Anaesth Crit Care Pain Med (2023) 101269

Contents lists available at ScienceDirect

Anaesthesia Critical Care & Pain Medicine

journal homepage: www.elsevier.com

Original Article

The effects of intrathecal morphine on urinary bladder function and recovery in patients having a cesarean delivery – A randomized clinical trial

Nicolas Gautier [a], Delphine Lejeune [a], Lilas Al Zein [a], Cédric Kesteloot [a], Yannick Ciccarella [a], Jean-François Brichant [b], Lionel Bouvet [c], Jirka Cops [d,*], Admir Hadzic [e,f], Philippe E Gautier [a]

[a] Department of Anesthesiology, Clinique Sainte-Anne Saint-Rémi - CHIREC, Anderlecht, Belgium
[b] Department of Anesthesiology and Resuscitation, Centre Hospitalier Universitaire de Liège, Liège, Belgium
[c] Department of Anesthesia and Critical Care, Hospices Civils de Lyon, Lyon, France
[d] NYSORA, New York, USA
[e] Department of Anesthesiology, Ziekenhuis Oost-Limburg, Genk, Belgium
[f] Department of Anesthesiology & Algology, Faculty of Medicine, KULeuven, Leuven, Belgium

ARTICLE INFO

Article history:
Available online xxx

Keywords:
Obstetrics
Regional anesthesia
Injections
Spinal
Analgesics
Opioid

ABSTRACT

Introduction: Spinal anesthesia with intrathecal morphine (ITM) is a common anesthesia technique for cesarean delivery. The hypothesis was that the addition of ITM will delay micturition in women undergoing cesarean delivery.

Methods: Fifty-six ASA physical status I and II women scheduled to undergo elective cesarean delivery under spinal anesthesia were randomized to the PSM group (50 mg prilocaine + 2.5 mcg sufentanil + 100 mcg morphine; n = 30) or PS group (50 mg prilocaine + 2.5 mcg sufentanil; n = 24). The patients in the PS group received a bilateral transverse abdominal plane (TAP) block. The primary outcome was the effect of ITM on the time to micturition and the secondary outcome was the need for bladder re-catheterization.

Results: The time to first urge to urinate (8 [6–10] hours in the PSM group *versus* 6 [4–6] hours in the PS group) and the time to first micturition (10 [8–12] hours in the PSM group *versus* 6 [6–8] hours in the PS group) were significantly ($p < 0.001$) prolonged in the PSM group. Two patients in the PSM group met the 800 mL criterium for urinary catheterization after 6 and 8 h respectively.

Conclusion: This study is the first randomized trial to demonstrate that the addition of ITM to the standardized mixture of prilocaine and sufentanil significantly delayed micturition.

1. Introduction

Cesarean delivery (CD) is common, now accounting for more than 21% of all childbirths according to the World Health Organization (WHO) [1]. This number is likely to increase in the coming decade, with nearly a third (29%) of all births predicted to be by CD by 2030 [1]. Spinal anesthesia is the anesthetic technique of choice for CD because it reduces maternal mortality compared to general anesthesia, and allows the mothers to experience birth and share the birthing process with their partners. Likewise, there appears to be a general perception among patients and obstetricians that it is beneficial to neonates as general anesthesia for CD is often associated with an increased risk of maternal adverse events [2]. The addition of intrathecal preservative-free morphine (ITM) is recommended for postoperative analgesia after CD [3,4]. Effective analgesia after CD is important to facilitate early mobilization, breastfeeding, and mother-newborn bonding.

As ITM results in adequate and long-lasting postoperative analgesia, it is the most widely used intrathecal opioid for analgesia after CD [5,6]. While the effects of ITM on postoperative analgesia, nausea, and vomiting are well-known [3,7], the effects on urinary bladder function and urinary retention have not been well-studied in randomized control studies. A confounding factor is that spinal anesthesia also may be associated with postoperative

* Corresponding author at: NYSORA, 2585 Broadway, Suite 183, New York, NY 10025, USA.
E-mail address: jirka@nysora.com (J. Cops).

https://doi.org/10.1016/j.accpm.2023.101269
2352-5568/

urinary retention [8,9]. Likewise, indwelling urinary bladder catheterization is commonly used in women after CD, which represents a risk for nosocomial urinary tract infection [10,11]. Apart from the infectious risk, the autonomy and self-esteem of the mother are affected by a long-lasting bladder catheter [12].

