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Clinical Investigation

CLINICAL INVESTIGATION

Intrathecal morphine and sleep apnoea severity in patients undergoing hip arthroplasty: a randomised, controlled, triple-blinded trial

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Abstract

Background: Intrathecal morphine prolongs analgesia after surgery, but has been implicated in postoperative respiratory depression or apnoeic episodes. However, this has not been investigated in a prospective trial using respiratory polygraphy. This randomised controlled triple-blinded trial tested the hypothesis that intrathecal morphine increases sleep apnoea severity, measured using respiratory polygraphy.

Methods: Sixty subjects undergoing hip arthroplasty under spinal anaesthesia received either 15 mg isobaric bupivacaine 0.5% with 0.5 ml normal saline 0.9% (control group) or 15 mg isobaric bupivacaine 0.5% with 0.5 ml intrathecal morphine 100 μg (intrathecal morphine group). Respiratory polygraphy was performed before surgery and on the first and third postoperative nights. The primary outcome was the apnoea–hypopnoea index in the supine position (supine AHI) on the first postoperative night. Secondary outcomes included supine AHI on the third postoperative night, oxygen desaturation index (ODI), and ventilatory frequency during the first and third postoperative nights.

Results: On the first postoperative night, mean (95% confidence interval) values for supine AHI were 20.6 (13.9–27.3) and 21.2 (12.4–30.0) events h^{-1} in the control and intrathecal morphine groups, respectively (P=0.90). There were no significant between-group differences for any of the secondary outcomes, except for a significantly higher central and mixed apnoea index preoperatively and significantly lower mean SpO_2 on the third postoperative night in the control group.

Conclusions: Intrathecal morphine did not increase sleep apnoea severity when measured using respiratory polygraphy. Of note, all patients had an increased number of apnoeic episodes on the third postoperative night.

Clinical trial registration: NCT02566226.

Keywords: hip arthroplasty; intrathecal morphine; perioperative medicine; sleep apnoea; spinal anaesthesia

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Editor's key points

- Co-administration of intrathecal morphine and a local anaesthetic prolongs the duration of analgesia after a spinal anaesthetic but may cause postoperative respiratory depression.
- Sixty patients undergoing spinal anaesthesia for hip arthroplasty were randomised to receive bupivacaine 15 mg with or without morphine 100 μg.
- Patients with obstructive sleep apnoea requiring continuous positive airway pressure, and any other major cardiac or respiratory problems were excluded, and preoperative and postoperative respiratory polygraphy was performed.
- The apnoea–hypopnoea index increased significantly on the first and third postoperative nights in both groups, but the differences between the groups were not statistically significant.

Intrathecal morphine is commonly used to prolong analgesia after surgery performed under spinal anaesthesia.[1] However, this practice has been implicated in postoperative respiratory depression or apnoeic episodes because of the rostral migration of the drug within the subarachnoid space towards the cisterns and then the pons.[2,3] The incidence of respiratory depression after administration of intrathecal morphine ranges from 0%[4] to 9%.[5] This variability is explained by the different doses injected, from 0.025 to 0.5 μg, and the heterogeneity of the definitions used for respiratory depression, such as reduced ventilatory frequency, decreased oxygen saturation, or increased sedation, which prevents any robust conclusion being made.[6]

Despite the limited evidence available, the American Society of Anesthesiologists Task Force on Neuraxial Opioids recommended that patients be continuously monitored 'at least once per hour for the first 12 h after administration, followed by monitoring at least once every 2 h for the next 12 h (i.e. from 12 to 24 h)'.[7] However, these recommendations might be perceived as excessively cautious and are responsible for increased health resource consumption.[8]

Respiratory polygraphy is a noninvasive system that records nasal airflow, oxygen saturation, and respiratory efforts, allowing a more thoroughly assessment of respiratory depression. Although full polysomnography inclusive of an EEG remains the gold standard diagnostic test, the American Academy of Sleep Medicine has recommended portable respiratory polygraphy as an alternative for the diagnosis of obstructive sleep apnoea (OSA) since 2017.[9]

No prospective trial has ever investigated the respiratory consequences of intrathecal long-acting opioids using respiratory polygraphy, especially in older patients who are at higher risk of experiencing the negative respiratory consequences of intrathecal morphine.[10] This randomised, controlled, triple-blinded trial was designed to test the hypothesis that intrathecal morphine worsens sleep apnoea severity, and therefore produces respiratory depression, in patients undergoing hip arthroplasty.

