Title
Effect of audiovisual distraction versus standard sedation on desaturation and airway interventions OSA-patients undergoing total knee arthroplasty under neuraxial anesthesia

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What is the condition or intervention to be studied?
The effect of audiovisual distraction (video goggles/headphones) on desaturation and airway interventions in OSA-patients undergoing total knee arthroplasty under neuraxial anesthesia compared to the events occurring using standardized pharmacologic sedation.

What is/are the research question(s)/specific aim(s)?
1) Is audiovisual distraction associated with a reduction of the number of desaturation events and airway maneuvers in OSA-patients undergoing total knee arthroplasty (TKA) under neuraxial anesthesia?
2) Can audiovisual distraction reduce the total amount of sedative requested without decreasing patient satisfaction?
3) Can audiovisual distraction replace pharmacologic sedation in OSA-patients undergoing TKA?

What is/are the hypothesis(es)?
1) Audiovisual distraction can reduce desaturation events in TKA-patients with OSA.
2) Audiovisual distraction can reduce airway intervention requirements in TKA patients with OSA.
3) Audiovisual distraction is an acceptable alternative to IV sedation for OSA patients undergoing TKA.

Primary outcome
Desaturation events (SpO2< 90% *for ≥ 10 sec*) measured during surgery and first half hour of PACU stay. This outcome will be analyzed as the number of desaturation events per hour.

Identify and define the secondary outcome(s) and when they will be measured
- Airway interventions (jaw thrust, oropharyngeal airway, nasopharyngeal airway, mask ventilation, larynx mask or intubation) measured during surgery and first half hour of PACU stay.
- Patient request for additional sedation during surgery
- Alertness levels on arrival to the recovery room, measured using the Modified Observer's Assessment of Alertness/Sedation Scale (MOAA/S)

Explain why these research questions are being asked:
OSA is associated with increased risk for adverse events, most prominently with airway complications and consequently desaturation in the perioperative setting[1]. Sedation may cause or worsen the risk for these complications[2]. Therefore, nonpharmaceutical methods, including audiovisual distraction, may pose a viable alternative to reduce stress and anxiety during surgery among OSA patients, while avoiding the negative impact of pharmacologically induced respiratory depression. Studies evaluating the impact of such devices on sedative requirements are rare with some data existing for children undergoing dental procedures[3-5]. However, to date virtually no data is available on the effect of audiovisual distraction for adults undergoing orthopedic surgery. Although joint arthroplasties can be performed under regional anesthesia,

US-patients typically expect additional sedation to shield them from a stressful operating room environment. However, the use of sedatives is associated with side effects such as depression in respirations, airway obstruction, hypotension, and changes in sensorium. Indeed, they have been proposed to be a contributing cause for post-operative delirium[6]. Some patient populations such as those with obesity and OSA may be especially vulnerable to airway and pulmonary effects[7]. Therefore, any intervention that could alleviate stress but does not affect airway and pulmonary function negatively would be of benefit in order to avoid adverse consequences associated with sedation. A randomized controlled trial directly comparing i.v.-sedation with audiovisual distraction with the primary outcomes of airway complications, desaturation events and patient satisfaction might thus be of important value.

1. Memtsoudis S, Liu SS, Ma Y, Chiu YL, Walz JM, Gaber-Baylis LK, Mazumdar M. Perioperative pulmonary outcomes in patients with sleep apnea after noncardiac surgery. Anesthesia & Analgesia 2011;112:113-21.
2. Opperer M, Cozowicz C, Bugada D, Mokhlesi B, Kaw R, Auckley D, Chung F, Memtsoudis SG. Does Obstructive Sleep Apnea Influence Perioperative Outcome? A Qualitative Systematic Review for the Society of Anesthesia and Sleep Medicine Task Force on Preoperative Preparation of Patients with Sleep-Disordered Breathing. Anesthesia & Analgesia 2016;122:1321-34.
3. Ram D, Shapira J, Holan G, Magora F, Cohen S, Davidovich E. Audiovisual video eyeglass distraction during dental treatment in children. Quintessence international 2010:673.
4. Prabhakar A, Marwah N, Raju O. A comparison between audio and audiovisual distraction techniques in managing anxious pediatric dental patients. Journal of Indian Society of Pedodontics and Preventive Dentistry 2007;25:177.
5. Mitrakul K, Asvanund Y, Arunakul M, Paka-Akekaphat S. Effect of audiovisual eyeglasses during dental treatment in 5-8 year-old children. European journal of paediatric dentistry : official journal of European Academy of Paediatric Dentistry 2015;16:239-45.
6. Coté GA, Hovis RM, Ansstas MA, Waldbaum L, Azar RR, Early DS, Edmundowicz SA, Mullady DK, Jonnalagadda SS. Incidence of sedation-related complications with propofol use during advanced endoscopic procedures. Clinical Gastroenterology and Hepatology 2010;8:137-42.
7. Lam KK, Kunder S, Wong J, Doufas AG, Chung F. Obstructive sleep apnea, pain, and opioids: is the riddle solved? Current Opinion in Anesthesiology 2016;29:134-40.