This randomized trial investigated the effects of ITM on urinary dynamics in women undergoing CD under spinal anesthesia. The hypothesis was that the addition of ITM will delay micturition in women undergoing CD. The primary outcome was the effect of ITM on the difference in time to micturition. The secondary outcome was the need for bladder re-catheterization.

2. Material and methods

2.1. Ethical approval

The study was carried out in accordance with the Declaration of Helsinki of the World Medical Association revised in 2013 for experiments involving humans. Ethical approval was received from the ethical committee at the University of Liège. The study was registered at clinicaltrials.gov on September 6th, 2021 (NCT05042817, https://clinicaltrials.gov/ct2/show/NCT05042817). Written informed consent was obtained from each patient. Patient enrollment was performed from October 2021 to March 2022.

2.2. Inclusion and exclusion criteria

Fifty-six ASA physical status I and II women with term singleton pregnancies, scheduled to undergo elective CD under spinal anesthesia from October 2021 to March 2022, were recruited (Fig. 1). Exclusion criteria comprised pre-existing or gestational hypertension, diabetes, cardiovascular disease, cerebrovascular disease, known fetal abnormalities, extremes of weight (< 40 or > 105 kg), contraindications to neuraxial anesthesia, twin pregnancies, or excessive intraoperative bleeding defined as blood loss exceeding > 1000 mL or requiring a blood transfusion.

2.3. Study design

The primary and secondary outcome variables were the effect of ITM on the time to micturition and the need for urinary bladder re-catheterization, respectively. Included patients were randomized into two groups: (1) the PSM group received an intrathecal injection of 100 mcg of ITM in 0.1 mL of 0.9% NaCl in addition to the mixture of hyperbaric prilocaine (50 mg) and sufentanil (2.5 mcg) or (2) the PS group received 0.1 mL of 0.9% NaCl in addition to the mixture of hyperbaric prilocaine (50 mg) and sufentanil (2.5 mcg).

2.4. Sample size calculation

The sample size calculation was based on data reported by Kuipers *et al.* in 2004 [13]. These authors reported a median value of 15.3 h for recovery of lower urinary tract function when using 100 mcg of morphine, and the standard deviation was estimated to be 2.5–4 h, depending on whether the min-max values or the interquartile range were used to estimate the standard deviation [13]. Note that the calculated standard deviation values were computed using the method described by Hozo *et al.* in 2005 [14]. We estimated that the mean difference in the time to micturition between the experimental (PSM group) and the control group (PS group) would be approximately 4 h. To reject the null hypothesis that the PSM and PS group population means are equal with a probability (power) of 0.95, and a type I error probability associated with this null hypothesis of 0.05, we needed to enroll 24 patients per group (n = 48). Thus, 56 patients were enrolled initially in anticipation of a 15% patient drop-off.

2.5. Randomization

Fifty-six patients were enrolled a day before the scheduled CD. Two patients were withdrawn due to the loss of baseline debimetry data before the start of the study. Both the PSM group and the PS group achieved the target sample size of 24 patients per group after the randomization of the first 48 patients. Only 3 patients in the PS group had missing debimetry data in contrast

