RESEARCH ARTICLE

REVISED Portable respiratory polygraphy monitoring of obese mothers the first night after caesarean section with bupivacaine/morphine/fentanyl spinal anaesthesia [version 2; peer review: 2 approved]

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Abstract

Background: Obesity, abdominal surgery, and intrathecal opioids are all factors associated with a risk for respiratory compromise. The aim of this explorative trial was to study the apnoea/hypopnea index 1st postoperative night in obese mothers having had caesarean section (CS) in spinal anaesthesia with a combination of bupivacaine/morphine and fentanyl.

Methods: Consecutive obese (BMI >30 kg/m²) mothers, ≥18 years, scheduled for CS with bupivacaine/morphine/fentanyl spinal anaesthesia were monitored with a portable polygraphy device Embletta /NOX on 1st postoperative night. The apnoea/hypopnea index (AHI) was identified by clinical algorithm and assessed in accordance to general guidelines; number of apnoea/hypopnea episodes per hour: <5 "normal", ≥5 and <15 *mild sleep apnoea*, ≥15 and <30 *moderate sleep apnoea*, ≥30 *severe sleep apnoea*. Oxygen desaturation events were in similar manner calculated per hour as oxygen desaturation index (ODI).

Results: Forty mothers were invited to participate: 27 consented, 23 were included, but polysomnography registration failed in 3. Among the 20 mothers studied: 11 had an AHI <5 (*normal*), 7 mothers had AHI ≥5 but <15 (*mild OSAS*) and 2 mothers had AHI ≥15 (*moderate OSA*), none had an AHI ≥30. The ODI was on average 4.4, and eight patients had an ODI >5. Mothers with a high AHI (15.3 and 18.2) did not show high ODI. Mean saturation was 94% (91-96%), and four mothers had mean SpO₂ 90-94%, none had a mean SpO₂ <90%.

Conclusion: Respiratory polygraphy 1st night after caesarean section in spinal anaesthesia with morphine in moderately obese mothers showed AHIs that in sleep medicine terms are considered normal, mild and moderate. Obstructive events and episodes of desaturation were commonly not synchronised. Further studies looking at

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Any reports and responses or comments on the article can be found at the end of the article.

preoperative screening for sleep apnoea in obese mothers are warranted but early postop respiratory polygraphy recording is cumbersome and provided sparse important information.

Keywords

Caesarean section, obesity, intrathecal morphine, respiration, respiratory depression, apnoea/hypopnea

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REVISED Amendments from Version 1

The manuscript is updated and amended based on valuable comments from referees. We have further tried to describe primary objective of the explorative observational study and the technique used. The respiratory polygraphy technique and how it is commonly assessed in "sleep medicine" is mentioned. We have amended the text in accordance to referees' comments, and added further data requested, ranges and rescue analgesia. The Discussion section is amended and we have tried to make it more focused on the explicit focuses of the study. We have addressed the findings and tried to put the observations in context as far as possible. Limitations are much further discussed, and further studies suggested.

See referee reports

Introduction

In caesarean section (CS), intrathecal morphine (ITM) is associated with better postoperative course with less pain and shorter time to mobilisation¹. Respiratory depression associated with morphine is well known side effect. The μ -receptor has been suggested to be the key target for the respiratory depressant effect of morphine and further the sophisticated neuronal interaction in the ventral part of the brain stem². Respiratory depression is the most feared adverse effect from intrathecal opioids, and although rare (0–0.9%), it is the reason for some anaesthesia units to withhold the addition of morphine to spinal anaesthesia for CS^{3–5}. It has been suggested that ITM in doses <0.3 mg (300 μ g) is associated with a lower risk of respiratory depression compared with doses >0.3 mg, and a tendency to a lower risk as compared to systemic opioids^{3,6}. No analgesic benefit and increased incidence and severity of side effects for doses exceeding 100 μ g intrathecal morphine for CS spinal anaesthesia have been described¹.

Respiratory depression is not well defined and there is still not a general definition of respiratory depression to opioids⁷. A recent meta-analysis around risks for respiratory depression commented that multiple definitions were used in the included studies⁸. Similarly, a review concerning the "definitions of respiratory depression", explicitly addressing ITM, found no common description⁹. They also clearly commented the need for further research for defining what is a clinically significant respiratory impairment caused by ITM and how it best can be monitored⁹. It has been proposed to define respiratory depression associated to opioids solely as a respiratory rate (RR) of <10 breaths per minute¹⁰.