Methods

Recruitment and randomisation

This trial was approved by the Ethics Committee of the Lausanne University Hospital (Commission d'Ethique Romande, protocol number CER 265/15) and was registered on clinicaltrials.gov (NCT02566226). All patients aged 18 to 85 yr scheduled to undergo hip arthroplasty between February 2016 and March 2019 at the University Hospital of Lausanne were eligible to participate in this study. Exclusion criteria included continuous positive airway pressure (CPAP) treatment for obstructive sleep apnoea, presence of severe respiratory or cardiovascular disease, malignant hyperthermia, preoperative consumption of benzodiazepine, chronic use of opioids ≥30 mg day^{-1} morphine equivalent, and pregnancy. After providing written informed consent, participating patients were randomly allocated on the day of surgery to either the control group or the intrathecal morphine group using a computer-generated randomisation table in aggregates of 10. Assignments were concealed in a sealed opaque envelope.

Measurement of sleep-disordered breathing

Sleep-related respiratory outcomes were measured using a portable respiratory polygraphy recorder (Embletta®; Embla, Flaca, Iceland). This portable recorder allows a noninvasive recording of nasal airflow through a nasal cannula, oxygen saturation (SpO_2) *via* finger pulse oximetry, respiratory efforts through thoracic and abdominal belts, and body position. All recordings were scored by a specialised sleep technician who was supervised and reviewed by a sleep specialist (both were unaware of treatment group allocation). An apnoea event was defined as breathing cessation lasting for ≥10 s, and a hypopnea as a >30% decrease in the respiratory flow signal associated with a ≥3% decrease in oxygen saturation. The apnoea–hypopnoea index (AHI) was defined as the number of apnoea and hypopnoea events per hour of recording. The oxygen desaturation index (ODI) represented the number of oxygen desaturation (≥3%) episodes per hour of sleep. All measurements were performed on the night before the surgery (baseline) and after surgery on postoperative nights 1 and 3.

Intraoperative and postoperative procedures

After application of routine monitors in the operating theatre, patients received spinal anaesthesia performed with the patient in the lateral position. After sterile skin preparation, a pencil-point needle (25 gauge) was inserted via a 21 gauge introducer needle at level L3–L4 or L4–L5, and 3 ml isobaric bupivacaine (5 mg ml^{-1}) with 0.5 ml morphine (200 μg ml^{-1}) or 3 ml isobaric bupivacaine (5 mg ml^{-1}) with 0.5 ml normal saline was injected. After prosthesis implantation, surgical site infiltration was performed with 50 ml ropivacaine 0.2%. As per our routine institutional practice, at the end of surgery all subjects received paracetamol 1 g intravenously (i.v.) and ketorolac 30 mg i.v., plus ondansetron 4 mg i.v. to provide multimodal analgesia and antiemetic prophylaxis, respectively.[11,12] In phase I recovery, pain (visual analogue scale [VAS] score ≥4 on a scale from 0 to 10, or subject request for analgesia) was treated with morphine 2 mg every 10 min as needed. Once oral intake was resumed, subjects received paracetamol 1000 mg every 6 h, ibuprofen 400 mg every 6 h, and oxycodone 5 mg every 3 h as needed. Antiemetic medications on the ward included ondansetron 4 mg i.v. as needed.