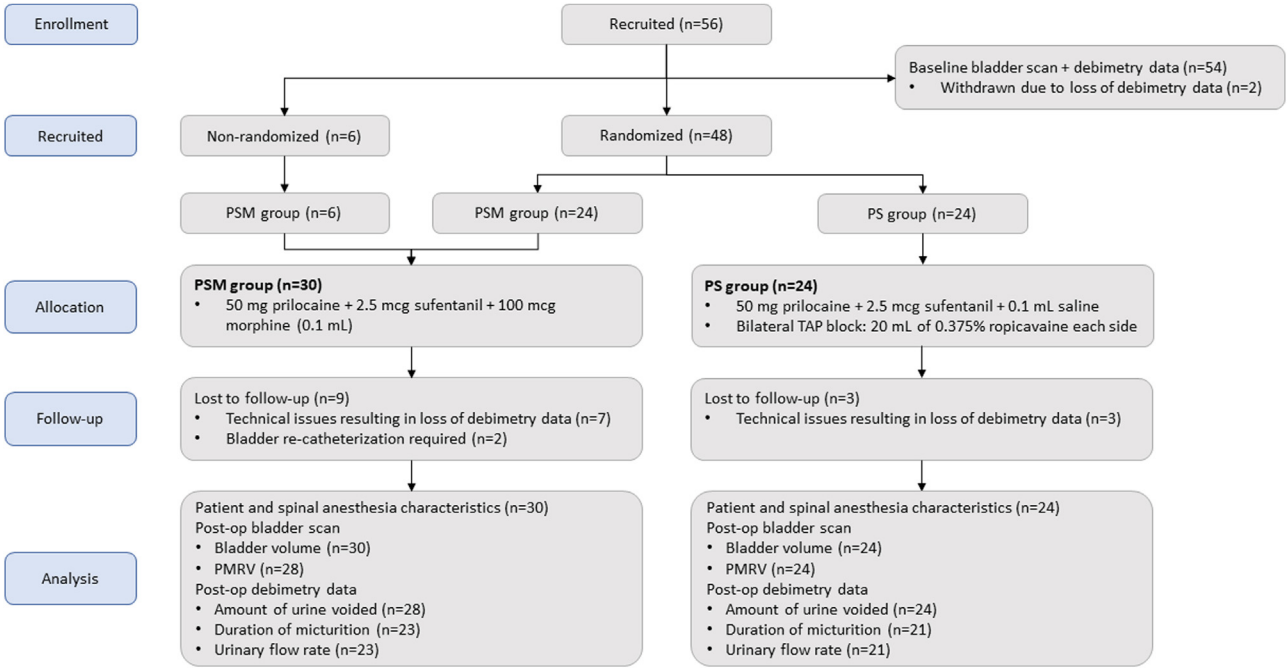

Fig. 1. The Consort flow diagram. PSM group, Prilocaine-Sufentanil-Morphine group; PS group, Prilocaine-Sufentanil group; TAP, transverse abdominal plane; PMRV, post-micturition residual volume.

to 7 patients in the PSM group. The 6 remaining patients were supplemented (non-randomly) to the PSM group to ensure that the missing debimetry data would not affect the results. Eventually, 30 patients in the PSM group and 24 patients in the PS group were analyzed on an intention-to-treat basis (Fig. 1).

Randomization was performed using the sealed envelopes method. A single research staff member, an unblinded anesthesiologist (PG), opened the envelopes, prepared the injection mixtures, drew up the spinal medications, and performed the TAP block. In this way, the rest of the research staff (DL, LAZ, CK, and YC) were kept blind to which patient belonged to which group (PSM or PS group). CK and YC administered anesthesia and perioperative care and performed the pinprick test and the Modified Bromage scale. DL and LAZ performed patient assessments and bladder urodynamic data collection. The sealed enveloped method was used again for the 6 remaining patients supplemented to the PSM group, to ensure that the research staff was also blind for the pre and postoperative assessment of these last 6 patients ("single block" randomization).

2.6. Study protocol

After the intrathecal morphine injection, a urinary bladder catheter was inserted in all patients. Carbetocin 100 mcg was administered intravenously after placenta delivery. Intraoperatively, all patients received a standardized intravenous multimodal analgesia protocol (paracetamol 1 g, diclofenac 75 mg, dexamethasone 10 mg, and ondansetron 4 mg). Postoperative multimodal analgesia was administered orally.

Perioperatively, the fluid intake was restricted to 1000 mL. Two hours after the intrathecal injection, IV fluids, and the urinary bladder catheter were discontinued while leaving the IV catheter *in situ*. Patients who had a bladder volume of $\geq$800 mL of urine at any time postoperatively, as determined by the bladder scan, were re-catheterized [15]. As per protocol, fluid intake was restricted to 100 mL/h orally thereafter.

