Effects of Obstructive Sleep Apnea Treatment On Opioid-Induced Respiratory Depression

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Primary ObjectiveTo determine the influence of treatment for OSA opioid-induced respiratory depression (minute ventilation (Vi); tidal volume (Vt); respiratory rate (RR); end-tidal pCO2; SpO2).Secondary ObjectivesAim 2: To determine the influence of...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON41933

Source
ToetsingOnline

Brief title
OSAS study

Condition

- Other condition
- Upper respiratory tract disorders (excl infections)

Synonym
Obstructive Sleep Apnea

Health condition

pijnsysteem

Research involving
Human

Sponsors and support

Primary sponsor: Sint Antonius Ziekenhuis
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: OSAS, remifentanil, respiratory depression, sleep apnea

Outcome measures

Primary outcome

Minute ventilation (Vi) (L/min; % change)

Tidal Volume (Vt) (ml; % change)

End-tidal pCO2 (kPa; % change)

Respiratory Rate (RR) (% change)

SpO2 (%; % change)

Secondary outcome

Electrical Pain Detection Threshold (mA)

Conditioned Pain Modulation (% EPDT)

Study description

Background summary

Between 5 and 50 million patients with obstructive sleep apnea (OSA) will undergo major surgery every year worldwide. OSA is independently associated with an increased risk of airway, respiratory and renal adverse outcomes in the early postoperative period1. Additionally, OSA has been implicated in severe unanticipated adverse respiratory events and sudden unanticipated death during postoperative opioid analgesic therapy4. Preoperative diagnosis and treatment for OSA with continuous positive airway pressure (CPAP) therapy or weight-loss surgery remains unusual. More than 80% of men and 90% of women who have OSA are undiagnosed and CPAP therapy adherence is a significant challenge. Preoperative risk-modification with CPAP therapy or bariatric surgery is poorly studied, providing a unique opportunity to rigorously evaluate it as a potentially

modifiable intervention to substantially reduce the risk of adverse outcome. Study investigators have previously shown that opioids are associated with reduction in genioglossus tone and increased airway instability. In recent years, our co-research group in Ann Arbor has shown that increased sensitivity to opioids and not increased opioid dose may be implicated in the occurrence of sudden unanticipated death4. Despite these concerns, little is known of the respiratory sensitivity to opioids in patients with OSA. Additionally, Sleep deprivation and fragmentation are associated with increased risk of acute or chronic pain states2. Patients with untreated OSA have increased pain sensitivity2. Thus untreated OSA may contribute to increased postoperative opioid analgesic requirements, which in turn, may increase perioperative respiratory morbidity in a dose-dependent fashion. Additionally, it appears that CPAP therapy may reduce this altered pain sensitivity. However, the duration of and predictability of treatment effect in different populations has not specifically been tested. Further, it is unknown if OSA treatment by weight loss is associated with similar alterations in pain sensitivity or respiratory sensitivity to opioids. Our contribution from the studies proposed in this application will be to identify the relationship between altered pain sensitivity and respiratory sensitivity to opioids in patients with OSA and determine the effect of treatment of OSA on these outcomes. This contribution is significant, because it has the potential to fundamentally change current preoperative management decisions in OSA and significantly alter postoperative outcomes in these high-risk patients.

Study objective

Primary Objective
To determine the influence of treatment for OSA opioid-induced respiratory depression (minute ventilation (Vi); tidal volume (Vt); respiratory rate (RR); end-tidal pCO2; SpO2).

Secondary Objectives
Aim 2: To determine the influence of treatment of OSA on experimental pain thresholds and endogenous pain modulation.

Study design

This is a prospective longitudinal study on the effect of obstructive sleep apnea treatment with CPAP therapy alone and CPAP therapy combined with bariatric surgery on hypoxic ventilatory response and pain sensitivity. Patients aged 18 yr or older, who are ASA I-IV, and are selected to undergo bariatric surgery are asked to complete the STOP-BANG questionnaire and the Brief Pain Inventory (BPI). The STOP-Bang questionnaire is a scoring model consisting of eight easily administered questions starting with the acronym STOP-Bang and is scored based on Yes/ No answers (score: 1/0). Thus, the scores range from a value of 0 to 8. A score of >=5 has shown a high sensitivity and

