Children After Tonsillectomy & Adenoidectomy | Kimmo Murto, MD |
| 4:45-5:00pm | Discussion/Q&A | |
| 5:00pm | i-Pad® Giveaway and Closing Remarks | Babak Mokhlesi, MD |

Wifi Access

To access Wifi in the meeting rooms during the 3rd Annual Meeting, please use the information below:

Network Name: PSAV EventSolutions

Password: SASM13

Research Grant Award

Congratulations to Principal Investigator, Dr. Susana Vacas, MD with the University of California, San Francisco for winning the first Society of Anesthesia and Sleep Medicine (SASM) Research Grant! Dr. Vacas will be awarded at the 3rd Annual Meeting Luncheon on Friday, October 11, 2013. Please find more details below.

Project Title: Obstructive Sleep Apnea and Postoperative Cognitive Decline

Principal Investigator: Susana Vacas, MD, UCSF

Senior Investigator: Mervyn Maze, MD, UCSF

Abstract Awards

Best Basic Research Awards

First Place Award

Abstract: GAL-021 Reverses Opioid-Induced Respiratory Depression and Decreases the Severity of Central Sleep Apneas and Obstructive Apneas in Rats

Main Author: Francis Golder, DVM, PhD, Galleon Pharmaceuticals

Co-Authors: *Matthew Hewitt PhD, *Santhosh Baby, PhD, *Ryan Gruber, BS, *Courtney Ideo, BS, *D Euan MacIntyre, PhD, *Galleon Pharmaceuticals

Second Place Award

Abstract: The Human Carotid Body Function - Neurotransmitter Release in Response to Acute Hypoxia

Main Author: Malin Jonsson Fagerlund, MD, PhD, Karolinska University Hospital and Karolinska Institutet

Co-Authors: Jessica Kåhlin, MD, Souren Mkrtchian, MD, PhD, Anette Ebberyd, BSc, Malin Jonsson Fagerlund, MD, PhD, Lars I Eriksson, MD, PhD

Best Clinical Research Awards

First Place Award

Abstract: Celecoxib for Pediatric Adenotonsillectomy: A Randomized Controlled Double Blinded Study

Main Author: Kimmo Murto, MD, FRCPC, University of Ottawa, Children's Hospital of Eastern Ontario

Co-Authors: Christine Lamontagne, MD, University of Ottawa, Children's Hospital of Eastern Ontario (CHEO), Johnna McCormick, MD, University of Ottawa, CHEO, Colleen Daly, MD, University of Ottawa, Kelly Ramakko, BSc, University of Ottawa, CHEO, David Rosen, MD, University of Ottawa, CHEO, Nick Barrowman, PhD, Clinical Research Unit, CHEO Research Institute and Regis Vailancourt, PharmD, CHEO

Second Place Award (1 of 2)

Abstract: Obstructive Sleep Apnea and Postoperative Complications: Matched Cohort Comparison of Respiratory and Cardiovascular Outcomes Before and After Diagnosis by Polysomnography

Main Author: Thomas Mutter, FRCPC, MSc, University of Manitoba

Co-Authors: Dan Chateau PhD, Manitoba Centre for Health Policy, University of Manitoba, Michael Moffatt, MD, FRCPC, MSc, University of Manitoba, Clare Ramsey, MD, FRCPC, MS, University of Manitoba, Leslie L. Roos, PhD, University of Manitoba, Meir Kryger, MD, FRCPC, Yale University School of Medicine, VA Connecticut Healthcare System

Second Place Award (2 of 2)

Abstract: GAL-021, A New Intravenous Selective Potassium-Channel Blocker, Reverses Opioid Induced Respiratory Depression with no Impairment of Opioid Analgesia

Main Author: Margot Roozkrans, MD, University of Leiden Medical Center

Co-Authors: Rutger van der Schrier, MD, Joop Van Gerwen, MD, PhD, Pieter Okkerse, MD, Sean Peng, PhD, Paul A. Hoskins, James F. McLeod, MD, Albert Dahan, MD, PhD

Acknowledgement of Commercial Support & Exhibit

Covidien,
Commercial Supporter

Fisher Paykel,
Commercial Supporter

Hospira,
Exhibitor

Masimo Corporation,
Commercial Supporter

Nihon Kohden,
Commercial Supporter

Philips Healthcare,
Commercial Supporter

ResMed,
Commercial Supporter

Respiratory Motion,
Commercial Supporter

Sleep Image, Exhibitor

QRxPharma, Exhibitor

Platinum Sponsor



Gold Plus Sponsor



Gold Sponsors



Silver Sponsors



Bronze Sponsors



Continuing Medical Education (CME) Certificate

IMPORTANT!

The online certificate site will be available at the end of the day on *October 11th* through *November 11th*. After that date, the site will be removed and certificates will no longer be available. If you need a CME / CE certificate, you must complete the evaluation and certificate process prior to that date; otherwise you will forfeit your credit for the course.

To get your certificate, just go to www.CmeCertificateOnline.com.

Scroll down to the SASM listing and click on the "SASM 3rd Annual Meeting" event. On the site, you will be asked to enter a password, which is **3AM**, and evaluate various aspects of the program. You may then print your certificate.

Please address any questions about the process to: Jillian Davis, Jillian@amedcoemail.com, 651-789-3722.

Abstract Table of Contents

| Abstract # | Page # | First Name: | Last Name: | Highest Degree(s): | Organization/Affiliation: | Abstract Title: | |
|----------------------|--------|-------------|------------|--------------------|--|---|--|
| MORNING BREAK | | | | | | | Moderators |
| 1 | 11 | Rebecca | Evans | MD | University of Utah | The Correlation Between Right Heart Dysfunction And The Stop Bang Questionnaire In The Preoperative Population | Dr. Dennis Auckley & Dr. Bhargavi Gali |
| 2 | 12 | Mohamed | Elhakim | MBBSch | University of Texas Medical School at Houston | Initiation Of A Computerized Physician Order System In An Academic Anesthesiology Department | Dr. Yandong Jiang & Dr. Michael Pilla |
| 3 | 14 | Mohamed | Elhakim | MBBSch | University of Texas Medical School at Houston | Measurement Of Esophageal Temperature At Two Separate Sites During Pulmonary Vein Ablation | Dr. Yandong Jiang & Dr. Michael Pilla |
| 4 | 16 | Mohamed | Elhakim | MBBSch | University of Texas Medical School at Houston | One Year Follow-Up After Computerized Physician Order System Implementation In An Academic Anesthesiology Department | Dr. Yandong Jiang & Dr. Michael Pilla |
| 5 | 18 | Philipp | Gerner | BSc | Stony Brook University | Sleep Apnea Is A Risk Factor For Inpatient Falls After Joint Arthroplasty | Dr. Dennis Auckley & Dr. Bhargavi Gali |
| 6 | 20 | Babak | Mokhlesi | MD | University of Chicago | Sleep-Disordered Breathing And Postoperative Outcomes After Bariatric Surgery: Analysis Of The Nationwide Inpatient Sample | Dr. Dennis Auckley & Dr. Bhargavi Gali |
| 7 | 21 | Maged | Andrewes | MD | Toronto Western Hospital, University Health Network, University of Toronto | Identification Of Factors Associated With Postoperative Elevation Of Apnea And Hypopnea In Surgical Patients Without Preoperative Sleep Apnea | Dr. Dennis Auckley & Dr. Bhargavi Gali |
| 8 | 23 | Yugo | Tagaito | MD, PhD | Teikyo University Chiba Medical Center | A Novel Method To Efficiently Detect Esophageal Misplacement Of Endotracheal Tubes | Dr. Yandong Jiang & Dr. Michael Pilla |
| 9 | 25 | Thomas | Mutter | FRCPC MSc | University of Manitoba | Obstructive Sleep Apnea And Postoperative Complications: Matched Cohort Comparison Of Respiratory And Cardiovascular Outcomes Before And After Diagnosis By Polysomnography | Dr. Dennis Auckley & Dr. Bhargavi Gali |
| 10 | 27 | James | Tse | MD, PhD | Rutgers-Robert Wood Johnson Medical School | A New And Low-Cost Tse-Alloteh Nasal CPAP/CF Mask/Circuit Improved Oxygenation Of A High-Risk Obese Patient With OSA Under MAC For TEE | Dr. Shiroh Isono |
| 11 | 29 | Lisa | Campana | PhD | Respiratory Motion | The Use Of A Non-Invasive Respiratory Volume Monitor To Detect And Quantify Obstructive Sleep Apnea In Postoperative Patients | Dr. Dennis Auckley & Dr. Bhargavi Gali |

Abstract Table of Contents Continued

| | | | | | | | |
|------------------------|----|------------|-------------|---------------|--|---|--|
| 12 | 32 | Edwin | Seet | M.Med (Anaes) | Kho Teck Puat Hospital, Alexandra Health Services | Incidence Of Unrecognized Obstructive Sleep Apnea In Major Noncardiac Surgery | Dr. Dennis Auckley & Dr. Bhargavi Gali |
| 13 | 34 | Susan | Kais | MD | Scripps Green Hospital, La Jolla California | Continuous Negative External Pressure (Cnep) Diminishes Obstructive Apneas And Improves Oxygenation During Colonoscopy | Dr. Shiroh Isono |
| 14 | 35 | James | Tse | MD, PhD | Rutgers-Robert Wood Johnson Medical School | A New And Low-Cost TSE-Alloteh Nasal CPAP/CF Mask/Circuit Improved Oxygenation Of A High-Risk Obese Patient With OSA Under MAC For Bronchoscopy | Dr. Shiroh Isono |
| 15 | 37 | Shinichiro | Kato | MD | Chiba University | Does Negative Pressure Applied To The Submandible Region Improve Collapsibility Of The Passive Pharyngeal Airway? | Dr. Shiroh Isono |
| 16 | 39 | Demet | Sulemanji | MD | Massachusetts General Hospital | Short-Term Succinylcholine Infusion During General Anesthesia May Not Result In Clinically Significant Phase II Block | Dr. Yandong Jiang & Dr. Michael Pilla |
| 17 | 41 | Meghan | Kirksey | MD, PhD | Hospital for Special Surgery | Diminished Sleep Efficiency After Total Knee Replacement Surgery May Be Ameliorated By Perioperative Melatonin: A Double-Blinded Placebo Controlled Study | Dr. Yandong Jiang & Dr. Michael Pilla |
| 18 | 43 | James | Tse | MD, PhD | UMDNJ-Robert Wood Johnson Medical School | A Technically Simple And Effective Nasal CPAP/CF Mask/Circuit To Improve Oxygenation Of Obese Patients With OSA Under Deep Propofol Sedation During EGD | Dr. Shiroh Isono |
| AFTERNOON BREAK | | | | | | | Moderators |
| 19 | 46 | Rajeev | Subramanyam | MD | Cincinnati Children's Hospital | Upper Airway Morphology In Children With Down Syndrome vs. Children With Normal Airway Under Dexmedetomidine | Dr. Suzanne Karan |
| 20 | 50 | Yandong | Jiang | MD, PhD | Massachusetts General Hospital | Evaluation Of Feasibility And Functionality Of A Video-Laryngoscope Equipped With A Ventilation Feature | Dr. Yandong Jiang |
| 21 | 52 | Peter | Liao | MD | Toronto Western Hospital, Toronto University Health Network | No Association Between Preoperative Polysomnography Parameters And Postoperative Opioids Requirement In Adult Patients With Obstructive Sleep Apnea | Dr. Anthony Doufas |
| 22 | 54 | Peter | Liao | MD | Toronto Western Hospital, Toronto University Health Network | Postoperative Opioids Requirement And Sleep Disordered Breathing | Dr. Anthony Doufas |
| 23 | 56 | Nicholas | Dalesio | MD | Johns Hopkins University | Morphine Metabolism In Diet-Induced Obese Mice Compared To Leptin-Deficient Obese Mice | Dr. Yandong Jiang |
| 24 | 58 | Francis | Golder | DVM, PhD | Galleon Pharmaceuticals | Gal-021 Reverses Opioid-Induced Respiratory Depression And Decreases The Severity Of Central Sleep Apneas And Obstructive Apneas In Rats | Dr. Yandong Jiang |
| 25 | 60 | Francis | Golder | DVM, PhD | Galleon Pharmaceuticals | Gal-021, A New Intravenous Selective Potassium-Channel Blocker, Is Well Tolerated And Stimulates Ventilation In Healthy Volunteers | Dr. Anthony Doufas |
| 26 | 62 | Kimmo | Murto | FRCPC | University of Ottawa, Children's Hospital of Eastern Ontario | Celecoxib For Pediatric Adenotonsillectomy: A Randomized Controlled Double Blinded Study | Dr. Suzanne Karan |
| 27 | 64 | Kimmo | Murto | FRCPC | University of Ottawa, Children's Hospital of Eastern Ontario | Validation Of The ASA OSA Prediction Tool In Children | Dr. Suzanne Karan |
| 28 | 66 | Michael | Wong | JD | Physician-Patient Alliance for Health & Safety | Results Of National Hospital Survey Of Patient-Controlled Analgesia Practices | Dr. Yandong Jiang |
| 29 | 67 | Margot | Roozekrans | MD | University of Leiden Medical Center | Gal-021, A New Intravenous Selective Potassium-Channel Blocker, Reverses Opioid Induced Respiratory Depression With No Impairment Of Opioid Analgesia | Dr. Anthony Doufas |
| 30 | 69 | Jessica | Kählin | MD | Karolinska University Hospital and Karolinska Institutet | The Human Carotid Body Function - Neurotransmitter Release In Response To Acute Hypoxia | Dr. Yandong Jiang |
| 31 | 71 | Jesse | Ehrenfeld | MD | Vanderbilt University | Impact Of A Post-Operative Obstructive Sleep Apnea Management Program On Perioperative Outcomes And Adverse Events | Dr. Suzanne Karan |

Morning Abstracts

The Correlation Between Right Heart Dysfunction and the STOP Bang Questionnaire in the Preoperative Population

Presenting author: Rebecca Evans, MD

Co-authors: Josh Zimmerman, MD, Ken Johnson, MD, Sonia Shishido, DO, Elise Heath, MD, Amber Bledsoe, MD

Background: The aim of this study was to assess the relationship between right heart dysfunction (RHD) diagnosed via transthoracic echocardiography and the number of positive responses to the STOP Bang questionnaire in patients presenting to the Preoperative Clinic at the University of Utah. We hypothesized that there would be a positive correlation between RHD and the number of positive responses to the STOP Bang questionnaire.

Methods: Between October-December 2012, 200 participants were consented and an abbreviated right-sided echocardiogram was performed by an anesthesiology resident with supervision from an anesthesiologist on the echocardiography team. Systolic function was measured using tricuspid annular plane systolic excursion (TAPSE) and tissue Doppler-derived tricuspid lateral annular systolic velocity (S'); diastolic function was measured using the tricuspid inflow E wave to tricuspid annular tissue Doppler e' wave ratio (E/e'). Two level III ASE qualified echocardiographers on the anesthesiology echocardiography team read each exam. Echocardiogram measurements were individually plotted as a continuous variable versus the patient's STOP-Bang score. Discrepancies between echocardiogram readings were analyzed using a Bland Altman plot.

Results: 181 echocardiograms were analyzed after exclusion of participants with incomplete STOP-Bang questionnaires. 52 patients reported 5 or more positive responses in the STOP-Bang questionnaire. Echocardiographers were able to interpret TAPSE 90%, S' 96%, and E/e' 82% of the time from the images obtained. Inter-reader variability of echocardiography measurements was within normal limits (average variability 6%, range 0-38%). Right heart dysfunction was found in 10 patients measured via TAPSE, 19 patients via S' , and 46 patients via E/e' . No correlation was observed between STOP-Bang scores and these metrics of RHD. Patients with echocardiographic evidence of RHD had a wide range of STOP-bang scores (0-8).

Conclusions: Our results did not confirm our study hypothesis. In this preliminary study, echocardiographic metrics of RHD did not correlate with positive responses to STOP-Bang scores suggesting that either there are numerous sources of RHD among one of which is sleep apnea, or the STOP-Bang questionnaire is not a sensitive tool for predicting right heart dysfunction.

Initiation of a Computerized Physician Order System in an Academic Anesthesiology Department

Authors: Mohamed Koronfel, Mohamed Elhakim, Paul Loubser

Affiliation: Heart and Vascular Institute, Hermann Memorial – Texas Medical Center, Department of Anesthesiology, University of Texas Medical School, Houston, Texas

Introduction: As hospitals move toward electronic health records, anesthesia departments are in various stages of transition toward Computerized Physician Order Entry (CPOE). However, the receptivity of physicians to CPOE has been mixed. (1) Last year, our facility implemented CPOE system in the Post-Anesthesia Care Unit. (PACU) In turn, an online survey of the department was conducted with respect to understanding the initial perceptions of the “usability” of the CPOE process

Methods: Prior to initiation of CPOE, all department members were offered training sessions using simulated CPOE workstations. As CPOE went live, facilitators were onsite in each PACU to guide providers through the process and troubleshoot problems as they arose. Approximately one month after CPOE initiation, an online survey of department members was conducted, including faculty and residents. The survey consisted on 10 questions that focused on experiences with orientation, training, support, ease of use, effect on efficiency, etc. Survey questions were structured using Likert scales that were amenable to scoring, or as a simple yes/no format. (Survey Monkey)

Results: Of the 128 surveys sent out, 60 responses were received (47% response rate). Sixty two percent of respondents were satisfied with the CPOE process. Although 67% of respondents described the institution’s orientation process as helpful, and 71% rated the onsite technical support as positive, only 42% reported that the CPOE system was user-friendly. In response to the question on impact that CPOE had on the ability to render patient care, 67 % of respondents stated that their efficiency was negatively impacted. The main benefit of CPOE was thought to be enhanced patient safety (55%). However, only 54% of respondents believed that CPOE would actually reduce medication errors. Receptivity to CPOE was mixed; 21% of respondents stated that colleagues were highly resistant to CPOE implementation. The institutional administration was perceived as the main driver for CPOE.

Conclusion: This survey revealed that initiation of CPOE in an academic anesthesiology department is challenging. Despite adequate support and orientation, some providers were negatively impacted in their patient care activities. Campbell et al describe this as “untended work consequences,” and have identified 9 such items. (2) This survey identified divergent opinion on the utility of CPOE; not all respondents viewed enhanced patient safety/reduced medication errors as a direct corollary of CPOE. Anesthesiology departments should be adequately prepared to deal with this

process, since efficiency may be impacted. Faculty and residents were included in this survey; an additional question is whether there are any differences in responses between the two groups, since residents tend to be main users of CPOE. Since familiarity with CPOE usage may improve with time, a follow-up survey after 12 months of CPOE usage would be helpful and elucidate any changes in the aforementioned responses.