The patients in the PS group received a bilateral transverse abdominal plane (TAP) block with 20 mL of ropivacaine 0.375% on each side in the postanesthesia care unit (PACU). The blocks were guided using an Aplio^{TM} I 700 ultrasound machine (Canon Medical System Europe) with an i18LX5 linear transducer and Stimuplex10 cm needle (BBraun, Mensulgen, Germany). Blinded research staff (LD, LAZ) performed preoperative and postoperative bladder assessments without participating in patient care.

Maternal arterial blood pressure was measured at 1 min intervals during the first 15 min after local anesthetic injection (starting at T0), and at 2.5 min intervals thereafter until the end of surgery. Hypotension was defined as a decrease in systolic blood pressure of $\leq$ 20% from baseline. In case of hypotension, and/or complaints of nausea or dizziness, ephedrine 5 mg or phenylephrine 100 mcg was administered to obtain 90% of the baseline value.

2.7. Patient and spinal anesthesia characteristics

Patient characteristics (Table 1), lowest blood pressure and heart rate, and spinal anesthesia characteristics were all recorded (Table 2). Sensitivity to pinprick at 10 and 120 min after intrathecal injection was used to assess the sensitive block in the lower limb (Table 2). The Modified Bromage scale at 10 and 120 min after intrathecal injection was used to investigate the motor block in the lower limb (Table 2). The time to first urge to urinate and the time to first micturition after spinal anesthesia were recorded (Table 3). After recovery from spinal anesthesia, the patients were allowed and encouraged to ambulate.

2.8. Bladder urodynamics

Baseline bladder urodynamic data were collected using the BladderScan® and urinary bladder debimetry measurements according to the manufacturer's instructions (MinzeUroflow®, HospiFlow, Antwerp, Belgium) the day prior to the surgery. Postoperative bladder scan and debimetry measurements were performed when the patient first urinated. The BladderScan® included bladder volume (Fig. 2A) and post-micturition residual volume (PMRV) (Table 3). The debimetry assessments included the amount of urine voided (mL), the duration of micturition (sec), and peak flow (mL/sec) (Fig. 2B–D).

2.9. Missing urodynamic data

The debimetry data were collected *via* a Wi-Fi connection. Unfortunately, the Wi-Fi connection failed during some data collections, likely due to an interruption or a weak Wi-Fi connection in some patients' rooms, resulting in missing debimetry data (Fig. 1). Nevertheless, urine volume was measured with a measuring cup as well. A maximal bias test was performed for outcome variables to simulate the effect of the missing data and to test the solidity of the results. In this maximal bias test, missing values were replaced by worst-case values (*e.g.*, the highest or lowest value depending on the results).

2.10. Statistical analysis

Data presented as median [interquartile range] or as the number (%) of patients were compared by a Mann-Whitney *U* test or a Chi^2 test (Table 2 and Table 3). Bladder urodynamic data (Fig. 2) were compared by an analysis of variance for repeated measures with mixed models. For all data, a $p < 0.05$ was considered statistically significant.

3. Results

A total of 56 patients consented and enrolled in the study a day before the scheduled CD. Two patients were withdrawn due to the loss of baseline debimetry data before the start of the study. Based

Table 1
Baseline patient characteristics of both the Prilocaine-Sufentanil-Morphine (PSM) and the Prilocaine-Sufentanil (PS) group.

	Prilocaine-Sufentanil-Morphine anesthesia (PSM group, n = 30)	Prilocaine-Sufentanil anesthesia (PS group, n = 24)
Age (year)	33 [29–37]	31 [28–37]
Weight (kg)	80 [72–101]	86 [75–94]
Height (cm)	163 [159–169]	160 [157–166]
Gravidity	3 [2–3]	3 [2–4]
Parity	1 [1–2]	1 [0–2]
Previous CD, n (%)	13 (43)	12 (50)
Number of previous CDs	0 [0–1]	1 [0–1]
Systolic (mmHg)	140 [119–151]	137 [121–144]
Diastolic (mmHg)	81 [74–89]	76 [62–87]
Heart rate (bpm)	95 [83–104]	88 [79–100]

Data are shown as median [interquartile range] or number (%) of patients. CD, cesarean delivery.