There are several factors that can contribute to postoperative respiratory depression. Residual effects from anaesthesia, abdominal surgery, obesity, immobilisation and opioid analgesics may all contribute to its occurrence^{7,11}. Postoperative respiratory depression after CS, performed in spinal anaesthesia including neuroaxial morphine, is found in low frequency (0/5036, 8/856, 6/1915)^{4,12,13}. Studies explicitly assessing the risk of respiratory compromise in obese patients, i.e. mothers with a high BMI (Body Mass Index) are sparse. No respiratory event, with need for naloxone, defined as RR $\leq$ 8 breaths/min, oxygen saturation

<90% or Richmond Agitation Sedation Scale <-2, was found in a retrospective study of 5036 mothers who had a CS with neuroaxial morphine, where 63% of patients were obese (BMI > 30 kg/m²), and the most commonly used morphine dose was 3 mg epidural and 0.15 mg spinal⁴. A study in women having intrathecal addition of 0.2 mg morphine in spinal analgesia for CS found 8/856 cases of respiratory depression, all eight cases were obese and naloxone treatment did not reverse the respiratory depression during sleep¹². A review published in 2008 addressing the risk, monitoring and prevention of respiratory depression associated with neuroaxial morphine in the obstetric setting supports the need for observation up to 24 hours following neuraxial morphine, due to the duration of the depressed CO₂ sensitivity³. This paper also commented on the present lack of efficient, simple and mother-friendly monitoring equipment; but support the monitoring of RR, and sedation monitoring in healthy mothers with addition of oxygen saturation in obese³.

Portable sleep test equipment so called at-home polygraphy monitors are commonly used for screening for obstructive sleep apnoea. This equipment assesses respiration; oro-nasal actual gas flow, thoracic and abdominal movements and saturation. The registration is analysed and processed in indices: apnoea-hypopnea index (AHI) and oxygen desaturation index (ODI) using defined algorithms.

The aim of this explorative trial was to study the apnoea/hypopnea index the 1st postoperative night in obese mothers having had caesarean section in spinal anaesthesia with a combination of bupivacaine/morphine and fentanyl. Our hypothesis was that the combination of risks, obesity, intrathecal opioids, and 1st postoperative night should show a high incidence of AHIs of more than 30.

Methods

Ethical statement

The study was approved by the Regional Ethical Review Board in Stockholm (2015/1257-31/2).

Patients

A prospective postoperative observational study was conducted from December 2015 to October 2017. Parturients with BMI >30 kg/m² at the first antenatal consultation, who were planned for elective CS with low transverse incision under spinal anaesthesia, were included in the study after informed verbal and written consent.

Patients with language difficulties and known diagnosed obstructive sleep apnoea (OSA) receiving treatment, as those with continuous positive airway pressure or mouth guard, or any known contraindication to ITM were excluded.

Patients were informed at the preanaesthetic consultation about spinal analgesia and that they would receive a mixture of local anaesthesia, bupivacaine, and two opioids, fentanyl and morphine, in order to optimize perioperative and postoperative anaesthesia, according to the standard routine at our department (Anaesthesia & Intensive Care Unit, Danderyd Hospital).

Spinal anaesthesia procedure

Spinal anaesthesia was performed with the patient in sitting or left lateral position, at the anaesthetists' preference, using a 25-gauge pencil-point needle. All patients received a mixture of heavy bupivacaine (11–12 mg), fentanyl (10 µg) and morphine (100 µg), per standard routines for CS in our department.

The mothers received preoperative 1.5 g paracetamol orally, and paracetamol was continued postoperatively 1 g every six hours or 1.330g every eight hours. Ibuprofen (400 mg) was administered every eight hours. A further rescue therapy for the handling of pain, nausea and vomiting or pruritus was administered per the department's routines.

Routine monitoring in the postoperative and obstetric ward after spinal anaesthesia includes the following: checking for sedation, and if sedated counting RR every hour; pain by NRS/VAS; heart rate and blood pressure; control of bleeding; urine output; mobilization; and breast feeding. First mobilization, to stand by the bed, is usually encouraged at about 5–6 hours postoperatively. Urine catheter is normally removed after the first postoperative night.