References:

1. Massaro TA: Acad Med. 1993 Jan;68(1):20-5.
2. Campbell TM et al: J Am Med Inform Assoc. 2006;13:547-556.

Measurement of Esophageal Temperature at Two Separate Sites During Pulmonary Vein Ablation

Authors: Mohamed Koronfel, MB ChB, Paul Loubser, MB ChB, Mohamed Elhakim, MB ChB, Bharat Kantharia, M.D, Nada B. Memon, M.D

Affiliation(s): Heart and Vascular Institute, Texas Medical Center, Departments of Anesthesiology and Cardiovascular Medicine University of Texas Medical School, Houston, Texas 77030

Introduction: Pulmonary vein ablation (PVA) has been used to treat persistent supraventricular arrhythmias, in which a cardiologist first isolates and then thermally ablates the source of the arrhythmia¹. Since the esophagus is in close proximity to the left atrium, heat induced injury to the esophagus may occur². Although the incidence is low, the mortality rate is high. Luminal esophageal temperature (ET) monitoring is one of the most effective measures to minimize the risk of injury³. In this retrospective study, we elected to analyze temperature changes during PVA at two different temperature monitoring sites in the esophagus.

Methods: The anesthetic technique was standardized and utilized general anesthesia, endotracheal intubation and an arterial line. ET monitors were placed at two mid-atrial locations, ET1 and ET2 separated by 1-1.5 inches in the esophagus, as determined by cardiologist using fluoroscopy. Temperatures at both ET1 and ET2 locations were recorded simultaneously when radio-frequency ablation was performed at different left atrial sites. The peak ET was recorded at each location. In particular, the increase over baseline ET and the difference between ET1 and ET2, were noted.

Results: Twenty five patients were studied. Ablation sites in the left atrium included the anterior, posterior, inferior regions and the pulmonary veins. The most significant increases in temperature were seen during ablation of the posterior left atrium ranging from 0.1 – 4.0 degrees. However, in 20 out of 25 patients, measurements of ET1 \neq ET2. The absolute value of difference of temperature between ET1 and ET2 ranged from 0.4 to 3.8, with a mean of 1.3 and a standard deviation of 1.1.

Discussion: These findings suggest that measurement of temperature at two separate esophageal locations is more sensitive than one location in detecting temperature increases during PVA. The ablating electrode during PVA moves from different areas within the left atrium, and therefore, a wide area of temperature measurement is needed for more accurate monitoring. Furthermore, the most significant increases in temperature occurred when ablation performed in the posterior left atrium, adjacent to the esophagus. The implications of these observations suggest that one location of temperature measurement may not be accurate enough in detecting a “true” esophageal temperature. Further studies are needed

to verify these findings in a prospective study and to ascertain whether this has any patient safety ramifications for preventing esophageal injury.

References:

1. Shuraih M, Frederick M, Shivkumar K, Buch E. Strategies to Prevent Esophageal Injury During Catheter Ablation of Atrial Fibrillation. *The Journal of Innovations in Cardiac Rhythm Management* 2012;719–726.
2. Sanchez-Quintana D, Cabrena JA, Climent V, Farre J, Mendonca MC, Ho SY. Anatomic relations between the esophagus and left atrium and relevance for ablation of atrial fibrillation. *Circulation* 2005;112:1400-1405
3. Perzanowski C, Teplitsky L, Hranitzky PM, Bahnson TD. Real-time monitoring of luminal esophageal temperature during left atrial radiofrequency catheter ablation for atrial fibrillation: observations about esophageal heating during ablation at the pulmonary vein ostia and posterior left atrium. *J Cardiovasc Electrophysiol* 2006; 17:166–170.

One Year Follow-Up After Computerized Physician Order System Implementation in an Academic Anesthesiology Department

Authors: Mohamed Koronfel, Mohamed Elhakim, Paul Loubser

Affiliation: Heart and Vascular Institute, Hermann Memorial – Texas Medical Center, Department of Anesthesiology, University of Texas Medical School, Houston, Texas

Abstract: We studied the perception of anesthesiology Faculty and residents 12 months following the implementation of CPOE in a post-anesthesia care unit. Respondents reported that clinical care was still negatively impacted by the majority of users. Nursing staff were identified as providers of technical assistance.

Introduction: Computerized Physician Order Entry (CPOE) was implemented in our facility one year ago. We performed an initial assessment of the anesthesiologist perceptions of this new system after one month of CPOE usage. More than half of the anesthesiologists surveyed stated that they were negatively impacted in their clinical care activities. We elected to repeat the survey after 12 months of CPOE usage, in an effort to elucidate whether the anesthesiologists' perceptions had changed in any way. In this study, we separated the faculty from the residents, since residents were the main users of CPOE.

Methods: An online survey of department members was conducted, including faculty and residents, 12 months following CPOE initiation and the first survey. The survey consisted on 10 questions that focused on experiences with orientation, training, support, ease of use, effect on efficiency, etc. Survey questions were structured using Likert scales that were amenable to scoring, or as a simple yes/no format. (Survey Monkey).

Results: Of the 128 surveys sent out, a total of 43 responses were received (26 Faculty and 17 Residents). With regard to actual CPOE system, 48% of faculty and 56% of residents were satisfied with the support and function of the system. Unfortunately, 60% of faculty and 76% of residents reported that their clinical care efficiency still was negatively impacted by CPOE. Approximately 50% of faculty and residents believed that CPOE would reduce medication errors. When technical problems were encountered, 38% of faculty and 35% of residents turned to nursing staff for assistance. "Paper persistence" was reported in 23% of residents and 11% of Faculty. The institutional administration was perceived as the main driver for CPOE by both Faculty and residents. Forty two percent of Faculty and 23% of residents responded that colleagues remained indifferent to CPOE. However, an overwhelming majority of Faculty (61%), and residents (82%) welcomed expansion of the methodology to other perioperative HER components.

Conclusion: This survey revealed that implementation of CPOE in an academic anesthesiology department is challenging activity. Clinical efficiency was still negatively impacted by CPOE by a high percentage of respondents, despite a prolonged period of system familiarization. Campbell et al describe this as "untended work consequences," and have identified 9 such items. (1) Nursing staff were identified as an important source of assistance to both faculty and residents when technical problems were encountered. Not all

anesthesiologists embrace CPOE, however, there is a willingness to expand HER to other perioperative arenas. Anesthesiology departments should be encouraged to study methodologies that minimize the unintended consequence of CPOE on clinical work routines, particularly for residents.

References:

1. Campbell TM et al: J Am Med Inform Assoc. 2006;13:547–556.

Sleep Apnea is a Risk Factor for Inpatient Falls After Joint Arthroplasty.

Gerner P, Danninger T, Stundner O, Rasul R, Memtsoudis S.

Background: In-patient falls (IF) are associated with significant risk for secondary injury and health care cost. Patients after joint arthroplasty are at especially high risk given their limitations on mobility in the postoperative period. While a number of studies have attempted to identify risk factors for these adverse events, none has considered the presence of sleep apnea as a covariate. Therefore, we utilized a large national database to test our hypothesis that sleep apnea would represent a risk factor for IF after knee arthroplasty.

Materials and Methods: Data provided by Premier Perspective, Inc. Charlotte, North Carolina was collected between 2006 and 2010. The database includes information from approximately 400 acute care hospitals located throughout the United States. We included subjects from the database undergoing elective total knee arthroplasty; Patient (age, gender, race, comorbidities) and health care system characteristics (anesthesia type, use of peripheral nerve block, hospital type, location and size, year of service) were determined for those that suffered an IF event and compared to non-IF patients. Among other comorbidities, the presence of sleep apnea was considered. To determine independent risk factors of IF, an initial multivariable logistic regression model was determined and then fitted on 100 bootstrapped samples using the forwards selection method. To robustly determine strong predictive covariates only, significant predictors occurring in at least 70% of the samples were selected for the final model and evaluated.

Results: We identified 191,570 entries with a procedure code for elective TKA that also had anesthesia type information recorded. The overall incidence of IF was 1.6%. The prevalence of sleep apnea was 9.2%.

Patients suffering IF were more commonly older (average age 68.9 vs 66.3 years, $P < 0.001$) and had a higher comorbidity burden (average Deyo Index 0.77 vs 0.66, $P < 0.001$). Sleep apnea was more commonly present in patients suffering an IF compared to those that did not (10.6% vs. 9.1%, $P = 0.0036$).

Patients suffering from an IF had significantly higher rates of major complications, including 30-day mortality (0.79% vs 0.12%, $P < 0.001$), higher rates of utilization of critical care services (9.0% vs 3.0%, $P < 0.001$), longer lengths of hospitalization (4.8 vs 3.5 days, $P < 0.001$) and higher average cost (\$19,487 (CI: \$19,095-\$19,879) vs. \$15,798 (CI: \$15,754-\$15,842), $P < 0.001$).

The multivariable logistic regression model showed that sleep apnea was an independent risk factors of IF (OR 1.21 (CI: 1.07;1.36), $P = 0.002$). Other risk factors were advanced age, male sex and increased comorbidity burden. The use of neuraxial and the combination of neuraxial/general anesthesia had lower odds in regard to IFs than general anesthesia alone (OR = 0.75 [CI: 0.67-0.85], $P < 0.0001$, OR = 0.86 [CI: 0.77-0.96], $P = 0.0068$, respectively). The use of a peripheral nerve block did not alter the odds for IF (OR=0.98 [CI: 0.88-1.10, $P = 0.764$]).

Discussion: In this study we were able to determine that amongst other factors, the presence of sleep apnea independently increased the likelihood of IF. The mechanism by which sleep apnea may contribute to this increased risk remains to be evaluated.

Sleep –disordered Breathing and Postoperative Outcomes After Bariatric Surgery: Analysis of the Nationwide Inpatient Sample

Babak Mokhlesi, MD, Margaret D. Hovda, MD, Benjamin Vekhter, PhD, Vineet M. Arora, MD, MA, Frances Chung, MD, David O. Meltzer, MD, PhD

Background: Sleep-disordered breathing (SDB) has been increasingly recognized as a possible risk factor for adverse perioperative outcomes in non-bariatric surgeries. However, the impact of SDB on postoperative outcomes in patients undergoing bariatric surgery remains less clearly defined. We hypothesized that SDB would be independently associated with worse postoperative outcomes.

Methods: Data were obtained from the Nationwide Inpatient Sample database, and included a total of 91,028 adult patients undergoing bariatric surgeries from 2004 to 2008. The primary outcomes were in-hospital death, total charges and length of stay. There were two secondary outcomes of interest: respiratory and cardiac complications. Regression models were fitted to assess the independent association between SDB and the outcomes of interest.

Results: SDB was independently associated with decreased mortality (OR 0.34, 95% CI 0.23-0.50, $p < 0.001$), total charges (-\$869, $p < 0.001$), and length of stay (-0.25 days, $p < 0.001$). SDB was independently associated with significantly increased odds ratio of emergent endotracheal intubation (OR 4.35, 95% CI 3.97-4.77, $p < 0.001$), noninvasive ventilation (OR 14.12, 95% CI 12.09-16.51, $p < 0.001$), and atrial fibrillation (OR 1.25, 95% CI 1.11-1.41, $p < 0.001$). Emergent intubation occurred significantly earlier in the postoperative course in patients with SDB. Although non-SDB patients had an overall lower risk of emergent intubation compared to SDB patients, their outcomes were significantly worse when they did get emergently intubated.

Conclusions: In this large nationally representative sample, despite the increased association of SDB with postoperative cardiopulmonary complications, the diagnosis of SDB was negatively, rather than positively, associated with in-hospital mortality and resource use.

Identification of Factors Associated with Postoperative Elevation of Apnea and Hypopnea in Surgical Patients Without Preoperative Sleep Apnea

Presenting author: Maged Andrewes M.D.¹

Co-authors: Yiliang Yang M.D.¹, Weimin Kang M.D.², Pu Liao M.D.¹, C Shapiro M.D.², Babak Mokhlesi M.D.³, Frances Chung MBBS¹

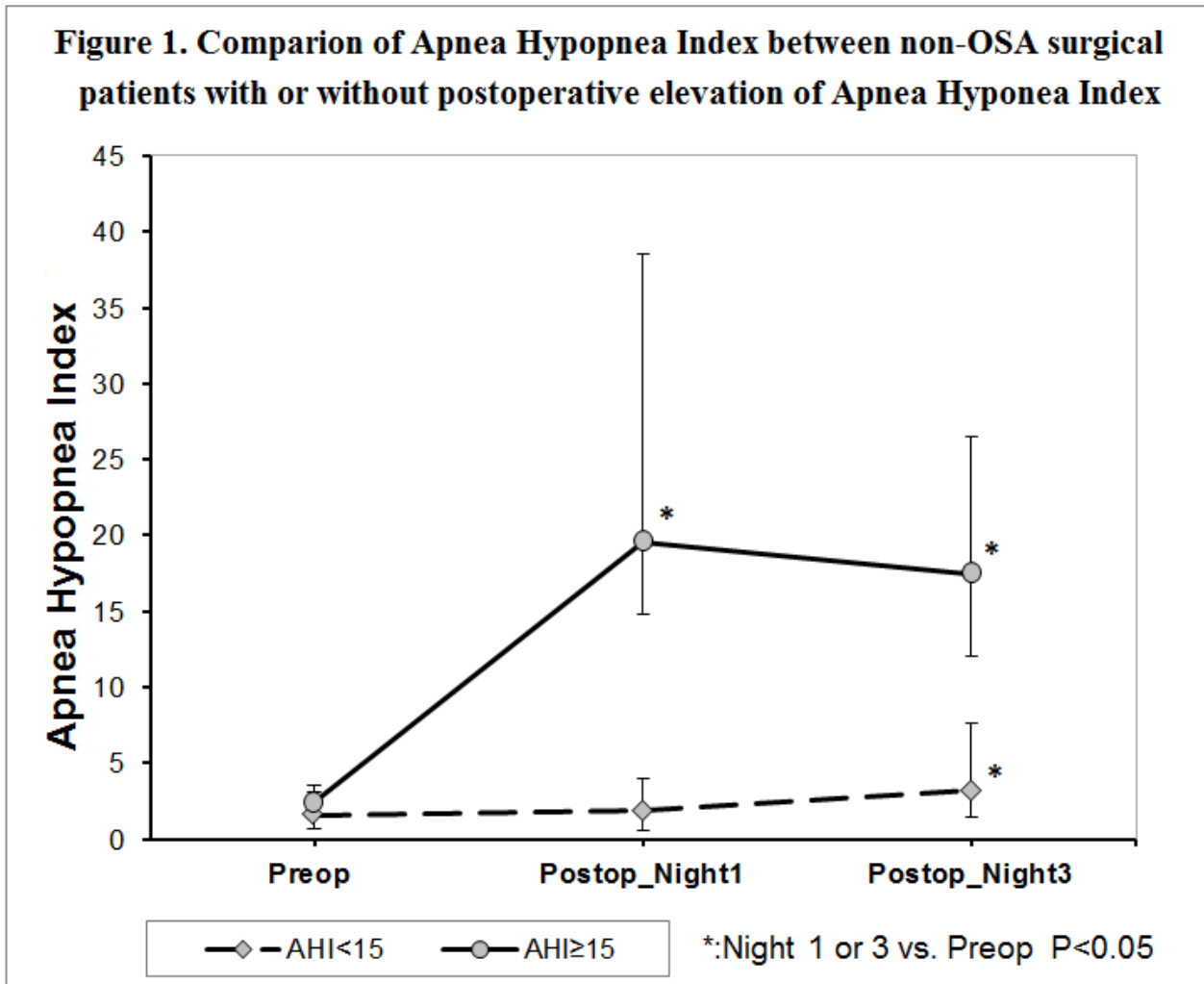
1 Department of Anesthesia, Toronto Western Hospital, University Health Network, University of Toronto 2 Sleep Research Unit, Toronto Western Hospital, University Health Network, University of Toronto 3 Sleep Disorders Center and the Section of Pulmonary and Critical Care Medicine, University of Chicago Pritzker School of Medicine, Chicago, IL .

Background: Respiratory depression and cardiac arrest may occur in patients receiving opioids for postoperative pain. Understanding the causes of postoperative increase in apnea, hypopnea and oxygen desaturation may elucidate the mechanism for respiratory arrest and enhance patient safety. The objective of this study is to investigate the factors associated with postoperative increase in apnea hypopnea index (AHI) in patients with no preoperative sleep apnea (OSA)

Methods: This is a prospective observational study. Following REB approval, consented preoperative patients were invited to undergo sleep studies with a portable device (Embletta x100) preoperatively (preop) at home, first (N1), and third (N3) postoperative night in the hospital or at home. The sleep study recordings were scored by a certified sleep technologist. The primary outcome was postoperative AHI. The data of patients with no preoperative OSA (defined as preoperative AHI<5) were examined. AHI ≥ 15 per hour (on either postoperative N1 or N3) was defined as a significant postoperative increase of AHI. Multivariate logistic regression was employed to evaluate the association of preoperative sleep parameters with postoperative AHI increase.

Results: 120 non-OSA patients completed postoperative N1 and/or N3 sleep studies. On either postoperative N1 or N3, 31 patients had elevation of postoperative AHI ≥ 15 and 89 patients had less increase: postoperative AHI <15 (Figure 1). Patients with postoperative AHI increase were older (60 ± 13 vs. 53 ± 12 yrs, $p < 0.01$) and had more smokers (32.3% vs. 15.7%, $p < 0.05$). Based on change of sleep parameters over perioperative PSG measurements, a multivariate logistic regression analysis revealed that Hypopnea Index ($p = 0.004$), Central Apnea Index ($p = 0.069$) and Age ($p = 0.009$) were important factors to contribute to postoperative AHI escalation in patients without preoperative OSA. Based on demographic data and preoperative sleep parameters, a predictive model was constructed for detecting patients who may develop a significant postoperative AHI surge. Preoperative AHI was associated significantly with postoperative AHI increase ($p = 0.0345$). However, BMI was inversely significantly associated with postoperative AHI increase ($p = 0.0472$). Age, smoker, Sleep Efficiency and Total Arousal Index also were associated with postoperative AHI elevation. When Total Arousal Index increased by 10 units, odds ratio of postoperative AHI increase was 1.94 (95% CI: 0.91-4.15).

Conclusions: Several factors are identified to be independently associated with a significant elevation in postoperative AHI. Preoperative sleep study parameters such as lower Sleep Efficiency, higher Sleep Fragmentation, higher AHI and higher Total Arousal Index are helpful for identifying non-OSA patients who may develop a significant postoperative increase in AHI.