Outcomes

The primary outcome was AHI in the supine position on the first postoperative night. Supine AHI was used rather than the overall AHI because sleep apnoea is generally more severe in this position and because subjects had to sleep in the supine position after the hip replacement. Secondary sleep-related outcomes were supine AHI on the third postoperative night, and global AHI, obstructive apnoea index, central apnoea index, hypopnea index, ODI, ventilatory frequency, percentage of recording time with SpO_2 <90%, and percentage of supine time on the first and third postoperative nights. Secondary pain-related outcomes were i.v. morphine equivalent consumption and pain scores at 2, 24, 48 and 72 h postoperatively (on a VAS from 0 to 10), rates of postoperative nausea and vomiting, and pruritus, at 24, 48, and 72 h after surgery, and satisfaction score (on a VAS from 0 to 10).

The subjects, postanaesthetic care unit recovery nurses, ward nurses, the research team, the sleep technician, the sleep physician, and the statistician were all unaware of treatment allocation.

Statistical analysis

It was calculated that 22 subjects per group (total 44) would be required to have 90% power to detect a between-group difference in supine AHI of 5 events h^{-1}, with a standard deviation of 5 and an alpha error of 0.05. The recruitment target was set at 60 subjects to allow for an estimated drop-out rate of 30% (protocol violation or consent withdrawal).

Categorical data were compared using the Fisher's exact test or Pearson χ^2 test with Yates' correction as appropriate. Continuous independent variables were analysed using general linear models (GLMs), whereas categorical and continuous repeated measurements were analysed using generalised estimating equations (GEEs) according to time, anaesthesia group, and interaction between time and anaesthesia effects. When more than one distribution fitted the model, the best one was chosen based on the lowest quasi-likelihood under independence model criterion for GEE and lowest Akaike information criterion for GLM. Briefly, GEE is an extension of GLM to longitudinal or clustered data, in which observations are no longer independent. The idea underlying the GEE approach is to extend the GLM estimating equations to the multivariate setting by replacing the vector of responses and the vector of means by their corresponding multivariate counterparts and using a matrix of weights. GEE takes into account the dependence of observations by specifying a working correlation matrix.[13] This increases the efficiency of the estimators of the parameters compared with those arising under the assumption that repeated observations from a subject are independent of one another, as long as this assumption is true, and the resulting estimators remain consistent in the absence of missing data.[14] This method uses all the available information, without excluding any individual even if they are missing at some time points. Multiple comparisons (for time or interaction effects) were performed using Bonferroni's *post-hoc* test.

Categorical and continuous data are summarised as rates and means with 95% confidence intervals (95% CI), respectively. Statistical analysis was performed using the IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA). Significance was considered at $P<0.05$ based on a two-tailed probability.

Results

Sixty subjects were recruited, and 47 completed the study for the primary outcome (Fig. 1). Eleven subjects did not perform the preoperative portable polygraphy because of logistic constraints (control group, $n=5$; intrathecal morphine group, $n=6$), whereas 13 and 17 patients ($P=0.16$) in the control and intrathecal morphine groups, respectively, did not perform the last portable polygraphy. Subject characteristics were similar between the two groups (Table 1).

Figure 2 presents the evolution of supine AHI during the study. Preoperative mean (95% CI) supine AHI was 22.8 (12.3–33.4) events h^{-1} in the control group and 16.1 (6.6–25.6) events h^{-1} in the intrathecal morphine group ($P=0.30$). Corresponding values on the first postoperative night were 20.6 (13.9–27.3) and 21.2 (12.4–30.0) events h^{-1} ($P=0.90$), and on the third postoperative night were 28.6 (10.4–46.9) and 45.2 (14.8–75.5) events h^{-1} ($P=0.24$). The GEE model showed no significant interaction ($P=0.84$) or group effect ($P=0.23$), but there was a time effect ($P=0.009$). Independent of treatment group allocation, there was a significant increase in supine AHI on the third postoperative night compared with the preoperative night ($P=0.049$), or the first postoperative night ($P=0.044$); there was no difference in supine AHI between the preoperative night and postoperative night 1 ($P=1.00$). Despite the difference in supine AHI over time, the rate of severe sleep apnoea (AHI >30 h^{-1}) on the third postoperative night was similar to that on the preoperative night (odds ratio [OR]=3.05; 95% CI, 0.87–10.70; P=0.08). Rates of severe sleep apnoea were also similar on the first postoperative night *vs* the preoperative night (OR=1.40; 95% CI, 0.31–6.46; P=0.66).