Data collection

Patients were informed at the preanaesthetic consultation about extended postoperative monitoring in addition to routine monitoring: nasal catheter to measure expiration flow; finger probe to measure oxygen saturation; thoracic and abdominal strings to collect breathing movements for polygraphy registration; a portable OSA breathing pattern monitor, Embletta (ResMed Sweden AB, Kista, Sweden)/Nox Sleep monitor (Nox Medical, Iceland); and a combined ear-probe for transcutaneous carbon dioxide (TcCO₂)/oxygen saturation (SpO₂) monitor (Tosca Radiometer Medical ApS, Denmark).

The respiratory polygraphy data was stored in the equipment and further analysed with a standard analysis program (ResMed Sweden AB, Kista, Sweden). The equipment software is screening for both the AHI and ODI^{14,15}. The program also provides each desaturation episode minimum blood oxygen saturation SpO₂ level measured, the *oxygen desaturation episode nadir*.

Apnoea was classified in accordance to the American Academy of Sleep Medicine (AASM) as a drop in the polygraphy peak signal excursion by $\geq 90\%$ of pre-event baseline air-flow signal¹⁶. The breathing disturbance was classified as mild AHI ≥ 5 and <15 , moderate ≥ 15 – <30 and severe ≥ 30 . The duration of the $\geq 90\%$ drop in sensor signal must be ≥ 10 seconds¹⁶. **Hypopnea** was classified by as a drop in the peak signal excursion by $\geq 30\%$ of pre-event baseline¹⁶. The duration of the $\geq 30\%$ drop in signal excursions must be ≥ 10 seconds¹⁶.

Respiratory monitoring, respiratory polygraphy and Tosca registration was in the late afternoon - evening of the first postoperative and continued during night. For the 3–5 first hours postpartum, the patients were observed awake in accordance to routines in the postoperative department.

All patients answered a standardised ESS (Epworth Sleepiness Scale) questionnaire at time of enrolment. With grading¹;

0–5 Lower Normal Daytime Sleepiness, 6–10 Higher Normal Daytime Sleepiness, 11–12 Mild Excessive Daytime Sleepiness, 13–15 Moderate Excessive Daytime Sleepiness, 16–24 Severe Excessive Daytime Sleepiness.

Statistical analysis

Data is presented as the mean and standard deviation; categorical data are presented as frequencies. The study is explorative and observational; thus, no power analysis has been conducted. Differences were tested with Student's t-test for continuous variables and Chi-squared test for categorical data. $P < 0.05$ was considered significant. Data was analysed with StatView (v1.04) for MAC.

Results

Forty mothers were invited to participate: 27 mothers consented but four of them had an early emergency CS delivery due to contractions, thus 23 mothers were included, but polygraphy registration failed in 3 (see Figure 1). Therefore, 20 mothers were included in analysis.

In all 20 mothers, mean age 35 ± 5 (24–43) years, mean BMI 35 ± 4 (30–42), and mean ESS 6 ± 3 (0–12) were studied.

Five mothers had an ESS of <5 , 12 had an ESS score between 5 and 10, and 3 scored >10 on the preoperative ESS screening.

All surgery and anaesthesia was uncomplicated.

Mean bed time during the polygraphic registration was 585 minutes (378–818).

Mean AHI was 6.6 ± 5.2 (0–18.2) and mean ODI was 4.4 ± 3 (0–10.3). A total of 11 mothers had “normal” (<5) AHI, 7 had an AHI between 5 and 15, and 2 had an AHI 15–30 (15.3 and 18.2). No mothers had an AHI ≥ 30 . The longest apnoea duration was (mean) 30 ± 27 seconds, and mean longest hypopnea duration 55 ± 25 seconds.

Mean saturation was 94% (91–96%) and four mothers had mean saturation between 90 and 94%, but no had a mean SpO₂ $< 90\%$. Nadir, lowest saturation registered, was in mean 71% (49–81%).

In total, 11 mothers had an ODI <5 , 8 had ODI between 5 to 10, and 1 mother had an ODI of 10.3. The 2 high AHI (15.3 and 18.2) mothers did not show high ODI or signs of hypercapnia on the transcutaneous CO₂ registration.

Mean TcCO₂ was 4.7 ± 0.3 (4.1–5.2) kPa, and mean of max TcCO₂ was 5 ± 0.5 kPa. There were no TcCO₂ >5.9 kPa.