specificity (88%) for OSA6. The BPI is used to assess the severity of pain and the impact of pain on daily functions. There is no scoring algorithm, but we will use "worst pain" as measure of pain severity. The worst pain is scored with numbers from 0 to 10, with 0 meaning *no pain* and 10 *worst pain. We will exclude patient with a score for worst pain of 5 and higher. Thereafter, a PSG will be performed in all patients, which is *standard care*. Patients with a STOP-Bang score of >=5, BPI *worst pain* < 5 and PSG with AHI<5 of >=15 are approached for consent for the study. According to the results of the PSG we will place the patients into two groups (AHI<5 and >=15). The patients with an apnea-hypopnea index (AHI) >= 15 are diagnosed with moderate or severe OSA. These patients are placed in group 2 . All these patient will have CPAP therapy. The Respiratory and Pain studies will be done before the start of CPAP treatment, 8 weeks after initiating the CPAP treatment and 9 months after the bariatric surgery. The CPAP treatment will not be stopped. With the studies after bariatric surgery we will look for an additional effect of the bariatric surgery and weight loss achieved with the surgery at top of the effect of the CPAP therapy. Also a PSG will be done 8 weeks after CPAP treatment and 9 months after bariatric surgery. 9 months after bariatric surgery there will be significant weight loss to expect an effect on OSA. The PSG 9 months after bariatric surgery will be done without CPAP. The patients who do not have OSA (confirmed with the PSG to have an AHI < 5 events per hour) will be the control group. In this group the Respiratory and Pain studies will be done before the bariatric surgery and 9 months after surgery. The patients who have OSA but not moderate or severe i.e. AHI >= 5 and < 15 will not participate in our study in order to achieve maximum contrast. The treatment of their OSA will follow the national guidelines. We will include 20 patients in both groups. It is know that in CPAP treatment the adherence can be an issue. Therefore we will include patients in the CPAP group until we have 20 patients who succesfully managed the 8 weeks of CPAP treatment. For excluding obesity hypoventilation syndrome, before the respiratory studies an arterial blood gas sample will be drawn (standard care). Anesthesia during the bariatric surgery will not be altered or standardised. The patients will receive routine analgesic therapy postoperatively.

Intervention

Intervention: patients accepted for bariatric surgery meeting all inclusion criteria and none of the exclusion criteria will be enrolled in the study, after informed consent is obtained. First, the patients will perform a STOP-BANG questionnaire (figure 1: study flow chart). Patients with a STOP-BANG score > 5 will be subjected to a PG (polygraphy). Both the questionnaire and PG is *standard care*. 20 patients without OSA (STOP-BANG>5; normal PG; AHI<5) will be enrolled in group 1 (control group). 20 patients with OSA (STOP BANG >5; PG proven moderate-severe OSA; AHI>15) will be enrolled in group 2. All study patients will be subjected to a pain threshold study and respiratory study (paragraph 3.2). Thereafter, bariatric surgery will be performed in group 1 patients. Group 2 will receive 8 weeks of preoperative CPAP therapy followed

by a 2nd respiratory and pain threshold study. 9 months after bariatric surgery, all study patients will undergo another respiratory and pain threshold study. Polygraphy before- and 8 weeks after initiation of CPAP is standard care. However, polygraphy 9 months after surgery is considered additional intervention.

Study burden and risks

Study subjects will undertake a 30-minute respiratory study 2 or 3 times at visits at the pulmonary outpatient clinic. Participation in this study has minimal risks for the patient. The effects of a small bolus of remifentanil is highly predictable and is thought to be mild. Remifentanil will be administered in a setting fully equipped for the monitoring and support of respiratory and cardiovascular function, and by persons specifically trained in the use of anaesthetic drugs and the recognition and management of the expected adverse effects of potent oplolds, includlng resplratory and cardiac resuscitation. Furthermore, quantitative sensory testing will be performed, including evaluation of endogenous analgesia pathways (conditioned pain modulation) using a cold pressor test (CPT). Risks during participation in this study are negligible. ECG electrodes attached to the skin during the use of the Nocitrack® device might give some local skin redness or irritability, however based on former clinical use this is expected to be minimal. Before the respiratory study starts, an arterial blood sample will be drawn to exclude for the obesity hypoventilation syndrome. Benefit exists in expanding our knowledge about the of OSA treatment on opiod induced respiratory depression and offers potential to fundamentally change current preoperative management decisions in OSA and significantly alter postoperative outcomes in these high-risk patients.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• age older than 18 years
• patients selected for bariatric surgery
• confirmed non-OSA (AHI<5) by PG for group Control
• confirmed OSA (AHI>=15) by PG for group CPAP and Surgery

Exclusion criteria

• age younger than 18 years
• CPAP treatment before the start of the study
• patients with a *worst pain* >5 on the BPI
• patients with PSG result indicating mild OSA (AHI >= 5 and < 15)

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-03-2016
Enrollment:	40
Type:	Actual

Medical products/devices used

Generic name:	Nocitrack
Registration:	No

Ethics review

Approved WMO Date:	21-08-2015
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	26-05-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL51445.100.15