There were no significant between-group differences in secondary sleep-related outcomes preoperatively or on the first and third postoperative nights, apart from significantly higher central and mixed apnoea index preoperatively and significantly lower mean SpO_2 on the third postoperative night

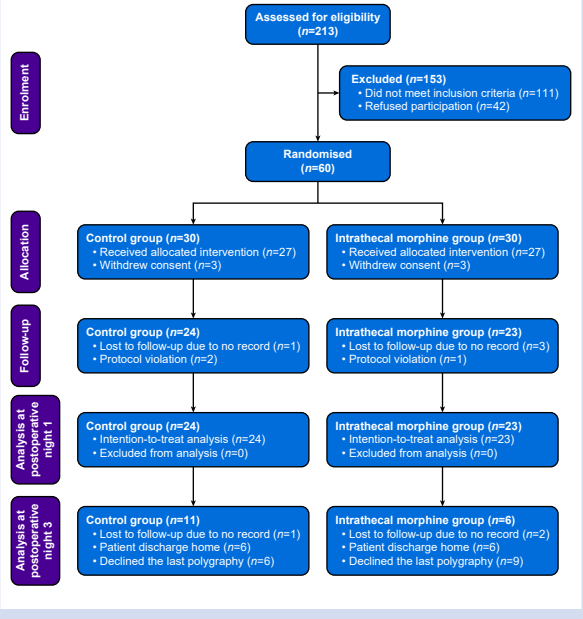

Fig 1. Patient flow through the study.

Table 1 Subject characteristics and clinical characteristics at baseline. Data are presented as means with 95% confidence interval or number of subjects (%). Missing data: hyperlipidaemia, n=2; AHI, n=11. AHI, apnoea–hypopnoea index; ASA, American Society of Anesthesiologists; NoSAS; STOP-BANG.

	Control (n=24)	Intrathecal morphine (n=23)	P-value
Male, n (%)	16 (66.7)	10 (43.5)	0.11
Age, yr	68 (61–75)	71 (67–75)	0.47
Weight, kg	77 (69–85).2)	78 (71–85) 6)	0.81
Height, cm	168 (164–172)	167 (163–171)	0.61
BMI, kg m^{-2}	27.0 (24.7–29)	27.8 (26.1–29)	0.52
ASA physical status, n (%)			0.46
1	2 (8.3)	1 (4.3)	
2	16 (66.7)	19 (82.6)	
3	6 (25.0)	3 (13.0)	
Duration of surgery, min	131 (117–145)	116 (105–127)	0.07
Hip arthroplasty, n (%)			1.00
Primary	22 (91.7)	21 (91.3)	
Secondary	2 (8.3)	2 (8.7)	
Comorbidities, n (%)			
Coronary artery disease	2 (8.3)	1 (4.3)	1.00
Hypertension	11 (45.8)	12 (52.2)	0.77
Renal failure	0 (0)	1 (4.3)	0.49
Diabetes mellitus	3 (12.5)	1 (4.3)	0.61
Hyperlipidaemia	7 (30.4)	2 (9.1)	0.14
Sleep apnoea scores, n (%)			
NoSAS score ≥8	14 (58.3)	16 (69.6)	0.55
STOP-BANG score ≥3	11 (45.8)	14 (60.9)	0.30
Berlin score ≥2	5 (20.8)	8 (34.8)	0.29
Preoperative AHI, n (%)			0.18
<5 events h^{-1}	3 (15.8)	7 (41.2)	
5–14.9 events h^{-1}	8 (42.1)	3 (17.6)	
15–29.9 events h^{-1}	5 (26.3)	6 (35.3)	
≥30 events h^{-1}	3 (15.8)	1 (5.9)	

in the control group (Table 2). The GEE model indicated that there was a time effect only (Table 3).