The pattern between AHI, ODI, BMI and ESS was overall scattered without correlation; Figure 2 describes the AHI and ODI pattern.

¹<http://epworthsleepinessscale.com/about-the-ess/>

Figure 1. Patient inclusion, polygraphy first night after CS in spinal anaesthesia with ITM in obese mothers.

Figure 2. The apnoea-hypopnea index (AHI) and oxygen desaturation index (ODI) measures plotted for each mother.

None of the mothers showed clinical signs or symptoms of severe respiratory depression as assessed by routine clinical monitoring. Six mothers required rescue buprenorphine oral 0.2 – 0.4 mg and one mother had 5 mg intravenous morphine for postoperative pain.

Dataset 1. Raw data for the study polygraphy on the first night after caesarean section in spinal anaesthesia with morphine in obese mothers by Hein *et al.* The three patients who were excluded from analysis are highlighted

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Discussion

We did not find any AHI defined as severe sleep apnoea in this at risk cohort; obese mothers 1st night after caesarean section in spinal anaesthesia including morphine and fentanyl. Two out of 20 mothers included in the present study had an AHI in the lower range of moderate sleep apnoea (15.3 and 18.2). Preoperative screening and testing for sleep apnea in accordance to guidelines is of course of value also mild/moderate sleep apnea may cause adverse effects¹⁷ but early postoperative respiratory polygraphy was found cumbersome and seems not to provide much critical information. Mothers with a high AHI did not show typical high oxygen desaturation index or TcCO₂ elevation. We cannot give any firm explanation to the discrepancy between the AHI and the ODI. Indeed, we did see frequent short episodes of oxygen saturation decrease, but we are unfortunately not able to assess whether these events were related to bradypnea or shallow breathing. We did not register any increase in TcCO₂. The TcCO₂ monitoring had a 5-minute averaging algorithm, thus it was not set for the detection of brief episodes of CO₂ elevation. Respiratory depression typically progresses slowly³.

Studies with polygraphy registration sleep apnoea signs, associated with ITM are sparsely performed. The effects of 30 mg oral morphine on patients with mild to moderate obstructive sleep apnoea has been investigated previously¹⁸. This study showed that morphine may paradoxically improve sleep apnoea¹⁸. Similarly, a study of the effects of remifentanyl infusion, and found a decrease in obstructive events, but a worsening in oxygenation during the infusion¹⁹. Cole *et al.* studied the respiratory effects of ITM (dose, 300 µg) in prospective randomized fashion among patients having knee replacement in spinal anaesthesia²⁰. They found similarly to the present study that night time respiratory polygraphy is cumbersome and associated with high patient non-compliance²⁰. Among the patients studied in that study, the incidence of apnoea and hypopnea episodes was not significantly different compared to the control group of patients that did not receive ITM²⁰. Median mean oxygen saturation was, however, significantly lower among the ITM patients and the occurrence of “mild and moderate hypoxia” was also high in the ITM group. In another previous study, 45 obese patients undergoing elective bariatric surgery with general anaesthesia were monitored in a similar fashion with portable polygraphy equipment during the first postoperative night on the general ward; only two patients with an AHI >5 and only three with an ODI >5 was found²¹.

Therefore, our findings, that registration during the first postoperative night following CS with spinal anaesthesia with a modest dose of morphine in obese mothers did not show any high incidence of AHI and ODI, might not be that surprising. It is also in line with a Cochrane review assessing the effects of opioid, hypnotic and sedating medications on sleep-disordered breathing in adults with obstructive sleep apnoea²². None of the studied drugs in the Cochrane review produced a significant increase in AHI or ODI and two trials have shown a beneficial effect on OSA²².

However, a recent paper, catastrophic events in patients related to obesity and sleep apnoea, stating that ‘Morbid obesity, male sex, undiagnosed OSA, partially treated/untreated OSA, opioids, sedatives, and lack of monitoring are risk factors for death or near-death events’²³. Preoperative assessment for sleep apnea should of course be performed eventually including polysomnography in at risk patient^{24,25}. For pregnant obese women, especially in case of hypertension, snoring and/or gestation diabetes, that are associated with increased incidence of OSA, assessment seems warranted already during pregnancy since untreated OSA may affect maternal and foetal outcome^{24,26,27}.