Table 2
Lowest blood pressure and heart rate, spinal anesthesia characteristics, and sensory and motor block levels of both the Prilocaine-Sufentanil-Morphine (PSM) and the Prilocaine-Sufentanil (PS) group.

	Prilocaine-Sufentanil-Morphine anesthesia (PSM group, n = 30)	Prilocaine-Sufentanil anesthesia (PS group, n = 24)	Mann-Whitney U Test or Chi^2 test *p*-value
Lowest blood pressure and heart rate			
Systolic (mmHg)	88 [80–106]	92 [86–112]	0.30
Diastolic (mmHg)	47 [39–56]	44 [42–50]	0.65
Heart rate (bpm)	61 [55–68]	60 [53–69]	0.84
Amount of IV ephedrine (mg)	12 [7–18]	9 [6–12]	0.08
Amount of IV phenylephrine (μg)	200 [31–328]	50 [0–275]	0.20
Spinal anesthesia characteristics			
Time from intrathecal injection to surgical incision (min)	18 [15–21]	18 [15–21]	0.61
Duration of surgery (min)	56 [45–65]	57 [45–65]	0.90
The number rating scale for drowsiness (0–10)	5 [1–7]	1 [1–6]	0.33
Number of patients with pruritus, n (%)	16 (43)	13 (54)	0.96
Duration of pruritus (min)	120 [0–1440]	120 [0–270]	0.24
Number of patients with nausea, n (%)	14 (47)	3 (13)	< **0.01****
Duration of nausea (min)	30 [0–600]	0 [0 – 0]	< **0.01****
Assessment of quality of anesthesia by the patients, n (%):			0.88
Excellent	16 (53)	13 (54)	
Good	9 (30)	6 (25)	
Average	3 (10)	2 (8)	
Unknown	2 (7)	3 (13)	
Time to ambulation (hours)	6 [6–8]	6 [4–6]	**0.001****
Sensitivity level to pinprick test			
10 min after intrathecal injection	Th2 [Th1 – Th3]	Th3 [Th1 – Th5]	0.80
120 min after intrathecal injection	Th2 [Th1 – Th3]	Th5 [Th4 – Th7]	**0.02***
Modified Bromage Scale			
10 min after intrathecal injection	1 [1–1]	1 [1–1]	0.70
120 min after intrathecal injection	5 [4–6]	6 [5–6]	0.71

A 6-point Modified Bromage scale was used [21]. Motor block in the lower limb was assessed with a modified Bromage scale (1 = complete motor blockade; 2 = almost complete motor blockade, the patient is only able to move the feet; 3 = partial motor blockade, the patient is able to move the knees; 4 = detectable weakness of hip flexion, the patient is able to raise the leg but is unable to keep it raised; 5 = no detectable weakness of hip flexion, the patient is able to keep the leg raised during 10 s at least; 6 = no weakness at all, the patient is able to perform partial knee bend while supine). Data are shown as median [interquartile range] or number (%) of patients. Data were compared by a Mann-Whitney *U* test or a Chi^2 test.
* $p < 0.05$.
** $p < 0.01$.

Table 3
Comparison of urodynamic data between the Prilocaine-Sufentanil-Morphine (PSM) group and the Prilocaine-Sufentanil (PS) group.

	Prilocaine-Sufentanil-Morphine anesthesia (PSM group)	Prilocaine-Sufentanil anesthesia (PS group)	Mann-Whitney U Test or Chi^2 test *p*-value
Time to first urge to urinate (hours)	8 [6–10] (n = 30)	6 [4–6] (n = 24)	< **0.001*****
Time to first micturition (hours)	10 [8–12] (n = 30)	6 [6–8] (n = 24)	< **0.001*****
Oral water ingestion before micturition (mL)	650 [363–900] (n = 30)	400 [210–500] (n = 24)	**0.01***
PMRV (mL)	110 [61–318] ($n_{baseline}$ = 30, n_{postop} = 28)	124 [61–201] ($n_{baseline}$ = 24, n_{postop} = 24)	0.57