A Novel Method to Efficiently Detect Esophageal Misplacement of Endotracheal Tubes

Yugo Tagaito, MD, PhD, Teikyo University Chiba Medical Center, Kunihiko Kawanaka, MD, Teikyo University Chiba Medical Center, Ryoko Kiuchi, MD, Teikyo University Chiba Medical Center, Kanehumi Matsuoka, MD, Teikyo University Chiba Medical Center, Fumiaki Mimura, MD, PhD, Teikyo University Chiba Medical Center, Satoshi Toyama, MD, PhD, Teikyo University Chiba Medical Center, Hidefumi Asano, MD, PhD, Teikyo University Chiba Medical Center, Alan R. Schwartz, MD, Johns Hopkins University School of Medicine, Megumi Shimoyama, MD, PhD, Teikyo University Chiba Medical Center

Introduction: Inadvertent esophageal intubation (EI) is a very common, but potentially a life-threatening complication of tracheal intubation (TI). Although various methods are employed to identify EI and to confirm proper placement of TI, no single technique currently in use is completely reliable.

We hypothesized that the endotracheal (ET) tube tip would generally remain patent as long as it passes through the airway, while it should be obstructed by the mucous membrane when it enters the esophagus leading to an elevated ET tube resistance. To obtain the tube resistance, we applied a flow of oxygen into the ET tube, since it would also enhance oxygenation.

Methods: American Society of Anesthesiologists (ASA) physical status 1-2 adult patients presenting for elective surgery under general anesthesia with orotracheal intubation were enrolled. After routine general anesthesia and muscle relaxation was achieved, anesthesiologists were asked to perform ET intubation by means of conventional laryngoscopy, where a constant flow of oxygen (6 liters per minute) was delivered through the tube. Upstream pressure (P_{US}) of the oxygen flow was monitored as a marker for the tube resistance during the whole procedure, but was not shown to the anesthesiologists. To prevent forcing gas into the stomach, an adjustable pressure limiting (APL) valve was placed between the oxygen source and the tube to limit pressure in the tube to 10 mmHg.

Results: One hundred and three intubation trials (46 males, 57 females) were analyzed. Accidental EI occurred in seven occasions (6.8%). In each case of inadvertent EI, the P_{US} promptly reached and maintained 10 mmHg, whereas in the

cases of successful TI, the P_{US} never exceeded 8 mmHg throughout the procedure (See table).

| Highest P_{US} | No. of EI cases | No. of TI cases | sum |
|------------------|-----------------|-----------------|-----|
| =10mmHg | 7 | 0 | 7 |
| <10mmHg | 0 | 96 | 96 |
| sum | 7 | 96 | 103 |

Fisher's exact test: $p < 0.001$

Accordingly, when we set the cutoff value of the highest P_{US} at 10mmHg, the sensitivity and the specificity of this method could become a 100% (95% CI; sensitivity: 0.764-1.0, specificity: 0.983-1.0).

In the seven cases of EI, time from the point when P_{US} reached 10mmHg to the point when each anesthetist realized that the attempt was EI was measured as a second endpoint. It was 42.6 ± 21.9 (mean \pm standard deviation) seconds, which corresponds to the time the anesthetists could have saved had they used P_{US} as indicator of EI.

Discussion: This study demonstrates the usefulness of monitoring ET tube resistance for EI recognition in the elective setting. Unlike capnography, performance of this method is independent of carbon dioxide production of the patients. More importantly, this method would enable us to prevent EI since it prompts us the possibility of EI real-time at the point of tube insertion. Further studies are warranted to test the feasibility of this method in various clinical settings including emergency situations.

Obstructive Sleep Apnea and Postoperative Complications: Matched Cohort Comparison of Respiratory and Cardiovascular Outcomes Before and After Diagnosis by Polysomnography

Thomas Mutter, FRCPC, MSc, University of Manitoba, Dan Chateau PhD, University of Manitoba, Michael Moffatt, MD, FRCPC, MSc, University of Manitoba, Clare Ramsey, MD FRCPC, MS, University of Manitoba, Leslie L. Roos, PhD, University of Manitoba, Meir Kryger MD, FRCPC, Yale University School of Medicine

Importance: Obstructive sleep apnea (OSA) is common in surgical patients(1) and is thought to increase the risk of postoperative complications, especially when unrecognized and untreated preoperatively(2,3,4). Consequently, current practice guidelines cautiously recommend diligent preoperative screening, diagnosis and treatment of OSA, with intensive postoperative monitoring of high-risk patients(2,3,4). However, no large postoperative outcome study of OSA patients, diagnosed by the reference standard, polysomnography, has ever been reported and, in many recent studies(5), surveillance bias from postoperative monitoring of OSA patients may have influenced results. The unique historical data of the present study, from a time period before the implementation of current practice guidelines, provide a large sample of postoperative outcomes before and after diagnosis of OSA by polysomnography.

Objective: To improve the preoperative risk stratification and postoperative care of OSA patients by determining the relative importance of preoperative recognition and treatment of OSA, OSA severity, other comorbidities and the type of surgery in predicting clinically important postoperative cardiovascular and respiratory complications.

Design, Setting and Participants: Matched cohort study with analysis of health administrative data from Manitoba, Canada, and polysomnography data from a clinical database. Postoperative outcomes in OSA patients up to 5 years before (unrecognized OSA, n = 1,571) and any time after (diagnosed OSA, n = 2,640) polysomnography were compared to controls without an administrative data diagnosis of sleep apnea (n = 16,277). Controls were matched by exact procedure, indication and approximate date of surgery. All surgical procedures on patients at least 18 years old between April 1, 1987 and March 31, 2008 were eligible for inclusion, except for procedures used to treat sleep apnea. Follow up was the latest of 7 postoperative days or hospital discharge.

Main outcome measures: Respiratory complications (adult respiratory distress syndrome (ARDS), respiratory failure or pneumonia) and cardiovascular complications (cerebrovascular accident, acute coronary syndrome, atrial fibrillation or shock and cardiac arrest) were reported as odds ratio [95% confidence interval] for OSA or subgroup versus controls.

Results: In multivariate analyses (Figure 1), OSA predicted increased risk of respiratory complications (2.08 [1.35-3.19], $p < 0.001$), primarily ARDS and respiratory failure, with no significant difference between diagnosed and unrecognized OSA ($p = 0.41$). The risk of cardiovascular complications, primarily cardiac arrest and shock, was significantly different ($p = 0.004$) between unrecognized OSA (2.20 [1.16-4.17], $p = 0.02$) and diagnosed OSA patients (0.75 [0.43-1.28], $p = 0.29$). For both outcomes, more severe OSA was associated with increased risk ($p < 0.05$ for trends) and surgical and patient characteristics were also important independent predictors.

Conclusions: Age, comorbid disease, the type of surgery and the severity of OSA are inadequately represented in current risk stratification tools used to guide the perioperative management of OSA patients. Preoperative diagnosis and initiation of continuous positive airway pressure therapy, particularly in patients with more severe undiagnosed OSA, may prevent important postoperative cardiovascular complications.

References:

- 1) *Sleep Med.* 2009;10(7):753-758.
- 2) *Anesthesiology.* 2006;104(5):1081-93.
- 3) *Anesth Analg.* 2012;115(5):1060-1068.
- 4) *Anesthesiol Clin.* 2010;28(2):199-215.
- 5) *Br J Anaesth.* 2012;109(6):897-906.

A New and Low-Cost TSE-Alloteh Nasal CPAP/CF Mask/Circuit Improved Oxygenation of a High-Risk Obese Patient with OSA Under MAC for TEE

Ankit Kapadia, MD, Shaul Cohen, MD, John Denny, MD, Rose Alloteh, MD, Kang Rah, MD, James Tse, PhD, MD

Introduction: Patients routinely receive IV sedation and nasal cannula (NC) O₂ during transesophageal echocardiography (TEE). Over-sedation and/or airway obstruction may cause severe desaturation, especially in obese patients. A simple plastic sheet was shown to improve oxygenation by transforming NC to a face tent (TSE "Mask") in sedated patients during TEE¹⁻². Obese patients with obstructive sleep apnea (OSA) require CPAP to keep nasopharyngeal airway open during sleep and under sedation. In light of a recent study showing the effectiveness of nasal ventilation in anesthetized patients³, we have developed a nasal TSE-Alloteh CPAP/CF (continuous flow) mask/circuit to improve oxygenation in obese patients with OSA under sedation². We wish to report a challenging case of a high-risk obese patient with OSA under MAC for TEE.

Clinical Case: An 84 year old male (ASA IV) with history of coronary artery disease status post bypass surgery, hypertension, diabetes mellitus, was undergoing TEE. He had a new onset of atrial flutter/fibrillation and was scheduled for TEE to evaluate the left atrial appendage for clot in preparation for electrophysiology study and ablation. He had OSA and tolerated poorly with a facial CPAP mask/machine. His BMI was 34 kg/m² and O₂ saturation was 89-91% with nasal cannula O₂ (5 liter/min). His LVEF was 20%. Anesthesia team was called to provide MAC for TEE because of severe cardiopulmonary disease. His O₂ saturation increased to 93-94% after the nasal cannula was transform to a TSE "mask". We then assembled a nasal CPAP mask/circuit using an infant face mask, a head strap holder and a flexible connector attached to a bag valve mask with PEEP valve attached. We showed him a fully inflated infant mask (10 cc air added) and obtained the photography consent him and his wife. We put the mask over his nose to make sure he could breathe through it easily. It was secured with head strap to obtain a good seal (Photo). Patient was breathing comfortably with the PEEP valve set at 10 cm H₂O and 10 liter/min fresh O₂ flow. After pre-oxygenation for 5 min, his O₂ saturation increased to 95-96%. A bite-block was then put in place. He then received etomidate (4 mg) followed by small boluses of propofol (a total of 40 mg). He maintained stable blood pressure and spontaneous respiration. He also received intermittent assisted nasal mask ventilation. His O₂ saturation was 93-96% throughout the 10-min procedure. He tolerated the procedure well and recovered from sedation quickly. He maintained 94-95% O₂ saturation with a TSE "mask". He subsequently underwent EP study and ablation of atrial flutter under general anesthesia the following day and tolerated the procedure well.

Discussion: This simple nasal CPAP/CF mask/circuit takes a few minutes to assemble using existing equipment. It improves oxygenation and prevents severe desaturation in obese patients with OSA undergoing EGD and TEE. It can be used to assist ventilation without interrupting the procedure. It may improve patient safety at a low cost.

References: 1. Anesthesia Analgesia 106 (SCA Suppl):105, 2008; 2. www.TSEMask.com; 3. Anesth 108: 998-1003, 2008;



The Use of a Non-Invasive Respiratory Volume Monitor to Detect and Quantify Obstructive Sleep Apnea in Postoperative Patients

Lisa Campana, PhD¹, Christopher Voscopoulos, MD², Edward George, MD, PhD³

¹Respiratory Motion, Inc., Waltham, MA, ²Brigham and Women's Hospital, Harvard Medical School, Boston, MA, ³Massachusetts General Hospital, Harvard Medical School, Boston, MA.

Purpose: Obstructive sleep apnea (OSA), while prevalent, remains underdiagnosed. This presents challenges after surgery, as OSA is associated with increased postoperative complications and often worsens with opioid administration. Currently, real-time identification of apneic events is difficult with standard monitoring technology and many events remain unnoticed and untreated. A novel, non-invasive, Respiratory Volume Monitor (RVM), which provides respiratory volume traces and accurately reports Minute Ventilation (MV), Tidal Volume (TV) and Respiratory Rate (RR), has the potential to detect and quantify apneic events post-operatively in real-time.

Methods: 142 patients undergoing elective orthopedic surgery were studied using an impedance-based RVM (ExSpirom, Respiratory Motion, Inc., Waltham, MA). Continuous RVM traces were obtained in the post-anesthesia care unit (PACU). Apneic events were defined as episodes with no detected breaths lasting at least 10 seconds, and hypopneic events were defined as episodes lasting at least 10 seconds with a reduction in tidal volume of 50% or greater. OSA was defined as more than 5 events per hour of PACU time. MV, TV and RR were calculated from 30-second RVM trace segments. Predicted adequate MV for each patient was calculated based on patient's body surface area. "At-Risk" MV was defined as MV <80% predicted. "Un-Safe" MV was defined as MV <40% predicted. The distribution of MV measurements was quantified post-operatively during 10 minutes of non-apneic and 10 minutes of apneic breathing for each patient.

Results: We focused our analysis on the 26 (18%) patients (mean age: 67.5, 53-86 yrs; mean BMI: 27.2, 15-38 kg/m², 15 males) who demonstrated OSA in the PACU. An average of 34.6 ± 4.2 apneic events (12.3 ± 1.2 events/hr) per patient were observed, with an average duration of 15.7 ± 0.6 s (12-24 s) seconds. Importantly, 21/26 patients (80%) were not previously diagnosed with OSA. During apneic breathing periods, average MV was significantly lower compared to non-apneic periods (104 ± 8.5% to 74 ± 5.7 % predicted, -37 ± 6%, p<0.001) (Fig 1). During non-apneic post-operative breathing 41% of MV measurements were below 80% of predicted ("At-Risk") and 7% were below 40% predicted ("Un-Safe"). Conversely, during apneic breathing MV was in the "At-Risk" zone 65% of the time, and in the "Un-Safe" zone 27% of the time, both a significant increase in time compared to non-apneic breathing (p<0.01).

Conclusions: RVM traces can be used to detect apneic episodes in the PACU and quantify the associated reduction in MV caused by OSA. MV measurements may be a clinically useful way to quantify the impact of OSA postoperatively. Traditional risk factors for OSA (age, sex, BMI) were not predictive of post-operative OSA. RVM provides non-invasive, real-time measurements that quantify respiration in patients with OSA. Since apneic episodes are associated with prolonged PACU stays, extra healthcare costs, and life-threatening post-surgical complications, the use of RVM to aid in decision-making regarding use of opioids may improve recognition and management of OSA in the PACU.

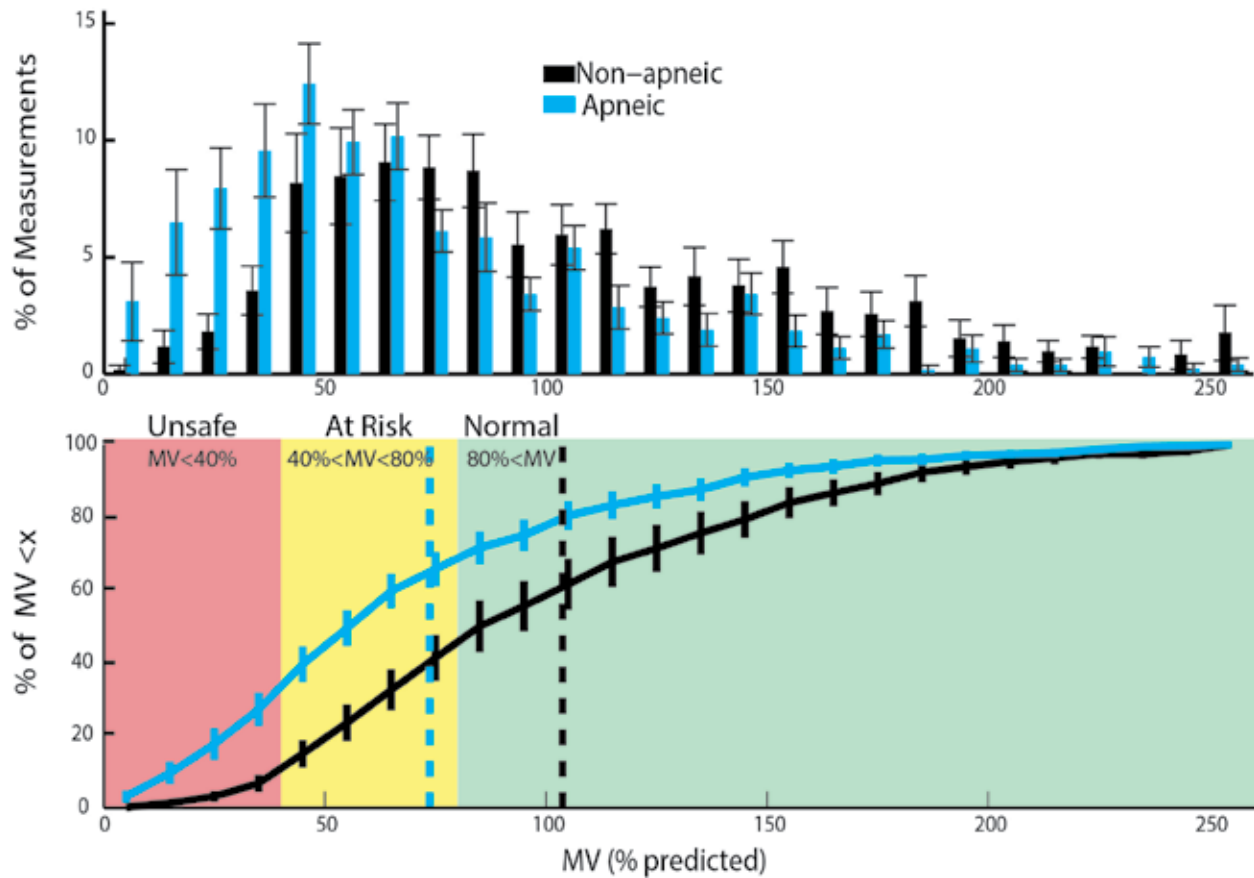


Figure 1. Top: Average histogram of the measured MV (as percent of the individually predicted MV) during 10 minutes of post-operative non-apneic breathing (black) and post-operative apneic breathing (blue) in patients with apnea. Bottom: The cumulative distribution of MV shows the fraction of measurements below a given MV level during non-apneic (black) and apneic breathing (blue). Vertical dashed lines represent the mean MV during each time period. Average MV drops from 104% to 74% of predicted during apneic breathing patterns. When no apnea is occurring, 7% of the MV measurements are below 40% predicted in the

“Un-Safe” zone (red), while during periods of apnea 27% of MV measurements fall below 40% predicted.

Incidence of Unrecognized Obstructive Sleep Apnea in Major Noncardiac Surgery

Edwin Seet¹, Matthew Chan², Chew-Yin Wang³, HY Lai³, Stanley Tam⁴, Frances Chung⁴, POSA Group.

¹Khoo Teck Puat Hospital, Alexandra Health Services.

²The Chinese University Hong Kong

³University of Malaya

⁴University Health Network, University of Toronto

Background: Obstructive sleep apnea (OSA) affects 9-17% of the general population, and it is more common in the tertiary care settings. Unfortunately, the majority of these patients are unrecognized at the time of surgery. The international Postoperative Vascular Events in Unrecognized Obstructive Sleep Apnea (POSA) Trial aims to determine the postoperative outcome of unrecognized OSA in moderate-to-high risk patients undergoing major noncardiac surgery > 2 hours duration. In an interim analysis, we present the prevalence of unrecognized OSA among POSA trial participants.