We cannot further comment on how and how long obese patients having ITM should be monitored. It seems still of importance to monitor respiration in patients at risk. Monitoring of AHI and ODI during the early postoperative period seems, however, not to be of major help. It may be that simple RR monitoring, TcCO₂ measure and SpO₂ are more feasible techniques^{28,29}. Kopka *et al.* suggest that TcCO₂ may be more effective in detecting respiratory depression compared to SpO₂ when patients receive supplementary oxygen³⁰. Ladha *et al.* studied oximetry after CS having 150 µg morphine intrathecal³¹. They found frequent mild desaturation events and increased risk in patients with obesity. Bauchat *et al.* studied TcCO₂ tension and found that hypercapnia events (>50 mm Hg for ≥2-minute duration) occurred frequently in women receiving 150 µg ITM for post-caesarean analgesia; higher baseline TcCO₂ readings were observed in women who had hypercapnia events³². Dalchow *et al.* studied both TcCO₂ and SpO₂ and found more frequent changes, hypercapnia as compared to desaturation³³. They concluded, ‘The incidence of opioid-induced respiratory depression detected by TOSCA is higher than previously reported by other monitoring methods. TOSCA may have a role in detecting subclinical respiratory depression in the obstetric population. Further studies including also a control population are warranted³³. Patients at risk should of course be assessed prior to surgery/anaesthesia. Optimal screening method is however not well defined¹¹.

There are several limitations with our study. It is merely an observational “explorative” study, and we could only include 23 mothers and gained registration form 20. We had a high number of mothers that declined to participate after having been informed about the monitoring techniques. The portable polygraphy is intended for use in the home for sleep apnoea screening instead of being in-hospital for a full polysomnography. The equipment involves straps around the thorax and abdomen, nasal prongs and a pulseoximetry probe all connected with cables to

the monitoring unit. We included mothers with a BMI between 30 and 42 (mean 35) and none of our mothers had a known sleep apnoea. Merely three had an ESS of more than 10. Higher BMI and higher number of patients, possibly with more signs and symptoms of sleep apnoea would have been of interest. We are not able to assess sleep time, whether the mothers studied were asleep or merely rested. A full polysomnography would be needed for further in depth analysis. One may however strongly question whether that is ethical in a mothers' first night after caesarean section. The number of mothers studied is low and it is indeed not possible to make any firm statistical assessments based on the sparse data available.

In conclusion, we found in this explorative study that portable polygraphy is cumbersome and many mothers decline its use. It seems also reasonable to conclude that although episodes of oxygen saturation decrease were not infrequently noticed, upper airway collapse, obstructive hypo/apnoea, role as risk factor for respiratory depression during the first night after caesarean section in spinal anaesthesia with addition of low dose intrathecal morphine even in obese mothers was not commonly seen. However, further studies with a combination of RR monitoring,

TcCO₂ monitor and SpO₂ seems warranted, especially in high risk mothers. Studies focused on preoperative screening with night time respiratory polygraphy in obese patients, at risk for sleep breathing disorder, are also warranted.

Data availability

Dataset 1: Raw data for the study polygraphy on the first night after caesarean section in spinal anaesthesia with morphine in obese mothers by Hein *et al.* The three patients who were excluded from analysis are highlighted. doi, [10.5256/f1000research.13206.d185388](https://doi.org/10.5256/f1000research.13206.d185388)³⁴

Competing interests

No competing interests were disclosed.

Grant information

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[Data Source](#)

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Sunil Kumar Chauhan

Rotunda Hospital, Dublin, Ireland

Patrick Thorton

Rotunda Hospital, Dublin, Ireland

Thank you author for addressing our comments and concerns about your study. The article gives appropriate insight of methodology and challenges you had while recruiting pregnant mothers for monitoring in post op period. It was well organised study, but with small sample size.

Competing Interests: No competing interests were disclosed.

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 12 February 2018

<https://doi.org/10.5256/f1000research.15048.r30644>

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Nina Stockfleth Buch

Department of Anesthesiology and Intensive Care, Aarhus University Hospital, Aarhus, Denmark

Lone Nikolajsen

Department of Anesthesiology and Intensive Care, Aarhus University Hospital, Aarhus, Denmark

The article has improved following revision. Did the authors use any statistical analysis to study the possible correlation between ODI and AHI? (Spearman's rho?).

It could still benefit from shortening (discussion) and a revision of the English language.