PMRV, post-micturition residual volume.
Data are shown as median [interquartile range]. Data were compared by the Mann-Whitney *U* test or the Chi^2 test.
* $p < 0.05$.
*** $p < 0.001$.

on the power analysis, 24 patients were required per group. As 24 patients were already randomized to the PSM and PS groups, and 7 patients in the PSM group had missing debimetry data in contrast to 3 patients in the PS group, the 6 remaining patients were supplemented (non-randomly) to the PSM group. Eventually, 30 patients in the PSM group and 24 patients in the PS group were analyzed on an intention-to-treat basis. During follow-up, 2 patients in the PSM group required bladder re-catheterization, and as a result, the PMRV and the amount of voided urine could not be obtained for these patients (Fig. 1). However, these parameters did not change after the maximal bias test and, therefore, the missing data did not influence the statistical conclusions.

Demographic (Table 1) and spinal anesthesia characteristics were similar in both groups (Table 2). Patients were 33 [29–37] years of age in the PSM group (n = 30) and 31 [28–37] years of age in the PS group (n = 24). The ability to feel the pinprick after 120 min (Th2 in the PSM group (n = 30) *versus* Th5 in the PS group (n = 24), $p = 0.02$) and the time to ambulation (6 [6–8] hours in the PSM group (n = 30) *versus* 6 [4–6] hours in the PS group (n = 24), $p < 0.001$) were both significantly delayed in the PSM group. The incidence of nausea (n = 14 (47%) in the PSM group *versus* n = 3 (18%) in the PS group, $p < 0.01$) and the duration of nausea (30 [0–600] minutes in the PSM group *versus* 0 [0–0] minutes in the PS group, $p < 0.01$) were both significantly higher in the PSM group (n = 30) compared to the PS group (n = 24) (Table 2).

3.1. Primary outcome

The addition of ITM 100 mcg to the mixture of prilocaine and sufentanil significantly prolonged the time to first urge to urinate (8 [6–10] hours in the PSM group (n = 30) *versus* 6 [4–6] hours in the PS group (n = 24), $p < 0.001$) and the time to first micturition (10 [8–12] hours in the PSM group (n = 30) *versus* 6 [6–8] hours in the PS group (n = 24), $p < 0.001$, Table 3). The oral water ingestion