What is the background of the topic that you believe is important for the reviewer to know in considering this protocol, including prior studies by this research team. Describe strengths and deficiencies of prior studies; explain how this study fits in. Include references.

Although regional anesthetic techniques can provide dense surgical anesthesia making additional sedation optional, patients frequently voice concern regarding being awake in the operating room for fear of “seeing and hearing” events. For this reason patients will usually be given sedatives and hypnotics while in the operating room. However, the use of sedatives is associated with side effects ranging from delirium[1], inability to monitor the patient’s neurologic status intraoperatively, airway obstruction, aspiration and in extreme cases airway loss. Patients of advanced age or those with sleep apnea may be especially at risk. Thus, reducing or eliminating sedation for patient groups at high risk for adverse effects associated with drugs of

this category, such as patients with obstructive sleep apnea (OSA)[2], may be associated with improved perioperative care. Listening to music and using audiovisual devices may not only reduce anxiety in the operating but can reduce sedation requirements during surgery under neuraxial anesthesia[3-5].

1. Sieber FE, Zakriya KJ, Gottschalk A, Blute M-R, Lee HB, Rosenberg PB, Mears SC. Sedation Depth During Spinal Anesthesia and the Development of Postoperative Delirium in Elderly Patients Undergoing Hip Fracture Repair. Mayo Clinic Proceedings 2010;85:18-26.
2. Gross JB, Bachenberg KL, Benumof JL, Caplan RA, Connis RT, Cote CJ, Nickinovich DG, Prachand V, Ward DS, Weaver EM, Ydens L, Yu S, American Society of Anesthesiologists Task Force on Perioperative M. Practice guidelines for the perioperative management of patients with obstructive sleep apnea: a report by the American Society of Anesthesiologists Task Force on Perioperative Management of patients with obstructive sleep apnea. Anesthesiology 2006;104:1081-93; quiz 117-8.
3. Athanassoglou V, Wallis A, Galitzine S. Audiovisual distraction as a useful adjunct to epidural anesthesia and sedation for prolonged lower limb microvascular orthoplastic surgery. Journal of clinical anesthesia 2015;27:606-11.
4. Kaur R, Jindal R, Dua R, Mahajan S, Sethi K, Garg S. Comparative evaluation of the effectiveness of audio and audiovisual distraction aids in the management of anxious pediatric dental patients. Journal of the Indian Society of Pedodontics and Preventive Dentistry 2015;33:192-203.
5. Lee DW, Chan AC, Wong SK, Fung TM, Li AC, Chan SK, Mui LM, Ng EK, Chung SC. Can visual distraction decrease the dose of patient-controlled sedation required during colonoscopy? A prospective randomized controlled trial. Endoscopy 2004;36:197-201.

Identify specific gaps in current knowledge that this study is intended to fill.
To date, the literature regarding the use of audiovisual distraction as an alternative to i.v.-sedation consists of mostly case reports. Our group is currently studying the effect of audiovisual aids on stress response in patients undergoing knee arthroscopies, but there are no relevant studies on the effect of audiovisual distraction on preventing airway complications or desaturation events. Since these complications may be detrimental to patient outcome and may occur more frequently in OSA-patients under sedation we sought to study if they can be reduced by using audiovisual distraction while providing adequate conditions for patients in the operating room.

How will answering these questions change clinical practice, change concepts about the topic or confirm the work of other investigators?
Audiovisual distraction may emerge as a feasible alternative to i.v.-sedation and could be considered as an easily applicable means to reduce stress and maintain patient satisfaction while avoiding complications of sedation in OSA patients undergoing surgery.