Methods: The study was approved by local research ethics committee (ClinicalTrials.gov Identifier: NCT01494181), and all patients gave written informed consents. Patients above 45 years, with a history of atherosclerotic disease (defined as > 1 risk factor of the revised cardiac risk index) received ambulatory polysomnographic monitoring (ApneaLink, Resmed, San Diego, CA) to determine the presence and severity of unrecognized OSA before surgery.

Results: As of June 2013, we analyzed data from 368 patients. The mean age (\pm SD) was 68 \pm 10 years, and 57% were males. A total of 232 patients (63%) had unrecognized OSA with apnea-hyponea index (AHI) > 5/h, 105 (29.5%) patients had moderate-to-severe OSA (AHI > 15/h) based on the polysomnographic results. Patients with unrecognized OSA had an increased body mass index ($p < 0.001$).

| | AHI < 5/h | AHI 5-15/h | AHI > 15/h | <i>p</i> value |
|--------------------------------------|----------------|----------------|----------------|----------------|
| No. of patients | 136 | 127 | 105 | |
| Age (years) | 66 \pm 10 | 69 \pm 10 | 68 \pm 10 | 0.101 |
| Body mass index (kg/m ²) | 25.3 \pm 5.2 | 27.0 \pm 5.8 | 28.2 \pm 5.1 | <0.001 |
| Ethnicity | | | | 0.053 |
| Chinese | 82 (43.2%) | 64 (33.7%) | 44 (23.2%) | |
| Malaysians / Indians | 36 (35%.0) | 36 (35.0%) | 31 (30.1%) | |
| Caucasians | 18 (24.3%) | 27 (36.5%) | 29 (39.2%) | |

Conclusions: Unrecognized OSA is prevalent in moderate-to-high risk patients undergoing major surgery. Further investigation is required to determine if this cohort of unrecognized OSA patients are at increased risk of vascular and other perioperative complications.

Funding support:

Health and Health Service Research Fund (09100351), Food and Health Bureau, Hong Kong; University Health Network Foundation, University of Toronto; High Impact Research Grant UM.C/625/1/HIR/067 from the University of Malaya; Alexandra Health Singapore, Small Innovation Grant

Continuous Negative External Pressure (cNEP) Diminishes Obstructive Apneas and Improves Oxygenation During Colonoscopy

S. Kais, S. Endemann, J. Aarestad, K. Klein, R. Rose and W. Coyle. Division of Gastroenterology, Scripps Green Hospital, La Jolla CA, and 5i Sciences, Inc., Rancho Santa Fe, CA

Respiratory complications during colonoscopy are reported to be infrequent, even when moderate sedation with intravenous propofol is used. However, the true incidence of respiratory impairment may have been underestimated by reliance on pulse oximetry as the sole measure of respiratory function in patients receiving supplemental oxygen. We performed an open label pilot study 1) to determine the frequency of apneas occurring during routine colonoscopy as assessed by a class III monitoring system (Nox T3, CareFusion) and 2) to investigate the effects of cNEP applied to the upper airway with a soft silicone collar (5i Sciences) on the occurrence of apnea and oxygen desaturation in this patient population. Twenty-four control subjects were enrolled to assess the frequency of apneas and hypopneas of greater than 30 seconds. Twenty two subjects were then studied with the application of cNEP at – 45cm H2O. The two groups were similar with respect to age, sex, BMI, STOP-BANG scores and dosage of moderate sedation. The results are summarized below:

| | control (n=24) | cNEP (n=22) |
|---|-----------------------|--------------------|
| Mean AHI | 12.9 | 5.5 |
| % of subjects with obstructive apnea (OA) | 87.5 | 13.6 |
| Mean episodes of OA/subject | 2.9 | 0.14 |
| % of subjects with O₂ desaturation \geq 5 mm for > 30 sec | 54 | 12.5 |
| % of subjects with O₂ saturation < 90% | 30 | 13.6 |
| % of subjects requiring increase in administered O₂ | 41.6 | 13.6 |

In addition, central apneas were observed in both groups and were particularly common during the initial phase of the procedure. These observations suggest that obstructive and central apneas are common during routine colonoscopy and can be associated with impairment in oxygenation. The application of cNEP is a safe and effective means of diminishing obstructive apneas and improving oxygenation in this clinical setting.

A New and Low-Cost TSE-Alloteh Nasal CPAP/CF Mask/Circuit Improved Oxygenation of a High-Risk Obese Patient with OSA Under MAC for Bronchoscopy

Neethu Kumar, MD, Rutgers-Robert Wood Johnson Medical School, Kang Rah, MD, Rutgers-Robert Wood Johnson Medical School, John Denny, MD, Rutgers-Robert Wood Johnson Medical School, Shaul Cohen, MD, Rutgers-Robert Wood Johnson Medical School, Rose Alloteh, MD, Rutgers-Robert Wood Johnson Medical School, James Tse, PhD, MD, Rutgers-Robert Wood Johnson Medical School

Introduction: Ambulatory patients undergoing flexible bronchoscopy routinely receive intravenous sedation and nasal cannula (NC) O₂. Over-sedation and/or airway obstruction may cause severe desaturation, especially in obese patients with obstructive sleep apnea (OSA). In light of the study showing the effectiveness of nasal ventilation¹, we have developed a simple nasal CPAP/CF (continuous flow) mask/circuit to improve oxygenation in sedated OSA patients². We wish to report a challenging case using this mask to improve oxygenation in an obese OSA patient with severe cardiopulmonary disease undergoing outpatient bronchoscopy evaluate a new RUL infiltrate.

Clinical Case: A 36 y/o obese male with BMI 40 kg/m² complains of dyspnea on exertion after walking 2 blocks. He has OSA and uses CPAP mask/machine during sleep. The patient also has asthma, restrictive lung disease, pulmonary hypertension and Behcet's disease (status post aneurysm repair of thoracic aorta, left renal artery and left ventricle). His LVEF is 40%.

The patient's baseline O₂ saturation (Sat) was 95%. He had no forced expiratory wheezes. He was pretreated with lidocaine and albuterol nebulizer and topical anesthesia. We assembled a TSE-Alloteh nasal CPAP/CF mask/circuit using an infant face mask and an adult breathing circuit attached to the anesthesia machine (Photo) as described². The patient breathed comfortably through this mask with the pop-off valve open and 10 L/min O₂ flow. After pre-oxygenation for 5 min, his O₂ Sat increased to 100%. A bite-block was then put in place and a NC with sampling line was secured on the lower rim of the bite-block for CO₂ and O₂ monitoring.

He then received 100 mg of lidocaine followed by small boluses of propofol (a total of 100 mg) and deep sedation was maintained with propofol infusion (150 mcg/kg/min). He maintained spontaneous breathing as indicated by capnography. There was some difficulty with entering the bronchoscope through the vocal cords by a pulmonology fellow. Upon passage through the vocal cords, he was found to have severe tracheomalacia at mid-trachea; the tracheal lumen was compressed over 80%. We closed the pop-off valve and delivered assisted nasal ventilation with PIP of 15-20 cm of H₂O. The video screen revealed that PIP opened the tracheal lumen and allowed bronchoscope to pass through the narrow lumen easily. He resumed spontaneous respiration with occasional assisted nasal ventilation. The pop-off valve was adjusted to

maintain CPAP of 5-10 cm of H₂O. His O₂ Sat was 99-100% throughout the procedure with FiO₂ of 0.6-0.8. He tolerated the procedure well and recovered from sedation quickly. He was very pleased and discharged home without delay.

Discussion: With this nasal CPAP mask/circuit, we were able to oxygenate and sedate an obese patient with OSA, severe cardiopulmonary disease and new findings of severe tracheomalacia while continuing to maintain spontaneous respiration. It improves oxygenation and pro-actively prevents severe desaturation in obese patients with OSA. When the patient becomes apneic, it can be used to deliver immediate assisted nasal ventilation without interrupting the procedure. It may improve patient safety at a very low cost.

References: 1. Anesth 108: 998-1003, 2008; 2. www.TSEMask.com



Does Negative Pressure Applied to the Submandible Region Improve Collapsibility of the Passive Pharyngeal Airway?

Shinichiro Kato, MD, Chiba University, Megumi Amemiya, MD, Shin Sato, MD, Yumi Sato, MD, Aya Ikeda, MD, Junko Okazaki, MD, Teruhiko Ishikawa, MD, Shiroh Isono, MD, Chiba University

Background: The passive pharynx behaves like a collapsible tube. Cross-sectional area of the tube is determined by transmural pressure, the difference between intraluminal and extraluminal pressure. Although dependence of the pharyngeal cross-sectional area on the intraluminal pressure is well documented, we lack knowledge of influences of the extraluminal pressure on the pharyngeal airway patency particularly in humans. We are testing a hypothesis that negative external pressure (NEP) application to the submandible region improves pharyngeal airway collapsibility. We report the preliminary results of this clinical study.

Methods: Static mechanical properties of the passive pharynx were compared before and during NEP (-25 and -50 cmH₂O) on the submandible region in seven anesthetized and paralyzed patients with sleep-disordered breathing. The NEP was applied with using a silicone collar covering the whole submandible region and a vacuum pump (the RestWell™ sleep system, 5i Science Inc.) while maintaining the head and mandible position (sniffing position). Static pressure/area relationships of the velopharynx and oropharynx were obtained by step changes in airway pressure during endoscopic cross-sectional area measurement of each segment. Exponential curve fitting to the measured pressure/area data yields three mechanical parameters such as A_{max} (maximum cross sectional area obtained), P_{close} (closing pressure) and constant K (an index of pharyngeal airway stiffness).

Results: As shown by the table, P_{close} at both the velopharynx and oropharynx significantly decreased in response to application of -50cmH₂O of submandible NEP whereas the A_{max} and K values did not significantly change probably due to small sample size.

| | Velopharynx | | | Oropharynx | | |
|---------|-------------------------------------|---|-----------|-------------------------------------|---|-----------|
| | A _{max} (cm ²) | P _{close} (cmH ₂ O) | K value | A _{max} (cm ²) | P _{close} (cmH ₂ O) | K value |
| NEP 0 | 1.9±1.1 | -2.2±2.5 | 0.16±0.04 | 3.1±1.4 | -2.5±2.1 | 0.19±0.03 |
| NEP -25 | 2.3±1.4 | -5.0±4.8 | 0.14±0.05 | 3.8±1.3 | -6.5±5.8 | 0.14±0.05 |
| NEP -50 | 2.1±1.1 | -4.1±3.7* | 0.14±0.04 | 3.5±1.4 | -6.4±4.9* | 0.15±0.04 |

*: P<0.05 versus control

Conclusion: Negative pressure applied to the submandible region appears to improve collapsibility of the passive pharyngeal airway particularly in non-obese patients with sleep disordered breathing. Continuous NEP could be an alternative treatment for pharyngeal airway obstruction.

Short-Term Succinylcholine Infusion During General Anesthesia May Not Result In Clinically Significant Phase II Block

Christopher Chenelle, BA, Massachusetts General Hospital, Geng Li, MD, Massachusetts General Hospital, Jingping Wang, MD, PhD, Massachusetts General Hospital, Mazen Maktabi, MB, BCh, Massachusetts General Hospital, Robert M. Kacmarek, RRT, PhD, Massachusetts General Hospital, Yandong Jiang, MD, PhD, Massachusetts General Hospital, Demet Sulemanji, MD, Massachusetts General Hospital

Introduction: Succinylcholine has many advantages as a muscle relaxant including quick onset and reversal and profound muscle relaxation. Although it is used frequently as a single bolus for endotracheal tube placement, continuous succinylcholine infusion is not commonly used due to anesthesiologists' fear of side effects including prolonged neuromuscular block due to deficiencies of plasma cholinesterase, the enzyme that metabolizes succinylcholine. The exact prevalence of the homozygous enzyme deficiency is unknown but the heterozygous prevalence is estimated at 2.5% in the general population (1). Previous studies suggest that a prolonged infusion is more likely to result in a prolonged block. However, the cut-off point for the duration of infusion to produce a clinically significant prolonged block and whether a short term infusion would also produce such a block remain unknown.

In this study, our aim was to determine if succinylcholine infusions of 60 minutes or less produced clinically significant prolonged neuromuscular block and/or increased the need for post-extubation ventilatory support.

Methods: Electronic anesthesia records of all laparoscopic cholecystectomy cases performed by a single surgeon over a seven-year period at our institution were retrospectively reviewed. Cases were allocated into 2 groups: Group S, patients who received succinylcholine infusion only (n=533), and Group N, patients who received no succinylcholine but only nondepolarizing neuromuscular agents (n=95). The time from extubation to leaving the operating room and the rate of post-extubation ventilatory support were calculated.

Results: There were no differences in gender, ASA category, age, height, or weight between the two groups. In Group S, the average duration of succinylcholine infusion was 26.5 ± 10.0 minutes, delivering a total median dose of 3.9 (3.3, 4.6) mg/kg. The requirement for post-extubation ventilatory support did not differ between the two groups, with 4 of 533 patients (0.75%) requiring additional support in Group S, and 1 of 95 patients (1.05%) requiring additional support in Group N. The time from extubation to leaving the operating room did not differ between Group S and Group N (1.0 (0.0, 3.0) vs. 1.0 (0.0, 3.0) minutes).

Discussion : With the increasing number of ambulatory surgeries, it is important to re-assess succinylcholine's value and risks. Our results demonstrate that a short-term succinylcholine infusion did not cause clinically significant prolonged neuromuscular block or alter the rate of patients requiring postoperative ventilatory support. A prospective study is warranted to validate these findings.

References

1. Hanel, H. K., Viby-Mogensen, J., de Muckadell, O. B. S., Serum Cholinesterase Variants in the Danish Population. *Acta Anaesthesiologica Scandinavica*, 1978, 22: 505–507.

Diminished Sleep Efficiency After Total Knee Replacement Surgery may be Ameliorated by Perioperative Melatonin: A Double Blinded Placebo Controlled Study

Meghan Kirksey, MD, PhD, Hospital for Special Surgery, Daniel Yoo, MB, Hospital for Special Surgery, Otto Stundner, MD, Hospital for Special Surgery, Thomas Danninger, MD, Hospital for Special Surgery, Stavros Memtsoudis, MD, PhD, Hospital for Special Surgery

Background: Melatonin is a key component in the regulation of circadian rhythms. Post-operative disturbances of melatonin levels have been associated with aberrant sleep/wake cycles, depression, and delirium [1,2]. Karkela et. al. have shown decreased levels of melatonin production post-operatively in patients after minor orthopedic surgery whether it was done under general or regional anesthesia [3].

Hypothesis: Sleep disruption occurs in the days immediately following total knee replacement surgery and perioperative melatonin administration can improve post-operative sleep quality.

Methods: Following IRB approval, we enrolled 50 patients in a double-blind, randomized, placebo-controlled clinical trial to compare sleep quality before and after total knee replacement surgery. Sleep quality was measured quantitatively using ActiGraph actigraphy wrist bracelets. Patients were randomly assigned to receive melatonin 5mg or placebo starting on the third night prior to surgery and continuing three nights after surgery as tolerated.

Results: In the control group, average post-operative sleep efficiency (time sleeping/time in bed) declined to 86% of baseline at 24 hours, 85% at 48 hours and 73% at 72 hours as measured by actigraphy. In the melatonin group, average post-operative sleep efficiencies were 97% (SD 24), 90% (SD 24), and 102% (SD 26) of baseline at 24, 48, and 72 hours respectively.

Conclusions: Sleep disruption is likely to occur in the inpatient period following total knee replacement surgery. Administration of perioperative melatonin may be an inexpensive and straightforward method of mitigating this highly disruptive post-operative complication.

References:

1. Am J Surg. 2001 Nov;182(5):449-54. Postoperative delirium and melatonin levels in elderly patients. Shigeta H, Yasui A, Nimura Y, Machida N, Kageyama M, Miura M, Menjo M, Ikeda K.

2. Chin Med J (Engl). 2007 Nov 20;120(22):1951-7. Postoperative neuropsychological change and its underlying mechanism in patients undergoing coronary artery bypass grafting. Yin YQ, Luo AL, Guo XY, Li LH, Huang YG.
3. Acta Anaesthesiol Scand. 2002 Jan;46(1):30-6. The influence of anaesthesia and surgery on the circadian rhythm of melatonin. Kärkelä J, Vakkuri O, Kaukinen S, Huang WQ, Pasanen M.

A Technically Simple and Effective Nasal CPAP/CF Mask/Circuit to Improve Oxygenation of Obese Patients with OSA Under Deep Propofol Sedation During EGD

James Tse, PhD, MD, UMDNJ-Robert Wood Johnson Medical School, Rose Alloteh, MD, UMDNJ-Robert Wood Johnson Medical School, Andrew Burr, DO, UMDNJ-Robert Wood Johnson Medical School, Sylviana Barsoum, MD, UMDNJ-Robert Wood Johnson Medical School, Shaul Cohen, MD, UMDNJ-Robert Wood Johnson Medical School

Introduction: Patients under monitored anesthesia care (MAC) receive intravenous sedation and O₂ via nasal cannula (NC). Over-sedation and/or airway obstruction may cause severe desaturation, especially in obese patients. A simple plastic sheet was shown to improve oxygenation by transforming NC to a face tent (TSE "Mask") in sedated obese patients during EGD¹⁻³. However, obese patients with obstructive sleep apnea (OSA) may require frequent chin-lift, jaw-thrust and/or insertion of nasal airways. Inserting nasal airways may cause bleeding despite using small, well lubricated nasal airways. In light of a recent study showing the effectiveness of nasal ventilation in anesthetized patients⁴, we have developed a nasal CPAP mask/circuit using an infant face mask to improve oxygenation in OSA patients under MAC.

Clinical Case: A 71 y/o male was hospitalized for bilateral posterior calf ulcer. His medical problems include atrial fibrillation, coronary arterial disease, hypertension, obesity and OSA. His height was 5 feet 8 inches, his weight was 312 lb and his BMI was 45 kg/m². His baseline O₂ saturation was 96%. Even though he was provided with a facial CPAP mask/ machine at bedside, he did not use it because of claustrophobia. He was scheduled for irrigation and debridement of the ulcers. After discussing with the patient and the surgeon, the procedure would be done under local anesthesia with MAC in right lateral decubitus position. After the patient was pre-oxygenated with a nasal cannula O₂ (4 L/min) and a TSE "Mask", his O₂ saturation increased to 100%. He received IV bolus of 40 mg of lidocaine and 50 mg of propofol and propofol infusion (125 mcg/kg/min). As soon as the patient was sedated, the nasal cannula was replaced with a nasal mask. Ten ml of air was added to the air cushion of an infant mask to obtain a good seal. The mask was then secured with head straps and was connected to an adult breathing circuit. The pop-off valve was adjusted to deliver CPAP of 5 cm H₂O with 5-7 L/min fresh O₂ flow and 2 L/min air flow. The patient maintained spontaneous respiration as indicated by capnography (see Photo) and the movement of the reservoir bag. The peak inspiratory pressure was about 10-12 cm H₂O. After injecting local anesthetics, the propofol infusion was reduced to 75 mcg/kg/min. His O₂ saturation was 99-100% throughout with FiO₂ of 0.8. He tolerated the procedure well and was awake soon afterward. Next day postoperative visit revealed no complaint. The patient was very pleased with the experience and stated that was the best sleep he ever had. He was encouraged to try a nasal prong or a nasal CPAP mask at night. Informed consent was obtained for photography and case report.