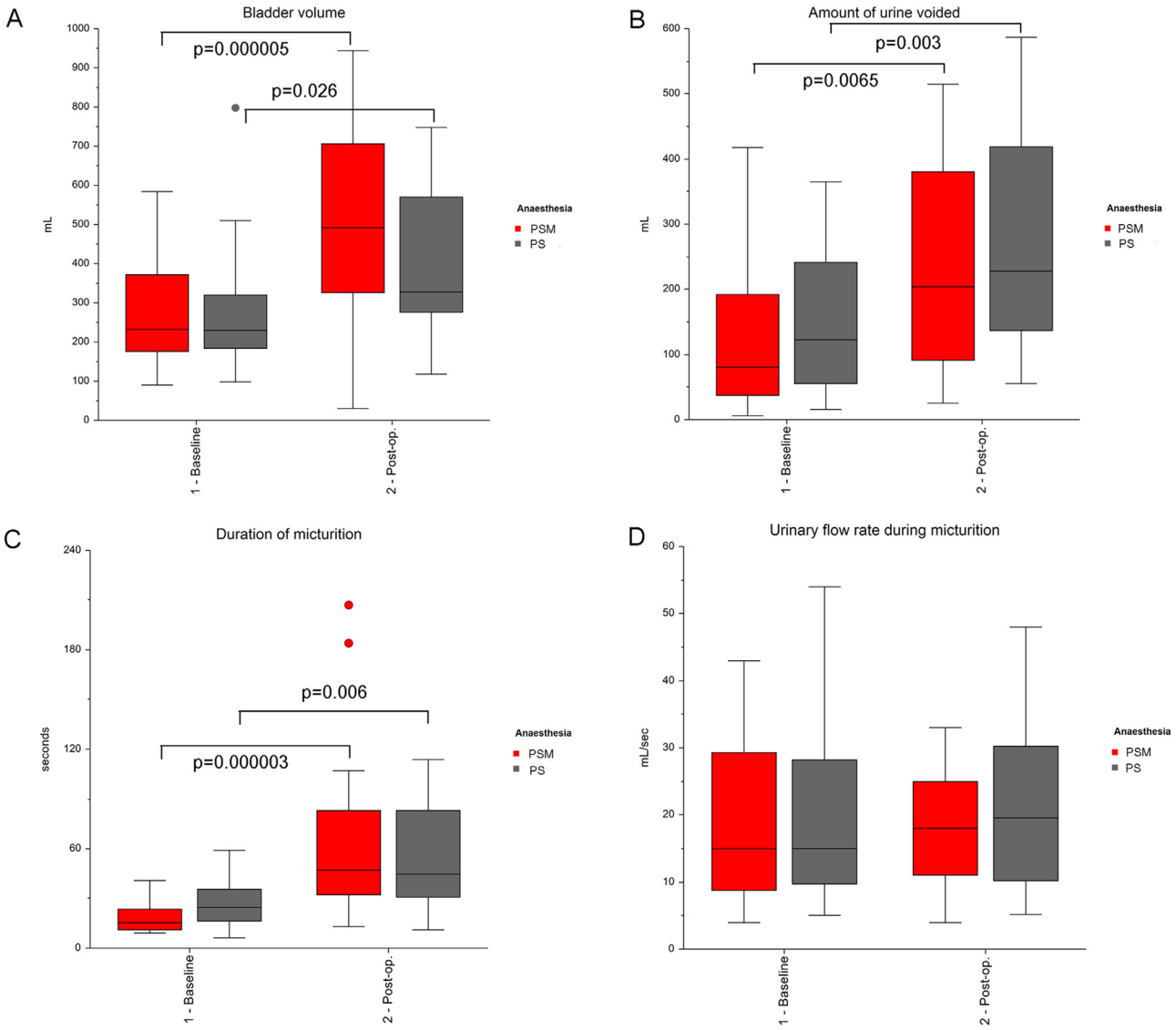

Fig. 2. Bladder urodynamic data. (A) Bladder volume measured with the BladderScan (PSM: $n_{baseline}$ = 30, n_{postop} = 30; PS: $n_{baseline}$ = 24, n_{postop} = 24). (B) Amount of voided urine (PSM: $n_{baseline}$ = 30, n_{postop} = 28; PS: $n_{baseline}$ = 24, n_{postop} = 24). (C) Duration of micturition (PSM: $n_{baseline}$ = 30, n_{postop} = 23; PS: $n_{baseline}$ = 24, n_{postop} = 21). (D) Urinary flow rate during micturition (PSM: $n_{baseline}$ = 30, n_{postop} = 23; PS: $n_{baseline}$ = 24, n_{postop} = 21). Data are shown as median, 25th percentile, and 75th percentile (the box limit). The whisker boundaries equal the Box edge ± 1.5x inter-quartiles range. Data were analyzed by a repeated measures ANOVA. Prilocaine-Sufentanil-Morphine group; PS group, Prilocaine-Sufentanil group.

before micturition was significantly higher in the PSM group compared to the PS group (650 [363–900] mL in the PSM group (n = 30) *versus* 400 [210–500] mL in the PS group (n = 24), p = 0.01 (Table 3). The PMRV of urine after the first micturition (PSM n_{postop} = 28, PS n_{postop} = 24, $p > 0.05$, Table 3) and the median urinary flow rate were similar in both groups (PSM n_{postop} = 23, PS n_{postop} = 21, $p > 0.05$, Fig. 2D).

3.2. Secondary outcome

Two patients in the PSM group met the 800 mL criterium for urinary catheterization after 6 and 8 h, respectively. After the catheterization, the catheters were immediately removed. No patient required re-catheterization with an indwelling catheter.