The only significant differences in pain-related outcomes between groups were a significantly lower pain score at 2 h after surgery and a significantly higher pain score at 2 days postoperatively in the intrathecal morphine group *vs* control (Table 4).

Discussion

The results of this randomised, controlled, triple-blind trial indicate that intrathecal morphine did not increase the supine AHI on the first postoperative night compared with the control group. The increased central apnoea index on postoperative night 1 in the intrathecal morphine group was too small to be clinically relevant, whereas decreases in mean SpO_2 and increases in the time spent with SpO_2 <90% on postoperative night 3 in the intrathecal morphine group are probably attributable to a type I error because of the low number of subjects in this group who underwent the third respiratory polygraphy assessment. Thus, our findings suggest that intrathecal morphine at a dose of 100 μg does not worsen sleep apnoea severity during the first and third postoperative nights and does not produce respiratory depression.

A meta-analysis of 28 studies has reported that the incidence of postoperative respiratory depression with intrathecal morphine doses below 300 μg was about 1.0%, whereas this may be as high as 9% with doses of 300 μg or more.[5] In patients undergoing Caesarean delivery, the rate of respiratory depression has been reported to vary between 0%[4] and 0.9%,[15] with intrathecal morphine doses of ≤200 μg. This variability could be attributed to the different definitions used for respiratory depression; indeed, in the absence of consensus, authors define respiratory depression as reduced ventilatory frequency, decreased oxygen saturation, hypercapnia, naloxone administration, increased sedation, and ventilatory response to progressive hypercapnia.[6] In the context of the high heterogeneity of definitions used,[6] we believe that our primary outcome provides more robust evidence because it is based on the different respiratory parameters provided by respiratory polygraphy.

In this trial, a 100 μg dose of intrathecal morphine was chosen as it has been shown to be a ceiling dose, and to offer a reasonable compromise between analgesic efficacy and minimal side-effects in a similar population undergoing hip and knee replacement.[16,17] However, physicians in different work environments might chose higher doses. If doses above 100 μg are injected intrathecally, caution is warranted because of the possibility of worsening sleep-related outcomes. In the absence of data, a dose–safety trial with a focus on AHI would be very important to address that issue. However, when intrathecal morphine doses of ≤100 μg are administered, our data suggest that patients can reasonably be transferred to the ward without continuous monitoring.

Nevertheless, if decision is made to monitor the patient, we can reasonably argue that it should be continued up to at least the third postoperative night, whether or not intrathecal

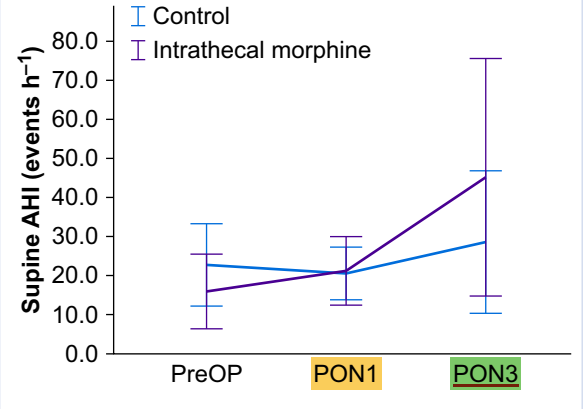

Fig 2. Evolution of the apnoea–hypopnea index (AHI) in supine position. Data are presented as mean with 95% confidence interval. PreOP, preoperatively; PON1, postoperative night 1; PON3, postoperative night 3.

Table 2 Sleep-related outcomes. Data are presented as mean (95% confidence interval). SpO_2, oxygen saturation.