Discussion: This simple nasal CPAP mask/circuit takes 2-3 minutes to assemble using existing anesthesia equipment. It improves oxygenation and pro-actively prevents desaturation in obese patients with OSA. It may improve patient safety at a very low cost.

References: 1. *Anesth* 102: 484, 2005; 2. *2010 ASA AM* A825; 3. www.TSEMask.com; 4. *Anesth* 108: 998-1003, 2008



Afternoon Abstracts

Upper Airway Morphology in Children with Down Syndrome vs. Children with Normal Airway under Dexmedetomidine

Rajeev Subramanyam MD*, Robert Fleck MD[‡], John McAuliffe MD, MBA*, Mario Patino MD*, Megan Schmitt RN*, Mohamed Mahmoud MD*

*Dept. of Anesthesia, and [‡]Dept. of Radiology Cincinnati Children's Hospital Medical Center

Summary: Increasing doses of Dexmedetomidine showed significant upper airway dimensions reduction in children with Down's syndrome and a history of obstructive sleep apnea compared to children with normal upper airway. These changes are significant at the narrowest points in the nasopharyngeal and retroglottal airways.

Background: Upper airway collapsibility is known to increase under sedation/anesthesia. Children with Down's syndrome are vulnerable to the development of significant upper airway obstruction due to relative macroglossia coupled with dynamic collapse of the airway. The objective of this study is to compare the upper airway dimensions of children with Down's syndrome with obstructive sleep apnea to those of children with normal airway under increasing doses of Dexmedetomidine (DEX).

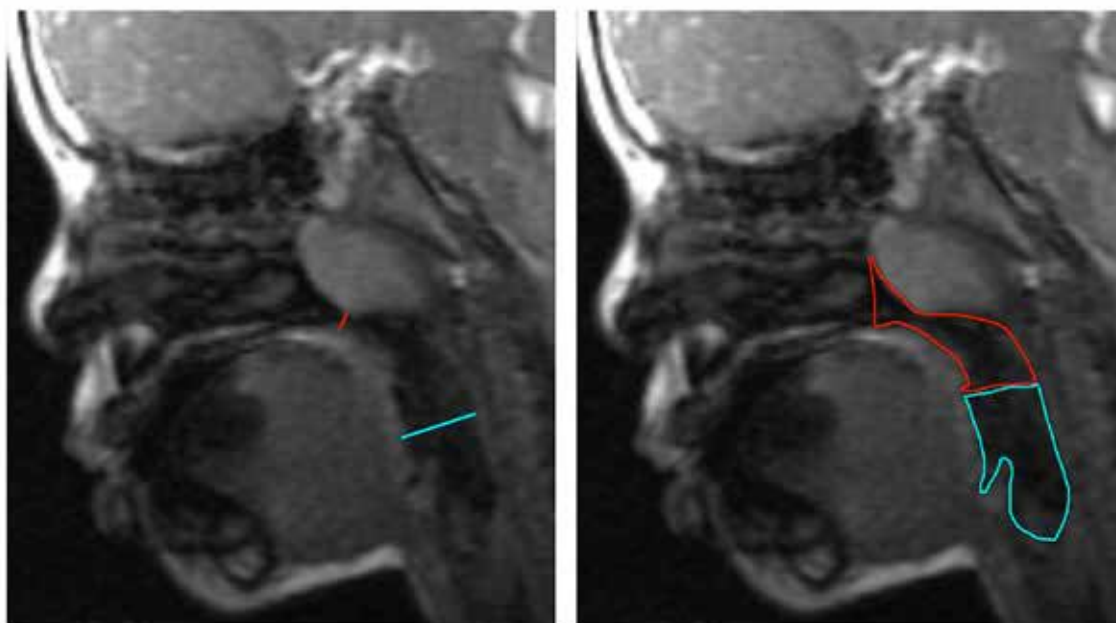
Methods: Institutional review board approval was obtained. All patients underwent clinically indicated magnetic resonance imaging under sedation. Dynamic sagittal midline Magnetic Resonance cine (fast gradient echo) images of the upper airway were obtained during low (1 mcg/kg/h) and high (3 mcg/kg/h) dose DEX sedation. Two independent observers manually measured airway anteroposterior diameter and sectional area. Sagittal airway measurements were done at the level of the soft palate (nasopharyngeal airway) and the base of the tongue (retroglottal airway) (Fig. 1). In general, the maximum sectional area was seen during exhalation, while the minimum was seen during inspiration.

Results: We studied 7 Down's children (mean age 5.2 ± 1.4 yr; 4 males; mean weight 26.0 ± 11.2 kg) and 23 normal airway children (mean age 5.6 ± 1.8 yr; 12 males; mean weight 21.6 ± 4.8 kg). Apnea Hypopnea Index in Down's children was 16.6 ± 11.3 (5.2-37.6) and the average minimal oxygen saturation observed during overnight sleep study in each patient was $80.7 \pm 5.3\%$ (72-85%). The minimum anteroposterior dimensions at nasopharynx was significantly reduced in Down's vs. normal airway at low (0.9 ± 0.9 vs. 4.7 ± 2.1 mm; $p < 0.0001$) and high dose DEX (1.1 ± 0.9 vs 4.6 ± 1.9 mm; $p < 0.001$). The minimum anteroposterior dimensions at retroglottal airway were significantly reduced in Down's vs. normal airway at low (1.9 ± 1.6 vs. 9.7 ± 3.9 mm; $p < 0.0001$) and high dose DEX (3.7 ± 3.1 vs. 9.0 ± 4.4 mm; $p = 0.012$) (Fig. 2). The minimum nasopharyngeal sectional area was significantly reduced in Down's vs. normal airway at low (157.4 ± 41.3 vs. 264.5 ± 79.8 mm²; $p = 0.0001$) and high dose DEX (171.16 ± 69.0

vs $262.3 \pm 75.1 \text{ mm}^2$; $p = 0.037$). Similar reductions were observed in retroglottal sectional area with Down's at low (107.7 ± 62.8 vs. $244.7 \pm 78.7 \text{ mm}^2$; $p = 0.0004$) and high dose DEX (120.8 ± 48.2 vs. $246.6 \pm 103.9 \text{ mm}^2$; $p = 0.001$) (Fig. 3).

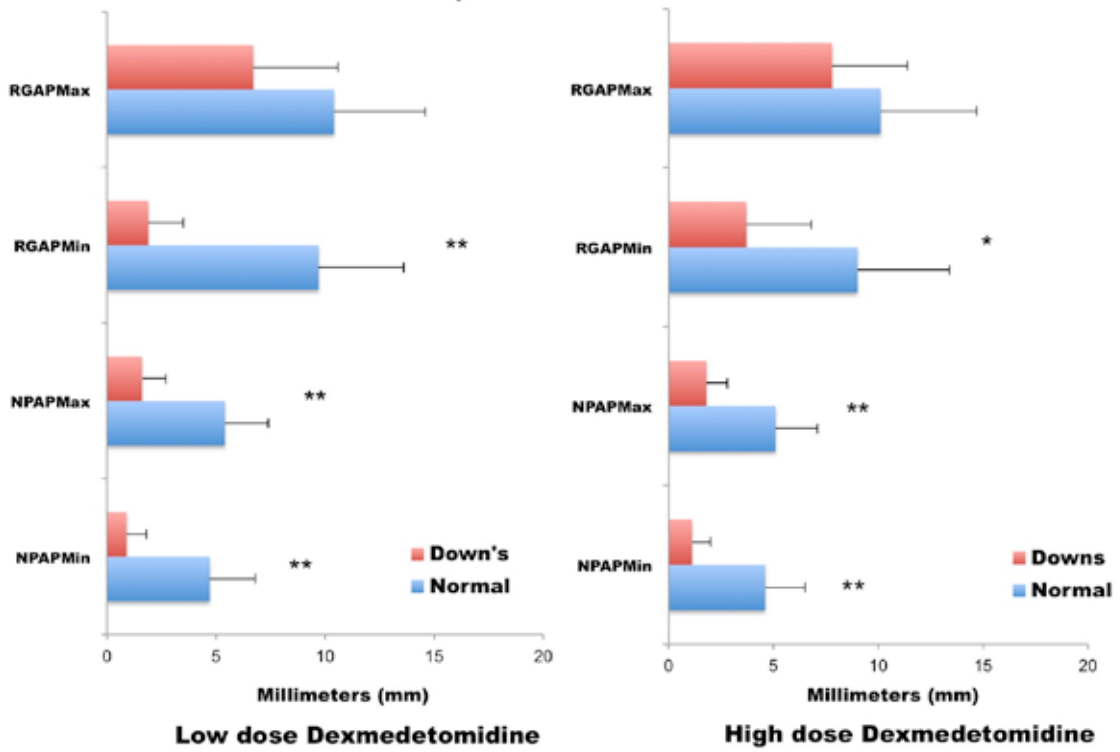
Conclusions: Under DEX sedation, children with Down's syndrome with obstructive sleep apnea show significant reductions in airway dimensions when compared to children with normal airway. The relative reduction in airway dimensions is equal at both low dose and high dose DEX, which argues that the observed differences are unique to Down's syndrome and not due to differences in sedation. These changes are significant at the narrowest points in the nasopharyngeal and retroglottal airways.

Figure 1: Dynamic sagittal airway measurements in a child with normal airway



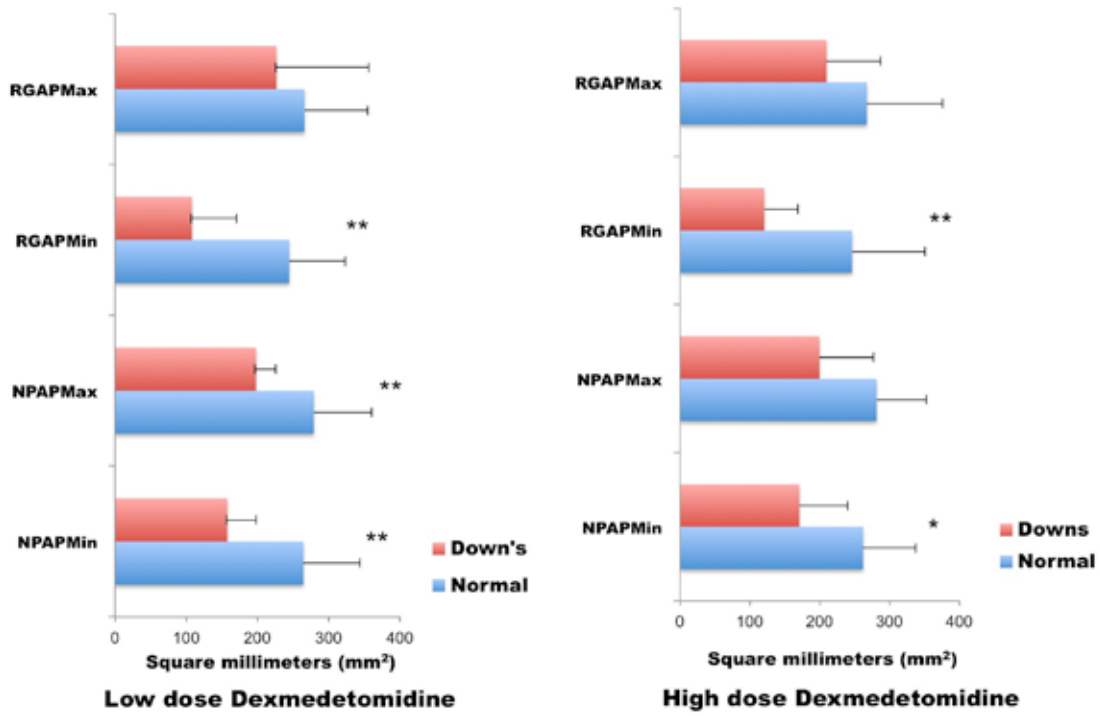
Midline sagittal magnetic resonance (MR) images from gradient echo cine sequence demonstrate method of measuring anterior to posterior diameter (left) and sectional area (right).

Figure 2: Dynamic anteroposterior diameter changes in children with Down's vs. children with normal airway



** p < 0.001; * p < 0.05; RGAPMax and RGAPMin = Retroglossal maximum and minimum anteroposterior diameter; NPAPMax and NPAPMin = Nasopharyngeal maximum and minimum anteroposterior diameter Sagittal view. All dimensions in mm.

Figure 3: Dynamic sectional area changes in children with Down's vs. children with normal airway



(** p < 0.001; * p < 0.05; RGAPMax and RGAPMin = Retroglossal maximum and minimum cross sectional area; NPAPMax and NPAPMin = Nasopharyngeal maximum and minimum cross sectional area. All sectional dimensions in mm²).

Evaluation of Feasibility and Functionality of a Video-Laryngoscope Equipped with a Ventilation Feature

Jun Oto MD, PhD, Massachusetts General Hospital, Christopher T. Chenelle, BA, Massachusetts General Hospital, Robert M Kacmarek PhD, RRT, Massachusetts General Hospital, Yandong Jiang, M.D., PhD, Anesthesia, Critical Care, and Pain Medicine, Massachusetts General Hospital

Introduction: Effective ventilation and oxygenation is critical for a patient with apnea, either induced or spontaneous occurring. However, to achieve this goal is still a great challenging for anesthesia care providers and emergency medical personnel as difficult mask ventilation and difficult intubations frequently occur. Video-laryngoscopes provide better visualization of the vocal cord, but it is unknown if this shortens the time for intubation. The aim of this study is to determine if a video-laryngoscope equipped with a ventilation feature produces effective ventilation prior to endotracheal intubation.

Methods: The study was conducted in a mannequin with its trachea connected to a model lung with compliance set at 50 ml/cm H₂O and airway resistance at 5 cm H₂O/L/s. Ventilation was produced via the Venturi effect by mounting a catheter with its tip at the end of the video-laryngoscope blade. Data was collected at three positions, corresponding to three different views of the vocal cords (fully visible, partially visible, and not visible). Ventilation was conducted with an ICU ventilator (ICU vent), a manual resuscitation bag (Bag), and a jet ventilator (JET). The driving pressure for the JET was 100 kPa. The inspiratory pressure of the ICU vent was set at 70 cm H₂O. The inspiratory pressure of the Bag was between 80 and 120 cm H₂O. Assessment of gastric distension was conducted with esophageal open pressure of 20 cm H₂O.

Results: The V_ts are listed in the table 1. The JET generated larger V_ts than the ICU vent or Bag ($p < 0.001$) when positioned with the vocal cord fully visible. Smaller V_ts were generated with partial visibility of the vocal cords than with full visibility for all methods ($p < 0.001$). With no visibility of the vocal cord, none of the ventilation methods generated a V_t (0 ml). Gastric distension was not seen in any position or ventilation device.

Conclusions: The video-laryngoscope with a ventilation feature may provide effective ventilation with any of the devices tested if the vocal cords are fully visualized. Because in general, video-laryngoscope provides great view of vocal cords, this system could potentially improve ventilation and oxygenation when cases of difficult mask ventilation or intubation are encountered. Further clinical studies are needed to validate and expand upon these findings.

Table 1. Mean tidal volumes for each device.

| | Fully visible | Partially visible | Not visible |
|----------|---------------|-------------------|-------------|
| JET | 538 | 142 | 0 |
| ICU vent | 225 | 30 | 0 |
| Bag | 372 | 43 | 0 |

Mean values (ml)

JET, jet ventilator; ICU vent, ICU ventilator; Bag, manual resuscitation bag

No Association between Preoperative Polysomnography Parameters and Postoperative Opioids Requirement in Adult Patients with Obstructive Sleep Apnea

Peter Liao, MD, Toronto University Health Network, Sazzadul Islam, MSc, Toronto University Health Network, Frances Chung, MB, MS, Toronto University Health Network

Introduction: Hypoxemia was associated with an increased sensitivity to opioids in children with obstructive sleep apnea (OSA). The objective of this study is to investigate if the preoperative polysomnographic parameters measuring sleep disordered breathing are associated with the postoperative opioid requirement in adults.

Methods: Following institutional REB approvals, patients were recruited from preoperative clinics. The consented patients underwent a home polysomnography (PSG) with a portable device (Embletta X100). The recordings were manually scored by a certified PSG technologist. The patients were followed postoperatively and charts were reviewed. The opioids administered were converted to intravenously morphine equivalent dose in milligram (mg). The correlation between the preoperative PSG parameters measuring sleep disordered breathing and the postoperative 72h opioids requirement was analyzed.

Results: 282 patients were studied, 66 non-OSA (apnea-hypopnea index (AHI) ≤ 5 events/h) and 216 OSA patients (AHI > 5 events/h). Age was 61.8 ± 11 years in OSA patients vs 56 ± 13 years in non-OSA patients ($p < 0.001$). Male accounted for 49% in OSA patients and 26% in non-OSA patients ($p = 0.001$). Body mass index was 31 ± 7 kg/m² in OSA patients and 28 ± 4 kg/m² in non-OSA patients ($p < 0.001$). Majority of patients were classified as 2 and 3 by American Society of Anesthesiologists Physical Status classification: 98% in OSA patients and 95% in non-OSA patients. The most common surgery was orthopedic surgery, 62% in OSA patients and 52% in non-OSA patients. General anesthesia accounted for 48% in OSA patients and 58% in non-OSA patients. The AHI was 19(11,31) events/h [median(25th, 75th percentile)] in OSA patients and 2(1,4) events/h in non-OSA patients. There was no significant difference between OSA and non-OSA patients in postoperative 72-hour opioids requirement, 55(15,84) mg in OSA patients and 54(8,85) mg in non-OSA patients.

In non-OSA patients, there was an inverse correlation between preoperative central apnea index with postoperative 72 hour opioids requirement ($r_s = -0.299$,

p=0.014). No other significant correlation between preoperative PSG parameters and 72h postoperative opioids requirement was found in OSA or non-OSA patients (Table 1).

Conclusion: In adult OSA patients, no correlation between preoperative PSG parameters measuring sleep disordered breathing and postoperative 72h opioids requirement was found.