Is this a pilot study that could lead to a more definitive protocol or different study?

No, this is not a pilot study. However, the results are expected to provide data which will inform and facilitate the design of future studies.

Experimental:
Randomized Controlled Clinical Trial
This is the "gold standard" for clinical research. These prospective studies have at least two groups. Patients meeting strict inclusion/exclusion criteria are enrolled and randomly assigned to receive either an experimental intervention or to receive what is considered to be an acceptable alternative – usually the current standard of care or a placebo (e.g., study of hylauronic acid injection versus cortisone for arthritis).

Specify all devices used on this study:

- HappyMed Video glasses
    - Investigational Device Not Yet Approved for use
    - This device is completely non-invasive. Participants in the study group will be asked to wear the glasses before, during and after their surgery. Participants will have the option to remove the glasses at any time should they feel any discomfort wearing the glasses. This use of this device for the study is aligned with the manufacturer's instructions. This device does not pose a significant risk to study participants and therefore does not need an IDE number.

- Zeiss Cinemizer OLED Glasses
    - Investigational Device Not Yet Approved for use
    - This device is completely non-invasive. Participants in the study group will be asked to wear the glasses before, during and after their surgery. Participants will have the option to remove the glasses at any time should they feel any discomfort wearing the glasses. This use of this device for the study is aligned with the manufacturer's instructions. This device does not pose a significant risk to study participants and therefore does not need an IDE number.

Assess the level of risk these devices pose to study participants:
Non-Significant Risks

Justify your risk assessment:
The devices used for the study do not pose a significant risk to participants due to their noninvasive nature. Both of the devices are being utilized according to the manufacturers' instructions. As with other audio devices, if the Cinemizer OLED/HappyMed glasses are worn for long periods of time at a very high volume setting hearing may be affected or participants may experience feelings of claustrophobia. Similar to computers and video games, when used for prolonged periods of time there are some side effects that users may experience when wearing the video glasses. This includes headaches, dizziness, disorientation or eye twitching. Participants will be made aware of their option to remove the Cinemizer OLED/HappyMed glasses should they experience any unwanted effects.

Inclusion Criteria:
Patients with known OSA (preexisting diagnosis or patients with a STOP BANG Score of 5 or above) scheduled for primary total knee arthroplasty under neuraxial anesthesia

Exclusion Criteria:
- Contraindications to neuraxial anesthesia or allergy to study medication
- Patients with audiovisual impairments prohibiting them from proper use of the study device
    - Patients who are blind
    - Patients with hearing aids
- Age < 18 years
- Patients with inability to communicate in English or understand the study requirements
- Patients with prior history of claustrophobia
- Patients with prior history of epilepsy or seizure disorder
- Patients undergoing a revision

Age Range
18 and above

Describe how you will identify and recruit potential subjects for participation in the study
Patients are currently being screened on EPIC the day before their surgery. They are approached in the holding area about 1 hour before surgery by a research assistant. When they are approached, the entire purpose of the study is explained in detail and all questions are answered before the patient is given time to read the consent form and decide whether or not they want to participate. We have also handed out flyers out during patient education classes to provide knee arthroplasty patients with some general information about alternatives to IV sedation before they come to the hospital for their operation. This general information is similar to the information we discuss during the consenting process in the holding area. In addition to the current consenting process, we would like to approach patients who are identified with OSA during their pre-surgical screening to give them information about the study. We would be going to the PSS nursing appointments and showing patients the device and giving them information about the study to think about before coming in for surgery. We would also leave them with the IRB approved flyers with our contact information.

Please select enrollment type from following drop down list:
Over Course of Study

Target Enrollment What is the maximum number of subject you plan to enroll in this study?
60

How subjects will be identified
- Potential subjects will be identified after a review of medical records of patients under the care of one or more of the study investigators

- Medical records and/or other Institution sources (databases, registries, billing records, pathology reports, and admission logs) will be reviewed to identify potential participants. May involve access of records by individuals not involved in the patient's care

Patients with known OSA (preexisting diagnosis of OSA or patients with a STOP BANG Score of 5 or above) undergoing primary total knee arthroplasty under neuraxial anesthesia will be asked to participate in this study. Before consent patients will be thoroughly informed about possible risks or benefits and about their possibilities to end the study at any time point or to ask for additional sedation if they feel uncomfortable or anxious. After they consent, they will be randomly assigned to either receive standard sedation (Group 1) or audiovisual distraction (Group 2). Each group will consist of 30 patients. The randomization schedule will be created by a member of the Healthcare Research Institute using SAS software, who is not otherwise involved in the trial.