Competing Interests: No competing interests were disclosed.

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 26 January 2018

<https://doi.org/10.5256/f1000research.14329.r28494>

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Sunil Kumar Chauhan

Rotunda Hospital, Dublin, Ireland

Patrick Thorton

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INTRODUCTION

The aim of this study was to assess monitoring capabilities of portable respiratory polygraph device in detecting respiratory depression due to intrathecal morphine in parturients for lower segment caesarean section. Although the number of factors causing respiratory depression is not just limited to intrathecal morphine, obesity, residual effect of anaesthesia, immobilisation and abdominal surgery itself are contributors for respiratory depression. The device used for the study seems good for diagnosing respiratory depression in community for patients with OSA, but its usefulness in peri-operative setting is still to be proved.

Comments:

- This study done on exploring the optimal monitoring device to diagnose respiratory depression with intrathecal morphine for LSCS in high BMI parturients, does not rule out undiagnosed OSA patients before abdominal surgery esp. when the patients were enrolled during the first antenatal visit and since that time till surgery patient had undergone changes in their BMI and usual respiratory physiological changes.
- The device respirator is not adequately described esp. it's functioning as well it's methodology to diagnose respiratory depression is seriously questionable as it fails to show basic correlation between AHI and ODI.
- The study design is prospective and observational, but would be of more use if it has compared with routine monitoring in subset of patients with intrathecal morphine for LSCS,

to give idea of usefulness of the device.

- Mean bedtime during which monitoring was done was never described as whether patient was asleep or was merely resting, which could seriously alter the results.
- There was no mention of type of breakthrough analgesia (opioid or non opioid) used postoperatively which could alter the results.
- The sample size to comment on correlation between AHI and ODI seems quite small to be conclusive and reproducible.
- The results showed comparison with routine monitoring but data in support of routine monitoring was not provided.
- Again high AHI and non reproducible ODI raises serious concerns about sensitivity of portable respirator.
- As far as studies statistical significance I have limited knowledge for which input from statistician would be highly recommended.
- I agree with the conclusion by authors that device is cumbersome with no reproducible results until proven otherwise by studying with large sample size in patients with preoperative screening in obese parturients (with already decreased respiratory reserve) at risk of OSA and comparing with routine monitoring.

Discussion:

- This study has some minor limitations in view of enrollments during first antenatal visit It would be better if more clarity with data was shown for duration of sleep rather than rest.
- Post operative analgesia for breakthrough pain needs to be explained.
- Any study to quote for the efficacy of device would be of great value before using it in peri-operative setting.
- Any comorbidity like PIH or chest infections before surgery or any major fluid shift with any major blood loss was not ruled out or if it was then not declared in the study design which may easily alter the results.
- Post operative analgesia for breakthrough pain needs to be explained.
- Any study to quote for the efficacy of device would be of great value before using it in peri-operative setting.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Partly

Are sufficient details of methods and analysis provided to allow replication by others?

Partly

If applicable, is the statistical analysis and its interpretation appropriate?

I cannot comment. A qualified statistician is required.

Are all the source data underlying the results available to ensure full reproducibility?

Partly

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.

Author Response (F1000Research Advisory Board Member) 26 Jan 2018

Jan Jakobsson, Danderyds University Hospital, Stockholm, Sweden

Dear Referee, thank you for important and adequate comments and criticism. The study is small and "explorative" - we still feel that it is of importance to present the available findings in structured fashion. We have tried to address all your comments and queries in Version 2 that has just been uploaded in the manuscript management system.

Comments:

This study done on exploring the optimal monitoring device to diagnose respiratory depression with intrathecal morphine for LSCS in high BMI parturients, does not rule out undiagnosed OSA patients before abdominal surgery esp. when the patients were enrolled during the first antenatal visit and since that time till surgery patient had undergone changes in their BMI and usual respiratory physiological changes.

We have in version 2 put strong emphasis on the need for further studies in pregnant women per se and especially in obese mothers. Sleep apnea should be considered and assessed for.

The device respirator is not adequately described esp. it's functioning as well it's methodology to diagnose respiratory depression is seriously questionable as it fails to show basic correlation between AHI and ODI.