Table 1 Spearman coefficient between preoperative polysomnographic parameters and 72h postoperative opioids requirement

| Polysomnographic parameters | AHI ≤ 5 | | AHI > 5 | |
|--|----------------|-------|----------------|-------|
| | r _s | p | r _s | p |
| Apnea-hypopnea index | -0.066 | 0.597 | 0.073 | 0.284 |
| Obstructive apnea index | -0.119 | 0.342 | 0.032 | 0.645 |
| Central apnea index | -0.299 | 0.014 | 0.109 | 0.111 |
| Mixed apnea index | 0.042 | 0.736 | 0.041 | 0.545 |
| Hypopnea index | -0.071 | 0.469 | 0.057 | 0.407 |
| Respiratory arousal index | -0.033 | 0.790 | 0.092 | 0.182 |
| Oxygen desaturation index | -0.076 | 0.548 | 0.110 | 0.109 |
| Cumulative time percentage with SpO ₂ < 90% | -0.101 | 0.462 | 0.057 | 0.448 |
| Lowest SpO ₂ | 0.133 | 0.247 | -0.033 | 0.631 |

Postoperative Opioids Requirement and Sleep Disordered Breathing

Peter Liao, MD, Toronto University Health Network, Sazzadul Islam, MSc, Toronto University Health Network, Frances Chung, MB, MS, Toronto University Health Network

Introduction: Opioids can induce central respiratory depression through mu- and kappa- opioid receptor. It also can inhibit central tonic outflow to the primary upper airway dilator, genioglossus muscle. The objective of the study is to investigate the relationship between postoperative opioids requirement and sleep disordered breathing (SDB).

Methods: Following institutional REB approvals, patients were recruited from preoperative clinics. The consented patients underwent a preoperative home polysomnography (PSG) and postoperative PSG on first night after surgery, with a portable device (Embletta X100). Recordings were manually scored by a certified PSG technologist. Patients were followed postoperatively and charts were reviewed. Opioids administered were converted to intravenously morphine equivalent dose. According to preoperative apnea-hypopnea index (AHI), patients were classified as obstructive sleep apnea (OSA, AHI>5 events/hr) or non-OSA (AHI≤5 events/hr). The correlation between 1st 24h opioids requirement and SDB on postoperative night 1 was analyzed.

Results: 354 patients were studied, 101 non-OSA and 253 OSA patients. There was more males in OSA group, 50% vs 30% in non-OSA ($p=0.001$). OSA patients were also older (age 60 ± 11 vs 55 ± 12 years, $p<0.001$) and more obese (BMI 31 ± 5 vs 27 ± 5 kg/m², $p<0.001$). Orthopedic surgery was most common type, 60% in OSA patients and 46% in non-OSA patients ($p=0.004$). There were more patients receiving general anesthesia, 52% in OSA patients and 63% in non-OSA patients. There was no significant difference between OSA and non-OSA patients in 1st 24h opioids requirement, 25(10,39) mg [median(25th,75th percentile) in OSA patients and 23(5, 35) mg in non-OSA patients ($p=0.155$).

On postoperative night 1 PSG, AHI was 18.4(5.6, 45.5) in OSA patients vs 4(1,13) events/hr in non-OSA patients ($p<0.001$), obstructive apnea index: 2.8(0.2, 12.6) vs 0.3(0,3) events/hr ($p<0.001$), central apnea index: 0(0,0) vs 0(0, 0) events/hr ($p=0.953$), hypopnea index : 9.3(2.9, 20.4) vs 2.4(0.6, 5.5) events/hr ($p<0.001$), respiratory arousal index: 7.1(1.8, 25.0) vs 1.6(0.4, 5.9) events/hr ($p<0.001$), oxygen desaturation index: 2.4(0.2, 16.2) vs 0.9(0, 4.7) events/hr ($p=0.001$), and lowest SpO₂: $86.4\pm 8.7\%$ vs $89.1\pm 7.1\%$ ($p=0.003$).

The Spearman correlation coefficient (r_s) between the 1st 24h opioids requirement and PSG parameters measuring SDB is shown in Table 1. In non-OSA

patients, there was a significant correlation between 1st 24h opioids requirement and central apnea index and mixed apnea index, $r_s=-0.231$, $p=0.020$ and $r_s=-0.252$, $p=0.011$ respectively. In OSA patients, a significant correlation was found between 1st 24h opioids requirement and AHI, obstructive apnea index, central apnea index, mixed apnea index, respiratory arousal index with r_s ranged from 0.155 to 0.220 and $p<0.05$.

Conclusion: In adult OSA patients, postoperative opioids requirement was associated with AHI, obstructive apnea index, central apnea index, mixed apnea index, respiratory arousal index. While in non-OSA patients, postoperative opioids requirement was only associated with central apnea index and mixed apnea index.

Table 1 Spearman coefficient between 1st 24h opioids requirement and sleep disordered breathing on postoperative night 1

| | AHI ≤ 5 (n=101) | | AHI>5 (n=253) | |
|---|-----------------|-------|---------------|--------|
| | r_s | p | r_s | p |
| Apnea-hypopnea index | 0.033 | 0.747 | 0.198 | 0.002 |
| Obstructive apnea index | 0.129 | 0.200 | 0.155 | 0.014 |
| Central apnea index | 0.231 | 0.020 | 0.17 | 0.005 |
| Mixed apnea index | 0.252 | 0.011 | 0.220 | <0.001 |
| Hypopnea index | -0.141 | 0.161 | 0.057 | 0.364 |
| Respiratory arousal index | -0.011 | 0.913 | 0.186 | 0.003 |
| Oxygen desaturation index | -0.034 | 0.738 | 0.089 | 0.171 |
| Cumulative time percentage with SpO ₂ <90% | -0.096 | 0.409 | 0.085 | 0.241 |
| Lowest SpO ₂ | 0.081 | 0.438 | 0.033 | 0.611 |

Morphine Metabolism in Diet-Induced Obese Mice Compared to Leptin-Deficient Obese Mice

Nicholas Dalesio, MD, Johns Hopkins University, D. Hale McMichael, MD, Johns Hopkins University, Rachael Rzasa Lynn, MD, University of Colorado, Huy Pho, BS, Johns Hopkins University, Rafael Arias, BS, Johns Hopkins University, Jeffrey Galinkin, MD, FAAP, University of Colorado, Alan R. Schwartz, MD, Johns Hopkins University, Myron Yaster, MD, Johns Hopkins University

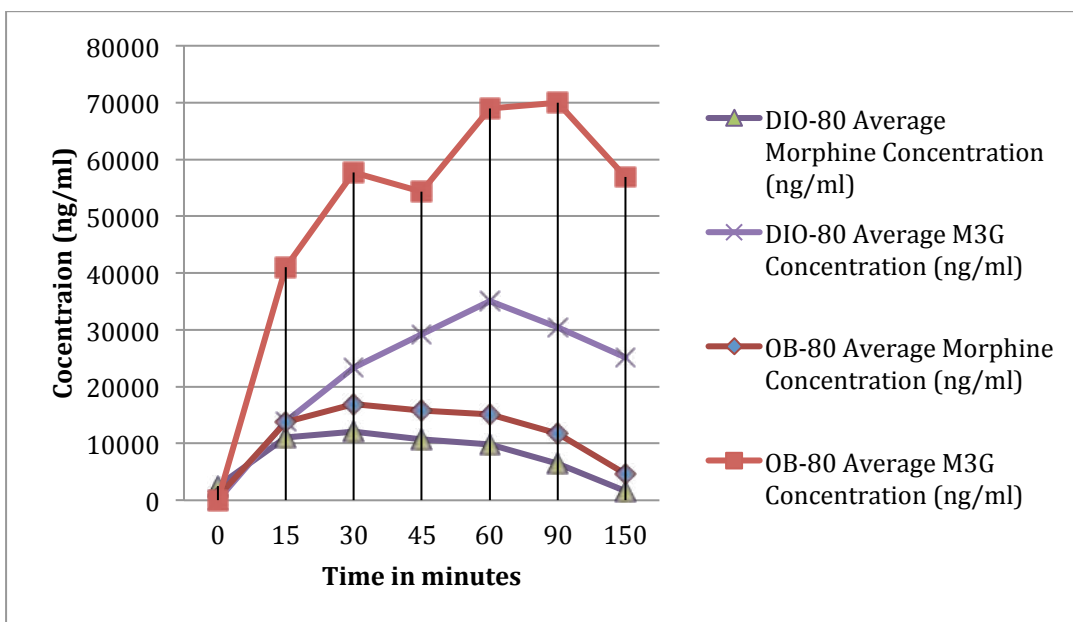
Background: Obesity has enormous perioperative implications including obstructive sleep apnea (OSA), abnormal liver function, and an increased sensitivity to opioids. Patients with OSA have been shown to be resistant to leptin, an adipose derived hormone that is key in regulating hunger and metabolism.¹ Leptin resistance is much higher in the OSA population when compared to weight-matched patients without OSA.² We hypothesized that opioid pharmacokinetics would differ in diet-induced obese wild type compared to leptin-deficient obese mice.

Methods: During a stable plane of anesthesia (1-2% of isoflurane), an intra-peritoneal (IP) injection of morphine was administered to C57BL/6J diet-induced obese (DIO) and leptin-deficient (OB) mice. Experiments were performed on 6 DIO and 6 OB mice that were age-matched (9 weeks) and weight-matched (30 grams). Each group of 6 DIO and OB mice received 80mg/kg of IP morphine. One drop of retro-orbital blood was obtained at 0, 15, 30, 45, 60, 90, and 150 minutes after IP injection. The collected blood was placed on Whatman 903 filter paper, dried, and analyzed in batches. Plasma morphine and its metabolite morphine 3-glucuronide (M3G) were extracted and quantified using high performance liquid chromatography- tandem mass spectroscopy as described by Clavijo et al.³ The enzyme to metabolize to morphine-6 glucuronide is not present in these mice strains and therefore, was undetected in all samples. The mice were anesthetized for each blood draw and allowed to recover between blood draws. Data were analyzed using Mann-Whitney test and p values < 0.05 were considered significant. Data are presented as average +/- standard deviation.

Results: Maximum morphine concentration (c_{max}) following IP injection was significantly less in the DIO mice as compared to the OB mice (12.8 +/- 2.6 mcg/ml and 18.1 +/-4.3 mcg/ml, respectively; $p < 0.05$). Time to maximum (t_{MAX}) morphine concentration in the DIO mice compared to the OB mice was equal at 30 minutes. At 150 minutes, the average morphine concentration in the DIO mice was smaller compared to the OB mice (1.6 +/- 0.8 mcg/ml and 4.6 +/- 2.8 mcg/ml, respectively; $p < 0.02$) The maximum serum concentration of M3G following IP injection reached a c_{max} statistically greater in DIO mice compared in the OB mice (37.7 +/- 13.5 mcg/ml and 79.1 +/- 27.2 mcg/ml, respectively; $p < 0.01$). At 150 minutes, the average M3G concentration in the DIO mice was approaching significance compared to the OB mice (25.2 +/- 18.2 mcg/ml and 56.9 +/-30.0 mcg/ml, respectively; $p = 0.09$). T_{MAX} to M3G was not statistically different (Figure).

Discussion: Leptin-deficient mice have significantly higher plasma morphine and morphine metabolite (M3G) concentrations when compared to weight and aged-match diet-induced obese mice. Leptin deficiency, more than just obesity, may play a role in morphine sensitivity in the OSA population. Further studies are necessary to identify the cause and implications of these findings.

Figure: Morphine and morphine-3-glucuronide (M3G) concentrations per unit time in diet-induced obese (DIO) and leptin-deficient obese (OB) mice.



References:

1. Marik PE. *Chest*. 2000;118(3):569–571.
2. Ip MS et al. *Chest*. 2000;118(3):580–586.
3. Clavijo CF, et al. *Anal Bioanal Chem*. 2011;400(3):715–728.

Blaustein Pain Foundation
 Richard J. Traytsman Endowed Chair

GAL-021 Reverses Opioid-Induced Respiratory Depression and Decreases the Severity of Central Sleep Apneas and Obstructive Apneas in Rats

Francis Golder DVM, PhD, Matthew Hewitt PhD, Santhosh Baby PhD, Ryan Gruber BS, Courtney Ideo BS, And D Euan MacIntyre PhD, Galleon Pharmaceuticals - Horsham, PA/US

Drug-induced control of breathing disorders such as opioid-induced respiratory depression (OIRD) and exacerbation of sleep-disordered breathing increase patient morbidity and are frequently encountered in the peri-operative period. GAL-021 is being developed as new therapeutic agent to restore breathing control. Here, we present pre-clinical data demonstrating that GAL-021 increases minute volume via carotid body stimulation, ameliorates OIRD without diminishing opioid-induced analgesia, and decreases the severity of central sleep apneas (CSA) and obstructive apneas (OA) in rats.

Carotid body-dependent ventilatory stimulation: Ventilation was measured in conscious drug-naïve rats using whole body plethysmography and in urethane anesthetized rats using direct tracheal spirometry. Intravenous boluses of GAL-021 (0.01 - 0.3 mg/kg) dose-dependently increased minute volume (\dot{V}_E), tidal volume, and respiratory rate. The ED_{50} for increasing \dot{V}_E was 0.08 mg/kg. The effects of GAL-021 on \dot{V}_E were decreased by up to 80% after bilateral carotid sinus nerve transection. The residual ventilatory stimulation was abolished by bilaterally denervating the aortic bodies.

OIRD: Based on the above results, we hypothesized that GAL-021 would also decrease the severity of OIRD. Acute respiratory depression (increased PCO_2 and decreased \dot{V}_E) was induced using an intravenous bolus of morphine (10 mg/kg IV) in conscious rats or an infusion of alfentanil (1 ug/kg/min IV) in urethane anesthetized rats. Subsequent GAL-021 infusions (0.1 – 1 mg/kg/min IV) dose-dependently diminished the effects of both opioids on breathing. Vehicle infusion had no effect on OIRD. Analgesiometry using the tail flick assay demonstrated that GAL-021 does not diminish morphine-induced analgesia in conscious rats.

CSA: We have established a novel model of opioid-exacerbated sleep disordered breathing in rats. Chronic morphine (0.6 mg/ml) added to the drinking water increases CSA frequency (Baseline: 4/hr; chronic morphine: 13/hr) and ventilatory variability during NREM sleep. Opioid tolerance was confirmed using analgesiometry. We hypothesized that GAL-021 would decrease the severity of CSA in this model. Sleep-wake state was scored as AWAKE, NREM or REM using EEG/EMG telemetry and breathing was measured using whole body plethysmography. GAL-021 infusion (0.007 – 0.20 mg/kg/min IV) dose-dependently decreased CSA frequency (lowest dose of GAL-021: 7/hr; highest dose of GAL-021: 0/hr) and stabilized breathing. Vehicle infusion had no effect on CSA. These effects of GAL-021 occurred without significant changes in sleep-wake state or minute volume.

OA: Urethane anesthetized supine rats spontaneously express pharyngeal obstructions (30 - 40 OAs/hr, mean length 9 s) with intermittent oxy-Hb desaturations. We hypothesized that

GAL-021 would decrease the severity of these obstructions. Rats were anesthetized, positioned in a head-out plethysmograph to measure airflow, and allowed to breathe room air. Sub-glottal tracheal pressure was measured to confirm respiratory effort during an apnea. Pulse oximetry was recorded continuously. GAL-021 infusion (0.025 – 0.050 mg/kg/min) dose-dependently decreased OA frequency (GAL-021: 9/hr), OA length (GAL-021: 5 s), and the severity of oxy-Hb desaturations.

Collectively, these results demonstrate that GAL-021 is a modulator of breathing control that can restore respiratory function in a variety of disorders commonly encountered in the peri-operative period.

GAL-021 A New Intravenous Selective Potassium-Channel Blocker is Well Tolerated and Stimulates Ventilation in Healthy Volunteers

Authors: Francis J. Golder, BVSc, PhD¹, Sean Peng, PhD¹, Lance Myers, PhD², Paul A. Hoskins¹, James F. McLeod, MD¹

1 – Galleon Pharmaceuticals Corporation, Horsham, PA, USA

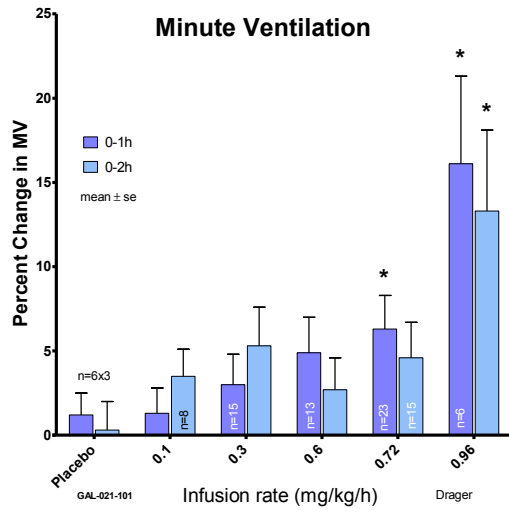
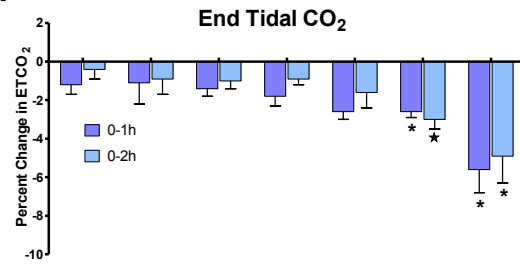
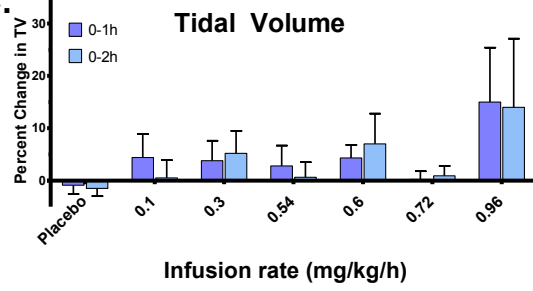
2- Vivonoetics, San Diego, CA, USA

Background: Potassium-channels in the carotid body and brainstem are important regulators of ventilation and contain response elements for CO, O₂, and CO₂. GAL-021, a new selective K⁺-channel blocker, increases carotid body signaling, phrenic nerve activity, and respiratory drive. GAL-021 increases minute ventilation and reduces ET_{CO₂} in rats and non-human primates. GAL-021 is being developed as a novel therapeutic agent to reverse drug-induced respiratory depression in the peri-operative setting. This first-human-study assessed the single dose safety, tolerability, pharmacokinetics, and pharmacodynamics of GAL-021 in healthy volunteers.

Methods: Thirty subjects participated in the study after approval by the ethic committee and Belgium health authority. In a 9-period, randomized, double-blinded, placebo-controlled, crossover, ascending dose study, subjects were divided into 3 cohorts (8 active and 2 placebo) in a rotating panel design with each subject receiving 3 treatments. Intravenous doses included 0.1 - 0.96 mg/kg/h for 1 hour and intermediate doses for 2 to 4 hours. Respiratory parameters (\dot{V}_E , RR, V_T, ET_{CO₂}) were assessed from 1 hour predose until 1 hour after infusion cessation. Safety and PK assessment were obtained from predose to 24 hours after the infusion initiation.