1. **Standard of care sedation** with 0.05 mg/kg bodyweight with a maximum dose of 5 mg midazolam in preparation for the administration of the neuraxial anesthesia; propofol infusion starting with 40µg/kg/min and then titrated to effect.
2. **Audiovisual distraction** during surgery and in the PACU using video goggles and headphones; patients can choose a movie from a preexisting library; 0.05 mg/kg bodyweight with an initial maximum dose of 5 mg midazolam in preparation for the administration of the neuraxial anesthesia, additional sedation with midazolam in 1 mg increments if requested by the patient or deemed necessary by the anesthesia provider.

The intraoperative anesthesia regimen will be standardized:
- All patients will be monitored according to ASA standard, receive either a radial arterial line or NIBP according to the preferences of the anesthesia provider and O2 via nasal cannula or face mask in the OR and the PACU.
- 4mg ondansetron, 4 mg of decadron and up to 30mg ketorolac may be administered as per clinical judgment of the attending anesthesiologist.
- Patients in both groups will receive neuraxial anesthesia. The attending anesthesiologist is free to add an ultrasound guided peripheral nerve block:
    - Neuraxial anesthesia (CSE, Epidural or spinal) as preferred by the attending anesthesiologist.
    - Decadron may be used as in addition to the local anesthetic if the anesthesia provider wishes to do so.
    - If a peripheral nerve block is performed the appropriate amount of 0.5% of bupivacaine will be administered under ultrasound-guidance as a single shot.
    - In case an epidural catheter was placed patients will receive a PCEA immediately after arrival at the PACU with 0.06% bupivacaine/10µg Hydromorphone at a basal rate of 4ml/h and bolus of 4ml on demand. Lockout time will be 10 minutes and maximum dose will be 20ml/h for postoperativepain management.
- Opioids and other medications with sedative or respiratory depressant side effects that are not specifically mentioned above should be omitted (if possible without harm for the patient)

Patients in the audiovisual distraction group will choose a movie, start watching it in the holding area and continue watching it in the OR as well as the first 30 min in the PACU. Audiovisual equipment will be removed for transfers or at patient request.

Alertness level will be determined by the research fellow preoperatively, intraoperatively (15 min after start of surgery), directly after PACU admission and 30 minutes after PACU admission using the Modified Observer's Assessment of Alertness/Sedation Scale (MOAA/S).

In the OR the research fellow will record if and why the patient receives additional sedation.

Further, desaturations ($SpO2 < 90\%$ for 10 sec or longer) or airway interventions defined as any of the following: jaw-thrust, oropharyngeal airway, nasopharyngeal airway, mask-ventilation, larynx mask or intubation; will be recorded both in the OR and in the first 30 min after PACU admission.

30 minutes after PACU admission we will ask the patients to fill out the Heidelberg perianesthetic questionnaire.

If the patients were in the audiovisual distraction group, providers will receive a survey about the audiovisual equipment at the end of the surgery day.

Data will be collected:
Patients in the study and the control group will be selected according to the same inclusion and exclusion criteria. Patients will be randomly assigned to one of two groups, each composed of 30 patients:
1. **Standard of care sedation** with 0.05 mg/kg bodyweight with a maximum dose of 5 mg midazolam in preparation for the administration of the neuraxial anesthesia; propofol infusion starting with 40µg/kg/min and then titrated to effect.
2. **Audiovisual distraction** during surgery and in the PACU using video goggles and headphones; patients can choose a movie from a preexisting library; 0.05 mg/kg bodyweight with an initial maximum dose of 5 mg midazolam in preparation for the administration of the neuraxial anesthesia, additional sedation with midazolam in 1 mg increments if requested by the patient or deemed necessary by the anesthesia provider.

Identical data will be collected for all 60 patients.