	Control	Intrathecal morphine	P-value
Preoperative baseline, *n*	19	17	
Apnoea–hypopnea index, events h^{-1}	15.0 (9.3, 20.7)	12.1 (6.2, 18.1)	0.51
Obstructive apnoea index, events h^{-1}	2.6 (0.8, 4.4)	1.3 (0.3, 2.4)	0.10
Central apnoea index, events h^{-1}	2.1 (−0.2, 4.4)	0.8 (−0.2, 1.7)	0.02
Mixed apnoea index, events h^{-1}	1.9 (−0.6, 4.3)	0.1 (0, 0.2)	<0.0001
Hypopnea index, events h^{-1}	8.4 (5.8, 11.0)	9.9 (4.5, 15.3)	0.52
Oxygen desaturation index, events h^{-1}	18.2 (11.6, 24.7)	15.0 (7.8, 22.1)	0.46
Mean SpO_2, %	92.4 (91.4, 93.3)	91.9 (90.8, 93.0)	0.46
Proportion of time with SpO_2 <90%, %	12.5 (1.9, 23.2)	19.5 (6.1, 32.8)	0.25
Ventilatory frequency, bpm	13.3 (11.9, 14.8)	14.0 (11.7, 16.3)	0.61
Proportion of time spent in the supine position, %	28.1 (15.0, 41.1)	36.8 (23.5, 50.1)	0.34
Postoperative night 1, *n*	24	23	
Apnoea–hypopnea index, events h^{-1}	19.5 (13.3, 25.7)	20.8 (12.0, 29.5)	0.82
Obstructive apnoea index, events h^{-1}	4.3 (1.5, 7.2)	7.5 (2.9, 12.0)	0.15
Central apnoea index, events h^{-1}	1.2 (0.4, 2.1)	2.7 (−0.7, 6.2)	0.04
Mixed apnoea index, events h^{-1}	2.6 (−0.9, 6.0)	0.9 (−0.2, 2.1)	0.06
Hypopnea index, events h^{-1}	11.3 (8.0, 14.7)	9.7 (5.2, 14.1)	0.51
Oxygen desaturation index, events h^{-1}	23.0 (15.9, 30.1)	18.7 (10.6, 26.9)	0.41
Mean SpO_2, %	91.5 (90.5, 92.6)	90.0 (88.5, 91.6)	0.09
Proportion of time with SpO_2 <90%, %	21.9 (11.4, 32.3)	36.5 (17.4, 55.5)	0.10
Ventilatory frequency, bpm	13.0 (10.3, 15.7)	12.3 (9.9, 14.7)	0.61
Proportion of time spent in the supine position, %	93.4 (87.9, 98.9)	94.4 (88.1, 100.8)	0.81
Postoperative night 3, *n*	11	6	
Apnoea–hypopnea index, events h^{-1}	24.5 (10.0, 38.9)	32.8 (4.4, 61.2)	0.52
Obstructive apnoea index, events h^{-1}	6.2 (0, 12.5)	15.8 (−4.9, 36.4)	0.09
Central apnoea index, events h^{-1}	2.4 (0.2, 4.6)	1.7 (−0.5, 3.8)	0.50
Mixed apnoea index, events h^{-1}	2.1 (0.4, 3.8)	3.9 (−2.9, 10.8)	0.33
			0.63
Hypopnea index, events h^{-1}	13.8 (5.2, 22.4)	11.4 (4.1, 18.7)	
Oxygen desaturation index, events h^{-1}	30.0 (13.3, 46.7)	37.6 (9.3, 65.8)	0.55
Mean SpO_2, %	92.7 (90.8, 94.6)	89.7 (87.5, 91.9)	0.016
Proportion of time with SpO_2 <90%, %	15.8 (−1.8, 33.5)	43.0 (5.2, 80.7)	0.03
Ventilatory frequency, bpm	14.1 (12.3, 15.9)	11.0 (4.7, 17.3)	0.12
Proportion of time spent in the supine position, %	87.6 (69.6, 105.5)	73.2 (31.0, 115.3)	0.45

morphine is used. Although there was no difference in sleep-related outcomes between the first and third preoperative nights, the supine AHI, AHI, obstructive apnoea index, and ODI increased significantly, and to a clinically relevant extent on the third postoperative night in all patients. However, continuously monitoring all orthopaedic patients undergoing hip arthroplasty up to the third postoperative night may not be feasible given the expansion of ambulatory surgery and overall reductions in length of hospital stays. We suggest, therefore, that a temporary prescription for CPAP therapy might represent a satisfactory and cost-effective approach to postoperative management,[18] especially in at-risk patients such as older individuals or those with sleep apnoea.