Results: Adverse events rates were generally similar among the dose levels and between placebo and actively treated subjects. In actively treated subjects at the higher doses, a mild/moderate burning sensation at the infusion site occurred during the infusion. No clinically significant changes in vital signs or clinical chemistries were noted. Minute ventilation increased (AUE_{0-1h} ≈ 16%, p<0.05) (Fig 1A) and ET_{CO₂} (Fig 1B) decreased (AUE_{0-1h} ≈ 6%, p<0.05) during the first hour at 0.72 and 0.96 mg/kg/h with ½-maximal \dot{V}_E and ET_{CO₂} changes occurring by 7.5 minutes. Drug concentration rose rapidly during infusion and declined rapidly initially with a distribution t_½ ≈ 20 minutes and then more slowly with a terminal t_½ of 5.6 hours. Exposure (AUC_{0-∞}) and the common time point among doses at 1 hour (C_{1h}) met statistical requirements for dose proportionality.

Conclusions: GAL-021 was generally safe and well tolerated and adverse events were comparable to placebo except for a burning sensation at the infusion site. GAL-021 simulated ventilation (\dot{V}_E and ET_{CO₂}) only at the highest doses suggesting that greater infusion rates may be required for maximum PD effects. GAL-021 was well-behaved pharmacokinetically with rapid rise in plasma concentrations and rapidly decline after ceasing infusion, consistent with drugs for use in acute care settings.

A.**B.****C.**

Celecoxib for Pediatric Adenotonsillectomy: A Randomized Controlled Double Blinded Study

Kimmo Murto MD¹, Christine Lamontagne MD¹, Johnna MacCormick MD², Colleen Daly MD³, Kelly Ramakko BSc¹, David Rosen MD¹, Nick Barrowman PhD⁴ and Regis Vaillancourt Pharm D⁵

1. Univ. of Ottawa Dept. of Anesthesiology, Children's Hospital of Eastern Ontario (CHEO), ON Canada

2. Univ. of Ottawa Dept. of Otolaryngology CHEO, ON Canada

3. Univ. of Ottawa Dept. of Anesthesiology

4. Clinical Research Unit, CHEO Research Institute, ON, Canada

5. Pharmacy Dept., CHEO, ON Canada

Introduction: Celecoxib is an effective analgesic in adult surgery patients, but no comparable pediatric literature exists. Adenotonsillectomy (T&A) is the most common surgery performed in children. The main indication is to treat "suspected obstructive sleep apnea (OSA)"¹. Children who have OSA have an increased sensitivity to the respiratory depressant effects of opiates². Our objective was to determine the effect of a short course of an oral celecoxib suspension on pain, analgesic consumption and functional recovery in pediatric adenotonsillectomy (T&A) patients.

Methods: With REB approval 282 children, 2-18 yrs, scheduled for elective T&A were randomized in a double blinded fashion to receive preoperative celecoxib 6 mg/kg or placebo. Anesthesia was standardized. After surgery patients received either celecoxib 3 mg/kg or placebo twice daily for 5 doses. Routine analgesics (acetaminophen and morphine) were administered as needed. Daily age appropriate diaries were completed by parents and children (≥ 5 yrs) to document recovery for postoperative days (PODs) 0-7. The primary outcome was a once daily score (100 mm scale) recording the "worst pain over previous 24 hours" for PODs 0-2. Total analgesic use was monitored. Celecoxib-related side effects were recorded and functional recovery in terms of QOL and fatigue were measured at POD 7 and compared to baseline. Reasons for hospital contact were recorded up to POD 14. Parent satisfaction was measured. The genotype of the CYP2C9 liver enzyme responsible for celecoxib metabolism including the "slow metabolizer" *3 allele was determined. Linear mixed-models, Fisher's exact and t-tests were used as indicated for comparisons.

Results: The intention-to-treat analysis included 206 (107 celecoxib and 99 placebo) children of which 195 (101 celecoxib and 94 placebo) were suitable for primary outcome analysis. Demographics including incidence of CYP2C9 genotypes were similar. Celecoxib significantly reduced "worst pain" on PODs 0 and 1, but not 2 (see Figure 1). It reduced pain at rest (mm, 95% CI) in the evening of POD 0 (45, 40-51 vs 54, 48-59, $p=0.04$) and with swallowing for POD 1 (47, 42-53 vs 58, 52-64, $p=0.02$) only. Total PODs 0-2 acetaminophen consumption (mg/kg \pm SD) was significantly lower in the celecoxib group (79 ± 57 vs 97 ± 60 , $p=0.03$) and morphine consumption trended lower (0.56 ± 0.47 vs 0.70 ± 0.56 , $p=0.06$). There was minimal difference in tonsil bleeds

requiring a hospital visit (8 celecoxib and 7 placebo) or surgery (3 celecoxib and 2 placebo). There was no difference in the incidence of celecoxib-related side effects, level of functional recovery or satisfaction. There was no difference in "worst 24 hour pain" or adverse events experienced over PODs 0-7 for patients who received celecoxib and were deemed "slow metabolizer" status (n=13) vs placebo.

Discussion: In children, a short course of an oral celecoxib suspension after T&A reduced early static and dynamic pain and analgesic consumption. It was well tolerated. However, it had no effect on functional recovery. A "slow metabolizer" status did not confer improved analgesia or increased adverse events in those who received celecoxib. Celecoxib appears to be beneficial for T&A in children.

References:

1. Otolaryngol Head Neck Surg 2009; 140:894.
2. Anesthesiology 2006; 105: 715-8

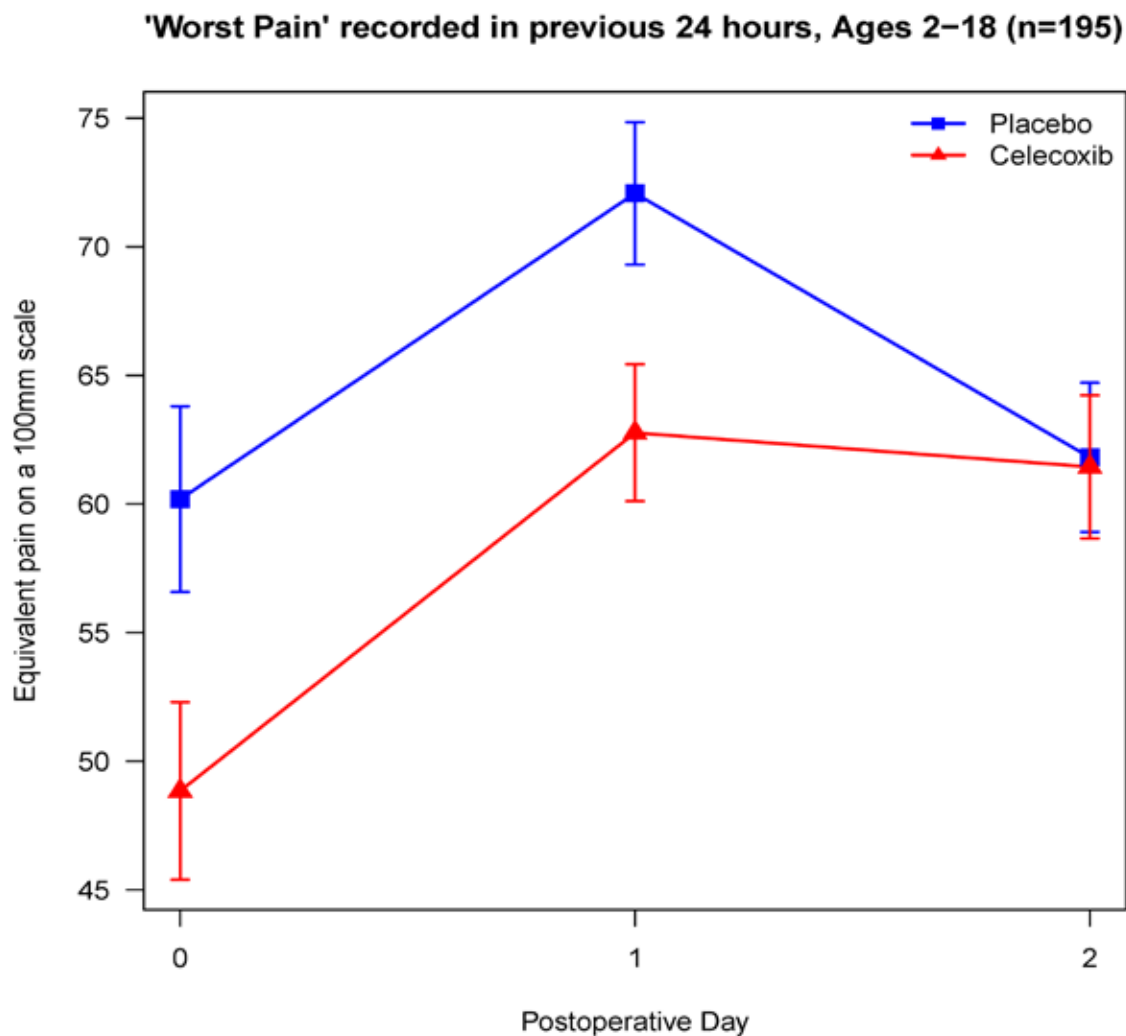


Figure 1. "Worst pain" experienced during first three PODs. Celecoxib group experienced significantly less pain at day 0 (p=0.02) and day 1 (p=0.02), but not day 2

z

Validation of the ASA OSA Prediction Tool in Children

Kimmo Murto MD¹, Sherri Katz MD², Carol Bradbury MD¹, Kelly-Ann Ramakko BSc¹, Nick Barrowman PhD³ and Gregory L Bryson MD⁴

1. Univ. of Ottawa Dept. of Anesthesiology, Children's Hospital of Eastern Ontario (CHEO), ON Canada

2. Univ. of Ottawa Dept. of Respiriology and Sleep Medicine, CHEO, ON Canada

3. Clinical Research Unit, CHEO Research Institute, ON, Canada

4. Univ. of Ottawa Dept. of Anesthesiology, The Ottawa Hospital, ON, Canada

Introduction: The American Society of Anesthesiologists (ASA) developed a tool to predict obstructive sleep apnea (OSA) in adults and children [1]. It consists of 16 predictor candidates (PCs) that are scored to predict none, moderate or severe OSA. This prediction tool has not been validated in children against polysomnography (PSG), the "gold standard". Our objectives were to assess tool performance and identify PCs both highly reliable and predictive of moderate to severe (MSOSA) in children.

Methods: After REB approval parents of children aged 2-18 yrs scheduled for PSG completed a questionnaire asking about the presence of 11 symptoms found in the ASA prediction tool. Patients were excluded if they had a previous diagnosis of OSA. A trained anesthesia resident assessed the child for the presence of three physical signs as per the ASA tool. A sleep lab technician measured neck circumference and height/weight for BMI percentile in a standardized fashion. All parents and personnel remained blinded to each other's responses and sleep study result. Severity of OSA was graded independently using the apnea-hypopnea index (AHI) from the PSG (grade definitions as per ASA tool) and the results of the questionnaire. Inter-rater reliability data (ICC and Kappa) for predictor variables were obtained from literature with permission [2]. Variables deemed reliable (ICC or Kappa ≥ 0.6) underwent univariate logistic regression to determine association with MSOSA. Variables with p values ≤ 0.15 were included in a multi-variate logistic regression model. Data are expressed as number (percent%) or mean (range).

Results: A total of 329 patients were enrolled (113-none, 137-mild and 79 MSOSA) for evaluation. The mean age yrs \pm SD [range] was 10.1 ± 4.5 [2.4-18.8], 45% were female, the majority were Caucasian (67%) and the mean BMI percentile \pm SD [range] was 71 ± 33 [0-100]. A non-OSA medical condition was present in 59% of patients. The ASA questionnaire predicted PSG diagnosis of MSOSA with: sensitivity (95%CI) 85% (75-91), specificity 22% (17-27), positive predictive value (PPV) 26% (21-31), negative PV 82% (71-89) and odds ratio (OR) 1.54 (0.78-3.05). Table 1 reports (un)adjusted and adjusted ORs for association of questionnaire items and MSOSA. Five PCs (frequent snoring, frequent somnolence/fatigue, falls asleep easily, tonsils touching/nearly touching and anatomical nasal obstruction) were excluded due to poor reliability.

Discussion: The ASA OSA prediction tool lacks specificity and PPV to be useful as a screen for MSOSA in a preoperative clinic. Tool performance limitations may be secondary to vaguely defined dichotomous PCs resulting in reduced reliability and predictive power. However, as in adults, loud snoring (heard through a door) and observed pauses expressed as dichotomous PCs were found to be both reliable and predictive of MSOSA in children.

References: 1. Anesthesiology 2006; 104:1081 2. ASA abstract A1067 2009

| Table 1. Unadjusted and adjusted ORs for questionnaire items associated with MSOSA. | | | | |
|--|------------------------------|------------------------|----------------------------|----------------|
| ASA Variable | Unadjusted OR (95%CI) | P value (≤0.15) | Adjusted OR (95%CI) | P value |
| Craniofacial abnormalities | 2.42 (0.74-7.86) | 0.14 | 2.62 (0.77-8.84) | 0.12 |
| Loud snoring | 2.37 (1.42-3.97) | 0.001 | 2.01 (1.16-3.51) | 0.01 |
| Observed pauses | 2.28 (1.36-3.81) | 0.004 | 1.91 (1.10-3.32) | 0.02 |

Results of National Hospital Survey of Patient-Controlled Analgesia Practices

Michael Wong, JD, Anuj Mabuyi, PhD, Northeastern Illinois University, Chicago, Beverly Gonzalez, PhD student, Northeastern Illinois University, Chicago

Objectives: Although use of patient-controlled analgesia (PCA) reduces the risk of oversedation, The Joint Commission [Sentinel Event Alert on safe use of opioids in hospitals](#) cautions, “While opioid use is generally safe for most patients, opioid analgesics may be associated with adverse effects, the most serious effect being respiratory depression, which is generally preceded by sedation.”

According to the Food and Drug Administration (FDA) based on [reports](#) it received between 2005 and 2009, more than 56,000 adverse events and 700 patient deaths were linked to PCA. One out of 378 post-surgical patients are harmed or die from errors related to patient-controlled analgesia (PCA).

Our goal was to benchmark the practices hospitals are using to initiate PCA with a patient and to continue to assess that patient’s use of PCA.

Methods: Hospitals across the United States were asked to complete a survey of PCA practices that asked respondents questions on the following five areas: (a) training and the need for training, (b) patient risk factors and information, (c) initiation and continuation of PCA, (d) types of PCA pumps and monitoring used, and (e) alarm fatigue. Survey questions were designed with the help of clinicians and prominent healthcare organizations familiar with PCA.

Results: Hospitals representing 40 of the 50 states responded. Respondents were primarily pharmacists (48%), with the remaining respondents (52%) being doctors, nurses, respiratory therapists, and other healthcare professionals.

Conclusions: The survey revealed inconsistencies in hospital practices and the recommendations of key healthcare organizations, particularly The Joint Commission, the Institute for Safe Medication Practices, and the Anesthesia Patient Safety Foundation. Key findings in this regard included: (a) patient risk factors are not always checked (for example, low body weight is considered only 62.8% of the time); (b) while pump settings are double checked 98.1% of the time, line attachment is only confirmed 68.1%; (c) continuous electronic monitoring is not routinely performed (only 60.9% monitor all patients with pulse oximetry); and (d) more than one out of every five hospitals are either not using PCA pumps that contain safety software and medication libraries, or using such pumps that are more than 10 years old. The survey also found that hospitals that continuously electronically monitor report adverse events were averted; and although alarm fatigue is not considered an unmanageable problem (61.1%), almost 90% would employ more monitoring if false alarms were not an issue.

GAL-021, A New Intravenous Selective Potassium-Channel Blocker, Reverses Opioid Induced Respiratory Depression with no Impairment of Opioid Analgesia

Margot H.J. Roozkrans MD¹, Rutger van der Schrier, MD¹, Joop Van Gerven, MD², PhD, Pieter Okkerse MD², Sean Peng, PhD³, Paul A. Hoskins³, James F. McLeod, MD³, Albert Dahan, MD¹, PhD.

1 – Leiden University Medical Center, Leiden Netherlands; 2 - Centre for Human Drug Research, Leiden Netherlands, 3 - Galleon Pharmaceuticals, Inc., Horsham USA.

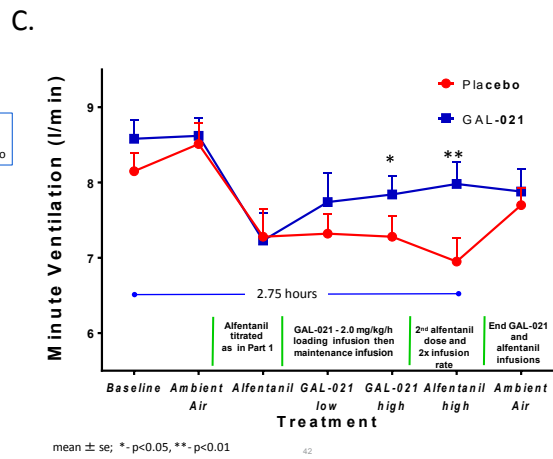
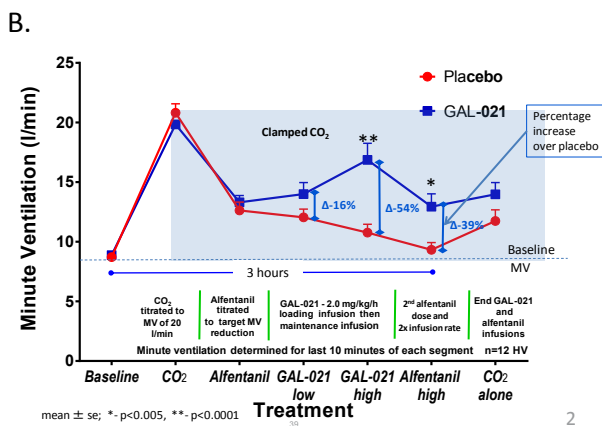
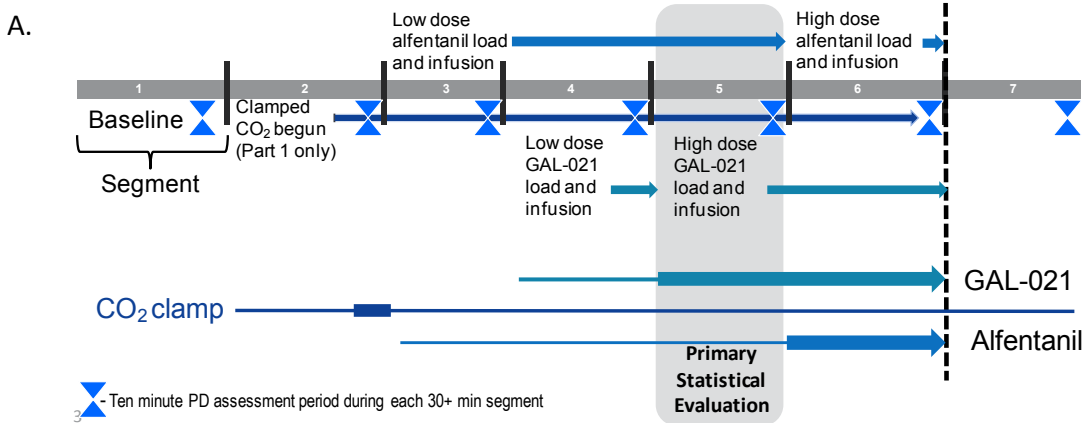
Background: GAL-021, a BK_{Ca}-channel blocker, is a novel therapeutic agent for the treatment and prevention of drug-induced postoperative respiratory depression. In rats and non-human primates, GAL-021 reversed opioid-induced hypoventilation and normalized minute ventilation (\dot{V}_E) and end tidal CO₂ (EtCO₂). In studies with humans, GAL-021 increased \dot{V}_E and decreased EtCO₂. To further evaluate the potential of the agent, the study assessed the effectiveness of GAL-021 to reverse alfentanil-induced respiratory depression under hypercapnic (dynamic-forced EtCO₂) and ambient air conditions in healthy volunteers. In parallel, transcutaneous electrical pain stimulation (TEPS) was used to assess GAL-021 effects on opioid analgesia.