We did use a standard ambulatory monitor, the Embletta and the NOx and subsequent the ResMed Sweden AB, Kista, Sweden analysis program with manual screening. The accuracy in the program has been assessed as adequate by the Swedish Agency for Health Technology Assessment and Assessment of Social Services. We did see a discrepancy between ODI and AHI, the exact reason for this is to us unclear. The group may have had

desaturation episodes due to low respiratory rate, atelectasis and thus alveolar hypoventilation, but we cannot exclude a monitoring error.

The study design is prospective and observational, but would be of more use if it has compared with routine monitoring in subset of patients with intrathecal morphine for LSCS, to give idea of usefulness of the device.

Agree, this would be of interest for further studies, but considering the cumbersomeness of the polygraphy I doubt it is worth the effort. I would much prefer preopstudies trying to find patients at risk during pregnancy. We have expanded on this in abstract, introduction and discussion.

Mean bedtime during which monitoring was done was never described as whether patient was asleep or was merely resting, which could seriously alter the results.

Indeed; this is also one of limitations, we do not have any objective measure of real sleep time, merely 1st night registration.

There was no mention of type of breakthrough analgesia (opioid or non opioid) used postoperatively which could alter the results.

The mothers provided rescue analgesics preferentially buprenorphine is added. All mothers had paracetamol regular prescribed.

The sample size to comment on correlation between AHI and ODI seems quite small to be conclusive and reproducible.

We have purposely not made any statistical assessment of AHI and OFI findings. This is a explorative observational study and we fully agree there is not data to make any firm statistical conclusions

The results showed comparison with routine monitoring but data in support of routine monitoring was not provided.

Again high AHI and non reproducible ODI raises serious concerns about sensitivity of portable respirator.

We cannot give any firm explanation to the discrepancy observed. We have further commented on this finding and we feel that there may be patient factors to possibly explain the finding and there are other studies also discussing discrepancy between ODI/AHI. Novel parameters for evaluating severity of sleep disordered breathing and for supporting diagnosis of sleep apnea-hypopnea syndrome. Kulkas A, Tiihonen P, Eskola K, Julkunen P, Mervaala E, Töyräs J. J Med Eng Technol. 2013 Feb;37(2):135-43.

As far as studies statistical significance I have limited knowledge for which input from statistician would be highly recommended.

We have purposely not made any statistical assessment of AHI and OFI findings. This is a explorative observational study and we fully agree there is not data to make any firm statistical conclusions

I agree with the conclusion by authors that device is cumbersome with no reproducible results until proven otherwise by studying with large sample size in patients with

preoperative screening in obese parturients (with already decreased respiratory reserve) at risk of OSA and comparing with routine monitoring.

Discussion:

This study has some minor limitations in view of enrollments during first antenatal visit It would be better if more clarity with data was shown for duration of sleep rather than rest.

Extensively commented in version 2

Post operative analgesia for breakthrough pain needs to be explained.

Added in version 2

Any study to quote for the efficacy of device would be of great value before using it in peri-operative setting.

Added in the Method section

Any comorbidity like PIH or chest infections before surgery or any major fluid shift with any major blood loss was not ruled out or if it was then not declared in the study design which may easily alter the results.

Mothers were considered "healthy" no obvious signs of infection or fluid overload was observed.

Post operative analgesia for breakthrough pain needs to be explained.

Added

Any study to quote for the efficacy of device would be of great value before using it in peri-operative setting.

On behalf of the authors Jan G Jakobsson

Competing Interests: None.

Reviewer Report 19 January 2018

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Nina Stockfleth Buch

Department of Anesthesiology and Intensive Care, Aarhus University Hospital, Aarhus, Denmark

Lone Nikolajsen

Department of Anesthesiology and Intensive Care, Aarhus University Hospital, Aarhus, Denmark

This observational study by Hein and Jacobsen examines the use of a portable respiratory polygraphy device for monitoring of obese mothers for respiratory depression the first night after caesarean section performed with bupivacaine/morphine/fentanyl spinal anaesthesia. The topic is interesting and relevant, as an increasing number of parturients is expected to present with high antenatal BMI in the future. A total of 20 women were monitored the first night after caesarean section. The authors conclude that the use of the polygraphy device is cumbersome and that obstructive events and episodes of desaturation were not commonly synchronized.

Comments:

Abstract: For the reader not familiar with this technique or the apnoe/hypopnea index (AHI), it is very difficult to interpret the results, e.g. AHI values of 5-15? And what does an ODI of 4.4 mean? For these reasons, the abstract is simply difficult to read.