Day of Surgery

- Preoperatively
  a. Patient demographics – date of birth, race, ethnicity, gender
  b. Alertness level (MOAA/S)

- Intraoperatively

a. Airway interventions
b. Number of desaturations
c. Number of requests for additional sedation
d. Alertness level (MOAA/S)

- Postoperatively/ PACU
  a. Airway interventions
  b. Number of desaturations
  c. Alertness level (MOAA/S)
  d. Patient Satisfaction (Heidelberg perianesthetic questionnaire)
  e. Provider feedback

When will the data be collected:
Data will be collected on the ay of surgery in the holding area, during the procedure, and in the PACU for 30 minutes.
The following source will be used:

- Medical Records
- Patient
- No Private Office Charts Please specify which private office:
- No Registries

Sample Size and Data Analysis

A computer generated randomization table will be generated by a statistician. Randomization will be done before the start of the study. A concealed allocation randomization schema will be used with randomization to occur after the patients consents to be in the research study. This is an unblinded study; group assignment is not concealed from the patients and the treating physician. The randomization will be generated by a statistician and carried ut by a research assistant otherwise not involved in this study.

Patients in the study and the control group will be selected according to the same inclusion and exclusion criteria. Patients will be randomly assigned to one of two groups, each composed of 30 patients:
1. **Standard of care sedation** with 0.05 mg/kg bodyweight with a maximum dose of 5 mg midazolam in preparation for the administration of the neuraxial anesthesia; propofol infusion starting with 40µg/kg/min and then titrated to effect.
2. **Audiovisual distraction** during surgery and in the PACU using video goggles and headphones; patients can choose a movie from a preexisting library; 0.05 mg/kg bodyweight with an initial maximum dose of 5 mg midazolam in preparation for the administration of the neuraxial anesthesia, additional sedation with midazolam in 1 mg increments if requested by the patient or deemed necessary by the anesthesia provider.

Survey administrations and the use of the audiovisual device are not standard of care. The Department of Anesthesiology Research and Education Fund will cover the associated costs.

Instruments and questionnaires to be used on this study:

- Heidelberg perianesthetic questionnaire

Describe any risks to participants in the Placebo of No-Treatment Arm of the study:
There are no known risks at this time to participants in the no-treatment arm of the study.

Provide a scientific or ethical justification for using a Placebo or No-Treatment Arm:
This is considered a desirable characteristic of randomized controlled trials. Since the protocols for both groups are otherwise identical, any differences between the groups may be attributed to whether or not patients are using the audio visual aid.

Sample size and Data Analysis

Is this is a case series based only on the patients available using descriptive statistics in lieu of a sample size calculation?
No

Data Analysis

The primary outcome (number of desaturation events per hour) will be compared between the standard-of-care and audiovisual distraction groups using a two-sample t-test or Wilcoxon rank-sum test, depending upon the distribution of the data. The corresponding effect size will be presented as difference in means or Wilcoxon-Mann-Whitney odds with a 95% confidence interval.

Continuous and ordinal secondary outcomes measured a single time per patient will be compared between groups using two-sample t-tests or Wilcoxon rank-sum tests, respectively. Categorical secondary outcomes measured a single time per patient will be compared between groups using $\chi 2$ tests, Fisher's exact tests, or Cochran-Armitage trend tests, as appropriate. Secondary outcomes measured longitudinally will be analyzed using the generalized estimating equations method. Effect sizes will be presented as difference in means, Wilcoxon-Mann-Whitney odds, or risk difference and relative risk with 95% confidence intervals. Analyses of secondary outcomes will be considered exploratory.

Balance on demographics and baseline characteristics will be assessed by calculating standardized differences (difference in means or proportions divided by the pooled standard deviation) between groups. An absolute value of 0.2 or greater will be interpreted as more imbalance than would be expected by chance (Austin 2009).

Data will be analyzed according to the intention-to-treat principle

References:
1) Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment group in propensity-score matched samples. Stat Med 2009; 28: 3083-107

Describe how, when and where the consent process will be initiated

Patients will be approached about the study in the holding area on the day of surgery. Written consent for all patients will be obtained by research staff or coinvestigators in the holding area on the day of surgery. Before consent patients will be thoroughly informed about possible risks or benefits and about their possibilities to end the study at any time point or to ask for additional sedation if they feel uncomfortable or anxious.