The worsening of different sleep-related outcomes up to the third postoperative night is probably attributable to rebound rapid eye movement (REM) sleep on the third postoperative night, because respiratory events occur predominantly during this sleep phase.[19] Unfortunately, our methodology did not allow us to measure the REM/non-REM sleep ratio because the respiratory polygraphy does not include EEG, EMG, and electrooculography channels. However, Dette and colleagues[20] showed that there was an 8% median reduction in REM sleep on the first postoperative night *vs* preoperatively, followed by an increase of 10% on the fifth postoperative night in a sample of 12 patients undergoing knee replacement under spinal anaesthesia. The reduction in REM sleep in the immediate postoperative period might be a consequence of pain[21] and opioid administration.[22]

Among the different pain-related outcomes that were assessed, only pain score at departure from the PACU was significantly reduced in the intrathecal morphine group *vs* control. The absence of difference in i.v. morphine equivalent consumption in the PACU and at 24 h might be a type II error. Indeed, a *post-hoc* analysis revealed that a total of 98 and 132 patients would be needed to detect a difference in analgesic use favouring the intrathecal morphine group in the PACU or at 24 h postoperatively.

The results of this study need to be interpreted in light of several limitations. Differences in sleep quality between the nights may account for part of the variations in AHI, and therefore the wide confidence intervals around some of our

Table 3 Details of the generalised estimating equations model for the secondary sleep-related outcomes, indicating the presence of a time effect. Data are presented as means with 95% confidence interval or number of patients (%). *P<0.05 *vs* preoperative night; #P<0.05 *vs* postoperative night 1. AHI, apnoea–hypopnoea index; SpO_2, oxygen saturation.

	Preoperative night	Postoperative night 1	Postoperative night 3	P-value
Supine AHI, events h^{-1}	19.6 (14.1–27.3)	20.9 (16.4–26.7)	34.5 (23.5–50.5)*#	0.009
AHI, events h^{-1}	13.6 (10.4–18.0)	20.1 (15.7–25.7)*	27.5 (18.6–40.6)*	0.001
Obstructive apnoea index, events h^{-1}	2.1 (1.2–3.5)	5.7 (3.8–8.7)*	9.7 (5.0–18.8)*	<0.0001
Central apnoea index, events h^{-1}	1.5 (0.6–3.3)	2.0 (0.9–4.5)	2.1 (1.2–3.9)	0.30
Mixed apnoea index, events h^{-1}	0.8 (0.3–2.2)	1.5 (0.6–3.7)	2.6 (0.8–8.3)*	<0.0001
Hypopnea index, events h^{-1}	9.1 (6.8–12.3)	10.5 (8.2–13.5)	12.8 (8.8–18.7)	0.09
Oxygen desaturation index, events h^{-1}	16.6 (12.7–21.6)	20.8 (16.4–26.5)	32.2 (22.6–46.0)*	<0.001
Mean SpO_2, %	92.1 (91.4–92.7)	90.8 (89.9–91.6)*	91.4 (90.3–92.6)	<0.0001
Proportion of time with SpO_2 <90%, %	15.6 (9.5–25.6)	28.2 (20.3–39.0)*	25.8 (15.0–44.4)	0.009
Ventilatory frequency, bpm	13.7 (12.5–14.9)	12.6 (11.1–14.4)	12.5 (10.1–15.3)	0.39
Proportion of time spent in the supine position, %	32.2 (24.7–41.9)	83.1 (69.2–99.9)*	93.9 (90.1–97.9)*	<0.0001