The introduction is a bit too long. The authors should consider omitting e.g. the sentence starting with Dahan in the first paragraph, and the second paragraph on definition of respiratory depression.

Methods and results: Parts of the text could be written more clearly, e.g. page 4 top: Additive medication to treat side effects, such as pain...??? Is pain a side effect?

The description of AHI, ODI etc. is very technical. Again, it is difficult for the reader not familiar with the technique, to interpret the values and relate them to the clinical setting. What is the clinical relevance of mild AHI/ ODI, mean nadir SpO₂, mean and max TcCO₂? The same applies to the ESS score: is a score of e.g. 5 good or bad?

Did the women receive opioids during the study period? (Respiratory depression could be caused by ex. oral opioids).

Discussion: Could be shortened.

Figure 2 is difficult to read.

Could some of the results be presented in a table?

The high number of abbreviations makes the paper more difficult to read.

The cohort described/studied by Subramani *et al.* (reference 20) might not be comparable with the group studied in this paper.

In summary, a nice paper on an interesting and relevant topic but it would benefit from a revision.

Review performed by MD Nina Stockfleth Buch, Department of Anesthesiology, Aarhus University Hospital, Denmark (approved by professor Lone Nikolajsen, Department of Anesthesiology, Aarhus University Hospital, Denmark).

Is the work clearly and accurately presented and does it cite the current literature?

Partly

Is the study design appropriate and is the work technically sound?

Partly

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.

Author Response (F1000Research Advisory Board Member) 22 Jan 2018

Jan Jakobsson, Danderyds University Hospital, Stockholm, Sweden

Comments to reviewers at Department of Anesthesiology, Aarhus University Hospital, Denmark).

Thank you for effective review of our paper and important comments and remarks. We used the American Academy of Sleep Medicine definitions, that the apnea/hypopnea index, the number of apnea/hypopnea events registered per hour are graded into three categories of Obstructive Sleep Apnea (OSA): Mild OSA: AHI of 5-15, Moderate OSA: AHI of 15-30 and Severe OSA: AHI of more than 30. Zero to 4 episodes, and AHI of <5 is commonly assessed as *normal*. According to the 2007 guidelines from the American Academy of Sleep Medicine, any event with a 3 percent drop in blood oxygen levels is counted as an oxygen desaturation, and the index is the number of desaturation episodes per hours. The screening and assessment for sleep apnea is updated in JAMA 2017 and criteria have not changed. The equipment software is screening for both the AHI and ODI. The program also provide each desaturation episode minimum blood oxygen saturation SpO2 level measured, the oxygen desaturation episode *nadir*.

We consider our findings as signs of normal/mild breathing pattern; all but 2 mothers showed an AHI well within normal and mild ranges and 2 had values in the moderate zone (15.3 and 18.2, thus in the lower edge of moderate 15-39). The apnea/hypopnea episodes had duration of 11 to 111 seconds with a lowest SpO2 60 mean 73 % (60 – 81).

None of the mothers showed a transcutaneous reading of above 5 kPa, thus none of our monitored mothers had a transcutaneous CO2 above normal.

The questionnaires used ESS for screening has been the standard tool at our department. We used the recommended grading;

0-5 Lower Normal Daytime Sleepiness
6-10 Higher Normal Daytime Sleepiness
11-12 Mild Excessive Daytime Sleepiness
13-15 Moderate Excessive Daytime Sleepiness
16-24 Severe Excessive Daytime Sleepiness

Also the ESS scores were low 3 mothers scored more than 10 commonly assessed as “threshold value”.

The description of pain and additional medication should be revised, to read easier. We provide our assessment of the “seemingly normal findings” from the polysomnography recordings in the first sentences of the discussion. We strongly believe that our study show that polysomnography is cumbersome and complex to use postoperatively and does not add valuable information. It is indeed intended for assessment of sleep apnea and is not primarily a monitoring device, it include no alarms to alert in case of major deviation it merely records and compile data for post recording assessment. Respiratory rate, SpO2 and CO2 monitoring seems of much more value. **Preoperative assessment** should of course be performed eventually including polysomnography in at risk patient . If positive findings CPAP should be recommended and used in conjunction to surgery/anesthesia.

We will make a version 2 as soon as we have and additional referee report.

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Competing Interests: None

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