Methods: The study was a 2-part study, 4-period, randomized, double-blind, placebo-controlled, stepped infusion design conducted in healthy subjects. Low and high doses of alfentanil and GAL-021 (or placebo) were used in each period (study design- Figure A). Clamped hypercapnia was used in Part 1 and inhaled CO₂ concentration was adjusted continuously to maintain a constant EtCO₂ during segments 3 to 7. A TEPS device placed over the anterior tibia assesses pain onset and maximum tolerated current.

Results: Adverse event (AE) rates were generally similar among the dose levels and between placebo and actively treated subjects with typical opioid AE associated with initial and subsequent changes in the alfentanil infusion. In Part 1, \dot{V}_E increased rapidly 2.3-fold with CO₂ administration. Alfentanil administration decreased \dot{V}_E by 7.3 l/min (63% of CO₂-stimulated increment in \dot{V}_E) which further declined during the subsequent segments with placebo treatment (Figure B). Low dose GAL-021 (0.4 mg/kg/h) increased minute ventilation by 0.7 l/min (16% vs. placebo, $p \approx 0.07$) with the high dose (1.1 mg/kg/h) further increasing minute ventilation by 3.6 l/min (54% vs. placebo, $p < 0.0001$). In Part 2, the CO₂ clamp technique was not used and analgesic effects were assessed. GAL-021 administration did not impair the analgesic effects of alfentanil. Under ambient air conditions (Figure C), high dose GAL-021 increased \dot{V}_E with low (8% vs. placebo, $p < 0.05$) and high alfentanil infusions (15% vs. placebo, $p < 0.01$).

Conclusions: GAL-021 was generally safe and well tolerated. Under hypercapnic conditions, GAL-021 (1.1 mg/kg/h) increased minute ventilation in the face of low and high dose alfentanil and prevented the progressive, opioid-induced, respiratory depression associated with placebo administration. Under ambient air conditions, GAL-021 had a similar pattern, but lower, of minute ventilation changes suggesting that elevated PCO₂ may increase the ventilatory response. In contrast to opioid antagonists, GAL-021 does not impair opioid

analgesic effects, thereby, allowing for treatment of post operative respiratory depression while maintaining good pain control.



The Human Carotid Body Function - Neurotransmitter Release in Response to Acute Hypoxia

Jessica Kåhlin, MD, Souren Mkrtchian, MD, PhD, Anette Ebberyd BSc, Malin Jonsson Fagerlund, MD, PhD, Lars I Eriksson, MD, PhD

Introduction: During the last years obstructive sleep apnea (OSA) has gained much attention in the field of perioperative medicine due to the fact that OSA patients are high-risk patients for postoperative complications (1, 2). OSA is strongly associated with several co-morbidities. The intermittent hypoxia (IH) in OSA causes autonomic dysfunction such as hypertension and elevated levels of catecholamines. This seems to be mediated via an abnormal chemoreflex control of sympathetic activation or inflammation by the carotid body (CB) that is the major oxygen sensor. IH causes potentiation of the acute hypoxic ventilatory response (HVR). The HVR is affected by several drugs used in anesthesia, such as neuromuscular blocking agents and propofol, suggested to cause depression of the CB oxygen sensing reflex (3-5). The primary excitatory neurotransmitters in the CB are ACh and ATP (6), acting on postsynaptic cholinergic and purinergic receptors to ultimately increase the afferent input to the brainstem where breathing is modulated. Although the CB structure and function is extensively studied in different animal species, the oxygen sensing and signaling mechanisms in the human CB are unknown. However, in two previous descriptive studies we have characterized the human CB with regards to oxygen sensing and signaling components (7, 8). In order to understand the mechanisms behind OSA, basic knowledge on human CB oxygen sensing is required as a basis for future studies on IH in humans.

Methods: Patients undergoing radical neck dissection were phenotyped with regards to HVR prior to surgery. During surgery, CBs (n=6) were removed and sectioned. The slices were exposed to acute hypoxia (10% O₂, 5% CO₂). Release of neurotransmitters (ACh and ATP) was analyzed after 5 min of hypoxia with luminometry and HPLC. Gene expression was analyzed after 60 min of hypoxia using microarray. In addition, we evaluated CB slices morphologically.

Results: We demonstrate a 30-50% increase in CB ACh and ATP release under hypoxia compared to control, with a subsequent return of neurotransmitter release to initial levels under recovery. The work is in progress to analyze the effect of hypoxia on the global gene expression in the human CB.

Conclusions: Here we provide new data on the mechanisms of oxygen sensing and signaling in the human CB. We confirm the release of ACh and ATP in response to hypoxia in the *human* CB. This indicates a regulatory role for ACh and ATP in human CB oxygen signaling. We have also mapped CB genomic changes in response to hypoxia. This is a basis for further studies on acute and intermittent hypoxia in humans.

References

1. T. S. Vasu et al. *J Clin Sleep Med* **8**, 199 2012
2. C. den Herder et al. *Bmj* **329**, 955, 2004.
3. M. Jonsson, et al. *Eur J Pharmacol* **497**, 173, 2004.
4. L. I. Eriksson, *Anesth Analg* **89**, 243, 1999.

5. D. Nieuwenhuijs, et al. *Anesthesiology* **92**, 46, 2000.
6. M. Zhang. *J Physiol* **525**, 143 2000.
7. M. J. Fagerlund et al. *Anesthesiology* **113**, 1270 2010.
8. S. Mkrtchian et al. *J Physiol* **590**, 3807, 2012.

Impact of a Post-Operative Obstructive Sleep Apnea Management Program on Perioperative Outcomes and Adverse Events

C. Riccio, M. Pilla, A. Ambrose, J. Wanderer, J. Ehrenfeld

Introduction: With the U.S. rate of obesity now exceeding 35% of adults and 17% of children,¹ obstructive sleep apnea (OSA) manifests as a significant and widespread preexisting condition for many patients presenting to hospitals for surgical or medical interventions.² These patients have been shown to be at heightened risk for perioperative respiratory complications and desaturation, often resulting in increased morbidity and mortality in this population.³ In order to optimally manage these patients, Vanderbilt University Medical Center has executed the first step of a hospital-wide OSA management program. As of November 2011, a protocol identifies pre-surgical patients who use CPAP. Upon admission to the hospital, respiratory therapy consult and CPAP initiation orders are automatically generated. The patient is subsequently evaluated by a respiratory therapist (RT), and either approved to continue using their personal CPAP for the duration of their hospital stay, or supplied with a hospital-owned, auto-titratable CPAP machine. Additionally, all patients evaluated in the Vanderbilt Preoperative Evaluation Center prior to surgery are screened for OSA using the STOP-Bang screening tool.⁴ Given these changes, we hypothesized that the program would decrease adverse perioperative respiratory events in this “at-risk” patient population.

Materials and Methods: The study was approved by the Vanderbilt Institutional Review Board (#120365). We utilized the perioperative data warehouse to obtain a list of patients who underwent surgery between January 1, 2009 and June 1, 2013. All completed cases of patients 18 years or older on the date of surgery were included. Cases were excluded if demographic (age, gender) or weight data were missing. Additionally patients presenting for organ harvest were excluded.

Results: We obtained data on 151,350 patients. Of these, 80,642 occurred before 11/15/11, the date on which the hospital-wide CPAP initiative was implemented, and 70,708 occurred after this date. Table 1 summarizes the demographics of the patient population.

| Table 1 | Patients 1/1/09-11/14/2011 | Patients 11/15/11-6/1/2013 |
|--|-----------------------------------|-----------------------------------|
| Gender, M/F (Total), n | 38,072/42,570 (80,642) | 34,061/36,647 (70,708) |
| Age, mean \pm SD, yr | 53.25 \pm 15.997 | 52.24 \pm 16.85 |
| BMI, mean \pm SD, kg/m² | 29.34 \pm 8.64 | 29.398 \pm 14.73 |
| BMI > 35 kg/m², n (%) | 14,660 (18.18) | 12,657 (17.90) |
| Diagnosed OSA, n (%) | 4,943 (6.13) | 4,347 (6.14) |
| ASA Status, mean \pm SD, n | 2.58 \pm 0.68 | 2.596 \pm 0.697 |
| ASA 1, n (%) | 3,019 (3.74) | 3,198 (4.52) |

| | | |
|---------------------|----------------|----------------|
| ASA 2, n (%) | 34,002 (42.16) | 28,905 (40.88) |
| ASA 3, n (%) | 37,786 (46.86) | 35,697 (50.49) |
| ASA 4, n (%) | 5,774 (7.16) | 5,359 (7.58) |
| ASA 5, n (%) | 61 (0.076) | 155 (0.22) |

Table 2 summarizes the outcomes before and after program initiation.

| Table 2 | Patients 1/1/09-11/14/2011 | Patients 11/15/11-6/1/2013 |
|--|-----------------------------------|-----------------------------------|
| Urgently reintubated after surgery, n (%) | 272 (0.337) | 90 (0.13) |
| Diagnosed OSA & Reintubated, n (%) | 17 (0.34) | 6 (0.14) |
| PACU Desaturation, n (%) | 26,948 (33.42) | 14,481 (20.48) |
| PACU Airway Obstruction, n (%) | 57 (0.07) | 50 (0.07) |
| CPAP Ordered, n (%) | 11 (0.014) | 2,292 (3.24) |
| CPAP Refused, n (%) | 0 (0) | 156 (0.22) |
| 15 Day Mortality, n (%) | 565 (0.70) | 551 (0.78) |
| 30 Day Mortality, n (%) | 913 (1.13) | 852 (1.20) |
| PACU Length of Stay, mean ± SD (minutes) | 163.82 ± 269.96 | 133.0708 ± 249.52 |
| ICU Length of Stay, mean ± SD (days) | 0.82 ± 4.04 | 0.89 ± 4.70 |
| Hospital Length of Stay, mean ± SD (days) | 4.00 ± 9.79 | 3.95 ± 9.99 |

This program proved to be successful in identifying those patients requiring CPAP, increasing the number of average visits by RTs for the initiation of home CPAP from 2 to 31 patients per day during the first 9 months of implementation.²

Prior to 11/15/2011, 0.34% of all patients with OSA were urgently reintubated after surgery. After initiation of the program, this rate has dropped to 0.14%. This represents a 59% drop in reintubations for patients with OSA. A chi-square with Yates correction was performed on these populations, which demonstrated a P-value of 0.0585 and suggests a trend towards significance.

Discussion: As previously described, with an increase in the incidence of obesity in America, the prevalence of OSA has become a significant factor that must be accounted for by anesthesiologists when developing an anesthetic plan. Prevalence of OSA is estimated to be as much as 25% of the general population,⁵ although many patients have not been officially diagnosed with OSA. It is estimated that in the bariatric surgery patient population, the rate of OSA incidence may be as high as 70%.⁵

While it is well established that sedatives and opioids used in anesthesia can lead to increased upper airway collapsibility, desaturation, and consequently an increased risk of postoperative complications, the majority of patients affected with OSA are undiagnosed and present a significant, postoperative risk of developing complications compared to those without OSA. In a case-control study by Liao et al., it was determined that OSA patients had more than 150% the rate of postoperative complications (44%) as did those who did not have OSA (28%).⁶ Adverse events, however, are not only limited to a higher rate of postoperative complications in those patients with confirmed OSA. In a study by Stierer et al., it was demonstrated that those with a $\geq 70\%$ calculated propensity for OSA based upon demographic and screening questionnaire data had increased rates of preoperative difficult intubation as well as intraoperative increased oxygen requirement and tachycardia.⁷ In a separate study by Lockhart et al., it was found that patients with diagnosed OSA also have an increased incidence of postoperative cardiac ischemia, hemodynamic instability, and arrhythmias.⁸

Based upon the known risks associated with surgical treatment of OSA patients, especially those at “high-risk” but without a confirmed diagnosis, Vanderbilt Medical Center instituted a CPAP identification and initiation program of VPEC-admitted patients with the hope of decreasing postoperative adverse respiratory events in this population. Step 1 involved identifying those patients currently prescribed to CPAP at home and automatically creating RT and CPAP consult orders. The results of this initiative were analyzed by Pilla et al in 2012, and yielded the conclusion that a reduction in the variability of care as well as a 15-fold increase in the number of patients seen for RT consultation and continued CPAP therapy while in the hospital was achieved.² Based upon this apparent success, the program was expanded with the intention to identify patients with diagnosed OSA who do not currently utilize home CPAP, as well as patients not currently diagnosed with OSA, but who are at significant risk for OSA as predicted by STOP-BANG screening results.

The main focus of this study was to identify the effect, if any, that this initiative has had on postoperative outcomes. Ideally, every “at-risk” patient that presents to the preoperative evaluation clinic would undergo nocturnal polysomnographic study (NPS) to confirm or rule out a diagnosis of OSA. Though challenging for many centers to have patients scheduled for NPSs in advance of their surgeries, a study by *Chong et al.* suggests that the same relative risk of postoperative adverse events can be achieved if “at risk” patients are managed on a perioperative risk reduction protocol.⁹ For this reason, it is important to accurately identify these “at-risk” patients through screening tests such as STOP-Bang. For the Vanderbilt Medical Center initiative, STOP-Bang was chosen based upon the available literature supporting it as the most sensitive test for the population of patients experiencing moderate to severe sleep apnea. According to a study by Abrishami et al., the STOP-Bang questionnaire is preferable to the Berlin and ASA surveys based upon its higher methodological quality and ease of scoring.¹⁰ More importantly, the STOP-Bang questionnaire exhibits consistently high sensitivity in detecting OSA at different apnea-hypopnea Index cutoffs. According to this study, the sensitivity achieved was $AHI \geq 5$: 84%, $AHI \geq 15$: 93%, $AHI \geq 30$: 100%, making it a very reliable, easily administered test for OSA.⁹

As STOP-Bang scores were unavailable for many patients prior to the initiation of our STOP-Bang screening in 2011, this study reviewed perioperative adverse outcomes in surgical patients with a previously confirmed diagnosis of OSA. In this population, we found that the rate of reintubation dropped from 0.34% to 0.14% after the implementation of our CPAP initiation program. While the p-value is slightly below the 95% confidence interval, it appears to demonstrate a trend in reduction of urgent and emergent reintubations in postsurgical OSA patients prescribed CPAP. More data is needed to demonstrate whether or not a stronger association between the CPAP initiation protocol and reduction in perioperative adverse events, including desaturation, mortality rates, and PACU length of stay. Additionally, costs, resource allocations, and the potential for other centers planning similar clinical protocols warrant cost-benefit analyses of this project.

References:

1. Ogden CL, Carroll MD, Kit BK, Flegal KM: Prevalence of obesity in the United States, 2009-2010. NCHS data brief 2012: 1-8
2. Michael Pilla MD, Paul St Jacques MD, Audrey H. Kuntz ED, Anna Ambrose RRT, Roger Dmochowski MD, William R. Furman MD: Implementation and Outcomes of a CPAP Initiation Program in a Large Academic Medical Center, *Anesthesiology* 2012, 2012
3. Chung F, Yegneswaran B, Liao P, Chung S, Vairavanathan S, Islam S, Khajehdehi A, Shapiro C: Validation of the Berlin questionnaire and American Society of Anesthesiologists checklist as screening tools for obstructive sleep apnea in surgical patients. *Anesthesiology* 2008; 108: 822-830
4. Chung F, Yegneswaran B, Liao P, Chung SA, Vairavanathan S, Islam S, Khajehdehi A, Shapiro CM: STOP questionnaire: a tool to screen patients for obstructive sleep apnea. *Anesthesiology* 2008; 108: 812-21
5. Vasu T, Grewal R, Doghramji K: Obstructive sleep apnea syndrome and perioperative complications: a systematic review of the literature. *Journal of clinical sleep medicine : JCSM : official publication of the American Academy of Sleep Medicine* 2012; 8: 199-207
6. Liao P, Yegneswaran B, Vairavanathan S, Zilberman P, Chung F: Postoperative complications in patients with obstructive sleep apnea: a retrospective matched cohort study. *Canadian journal of anaesthesia = Journal canadien d'anesthésie* 2009; 56: 819-828
7. Stierer T, Wright C, George A, Thompson R, Wu C, Collop N: Risk assessment of obstructive sleep apnea in a population of patients undergoing ambulatory surgery. *Journal of clinical sleep medicine : JCSM : official publication of the American Academy of Sleep Medicine* 2010; 6: 467-472
8. Lockhart E, Willingham M, Abdallah A, Helsten D, Bedair B, Thomas J, Duntley S, Avidan M: Obstructive sleep apnea screening and postoperative mortality in a large surgical cohort. *Sleep medicine* 2013; 14: 407-415
9. Chong C, Tey J, Leow S, Low W, Kwan K, Wong Y, Lew T: Management plan to reduce risks in perioperative care of patients with obstructive sleep apnoea averts the need for presurgical polysomnography. *Annals of the Academy of Medicine, Singapore* 2013; 42: 110-119
10. Abrishami A, Khajehdehi A, Chung F: A systematic review of screening questionnaires for obstructive sleep apnea. *Canadian Journal of Anesthesia/Journal canadien d'anesthésie* 2010; 57: 423-438