data points (indication imprecision of the estimates). Although portable respiratory polygraphy is commonly used in clinical practice and is recommended for the diagnosis of sleep apnoea, it does not provide data on sleep stages; as mentioned previously, full polysomnography (with EEG, EMG, and electrooculogram) remains the reference diagnostic test and would have allowed assessment of sleep quality in addition to breathing disturbances. However, the large number of sensors required for polysomnography could have further disturbed participants' sleep quality and would have been difficult to use on the ward. Another limitation of the study was the proportion of subjects who withdrew during the course of the study owing to the discomfort of the recordings or who were discharged home on postoperative day 2. However, we included enough subjects to evaluate the primary outcome according to the power analysis. In addition, our results should be interpreted in light of our anaesthetic management approach, including a low-to-moderate dose of intrathecal morphine and surgical infiltration. Finally, the mean BMI of our population was 27 kg m^{-2}, whereas the literature reports that patients with a preoperative diagnosis of OSA have a BMI ranging from 29 to 34 kg m^{-2}.[23–25] Therefore, our results may not be applicable to populations with a higher BMI, and should be considered as exploratory and requiring further validation.

Table 4 Pain-related outcomes. Data are presented as means with 95% confidence interval. VAS score, from 0 to 10. Missing data: pain score at 2 h postoperatively, *n*=1; pain score, postoperative nausea and vomiting, and pruritus at 48 h postoperatively, *n*=2; pain score, postoperative nausea and vomiting, and pruritus at 72 h postoperatively, *n*=8; satisfaction score, *n*=2.

	Control group	Intrathecal morphine	P-value
2 h postoperatively			
I.V. morphine equivalent consumption, mg	3 (0–5)	1 (0–1)	0.06
Pain score (VAS, 0–10)	0.9 (0.2–1.5)	0 (0–0.1)	0.004
24 h postoperatively			
I.V. morphine equivalent consumption, mg	6 (3–8)	3 (2–5)	0.20
Pain score (VAS, 0–10)	1.6 (0.9–2.3)	1.4 (0.6–2.2)	0.52
Postoperative nausea and vomiting, *n* (%)	1 (4.2)	1 (4.3)	1.00
Pruritus, *n* (%)	0 (0)	1 (4.3)	0.49
48 h postoperatively			
I.V. morphine equivalent consumption, mg	7 (3–10)	6 (3–9)	0.83
Pain score (VAS, 0–10)	0.9 (0.3–1.5)	2.0 (1.0–3.0)	0.001
Postoperative nausea and vomiting, *n* (%)	1 (4.3)	5 (22.7)	0.10
Pruritus, *n* (%)	0 (0)	3 (13.6)	0.11
72 h postoperatively			
I.V. morphine equivalent consumption, mg	7 (3–11)	5 (0–10)	0.53
Pain score (VAS, 0–10)	1.4 (0.6–2.1)	1.5 (0.5–2.5)	0.65
Postoperative nausea and vomiting, *n* (%)	2 (10.0)	2 (10.5)	1.00
Pruritus, *n* (%)	0 (0)	0 (0)	–
Satisfaction score (VAS, 0–10)	8.9 (8.3–9.6)	8.5 (7.7–9.2)	0.60

In conclusion, we have shown that intrathecal morphine does not worsen postoperative sleep apnoea severity in patients undergoing hip arthroplasty. This suggests that current recommendations for increased monitoring of patients receiving intrathecal morphine should be revised. It is important to note the increased number of apnoeic/hypopnoeic episodes on the third postoperative night, which needs further investigations.

Authors' contributions

Study design: EA, RH
Study registration: EA
Data interpretation: EA, VB, RH
Patient inclusion: AA
Statistical analysis: CH
Primary manuscript preparation: EA
Manuscript editing: VB, CH, AA, RH

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Declarations of interest

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