4. Discussion

The main result of this study was that the addition of ITM to the standardized mixture of hyperbaric prilocaine and sufentanil delayed micturition by around four hours compared to patients receiving hyperbaric prilocaine and sufentanil in combination with a bilateral TAP block. Moreover, only 2 out of 30 patients required urinary catheterization 6 and 8 h after CD. Although the addition of ITM delays micturition by about 4 h, there was no need for prolonged indwelling catheterization with or without ITM. Modern obstetrical anesthesia aims to offer an experience to a patient undergoing CD similar to normal vaginal delivery and facilitate early parenteral bonding. Currently, this is accomplished through a combination of spinal anesthesia, adequate analgesia, and early removal of the bladder catheter. The current study suggests that bladder catheter removal may be feasible within ≤ 6 h in patients receiving ITM for post-CD.

Obstetric anesthesia aims to achieve a similar maternal experience after cesarean or vaginal delivery, with regards to the ability to ambulate, postoperative discomfort, elimination of the bladder catheter, and early discontinuation of the IV fluids. Adequate postoperative analgesia is one of the most important aspects of a mother's experience after CD. While analgesia may be

most consistent with intrathecally administered morphine, this long-acting opioid did impair urinary function for a longer period than the shorter-acting opioids (*e.g.* sufentanil) [13]. The effects of intrathecal local anesthetics have been well studied. Due to its shorter duration [16], prilocaine is regarded as a good choice for a normal CD [17,18]. Our choice of prilocaine for this study allowed us to minimize the possibility of confounding the lingering effects of intrathecal local anesthetics *versus* ITM.

Previous studies have assessed bladder function in volunteers following IT injection of 10 mcg of sufentanil or 100 mcg of morphine. Kuipers *et al.* demonstrated that bladder dysfunction is dose-dependent and approximately twice as long in duration with IT morphine *versus* IT sufentanil, despite that the clinical action of morphine as spinal analgesia is an order of magnitude more than sufentanil [13]. Herman *et al.* reported that IT morphine reduced bladder spasticity for more than 12 h [19]. Zanfini *et al.* showed that bladder function was significantly depressed in women after CD under spinal anesthesia with bupivacaine and sufentanil [11]. Only 47% and 40% of patients were able to void after 4 and 6 h, respectively, despite the return of the first bladder awareness and urge to void [11]. According to Kamphuis *et al.*, bladder contractility lags behind the recovery of sensory function [20]. Hence, patients may be unable to void even when experiencing the urge to void, resulting in bladder distention [20]. Therefore, the current study findings are valid to patients receiving prilocaine and sufentanil but may be not generalizable to all patients receiving ITM. Moreover, while 2 patients in our study in the ITM group required single re-catheterization without the need for an indwelling catheter, the study was not designed or powered to study the difference in the incidence of re-catheterization.

5. Limitations

In interpreting the findings of our study, it is important to consider the possibility that the protocoled fluid restriction to 1 L intravenously perioperatively and 100 mL/h orally postoperatively and the lack of estimated blood loss monitoring, are confounders that may have diminished any potential differences in bladder function between ITM and intrathecal sufentanil. Moreover, prilocaine is not always the local anesthetic of choice commonly used for CD around the world and these findings should be replicated with other local anesthetics. Third, only the patients in the PS group received a bilateral TAP block as the patients in the PSM group did not receive a sham TAP block. As a result, the patients were unblinded to the group assignment, however, this was unlikely to affect the primary and secondary outcomes. Finally, the remaining 6 patients were supplemented non-randomly to the PSM group, however, the authors believe that this allocation procedure was unlikely to affect the primary and secondary outcomes. To avoid this design flaw in the future, 12 patients should have been randomized to both the PSM and PS groups.

6. Conclusion

In summary, our study investigated the effects of ITM on urodynamics after CD under spinal anesthesia. The addition of ITM with a mixture of hyperbaric prilocaine and sufentanil delayed urinary voiding by 4 h, with no effect on urodynamics or PMRV. Anecdotally, none of the subjects in our study required re-catheterization of an indwelling catheter. Future studies should investigate the risk-benefit ratio of adding ITM in spinal anesthesia for elective CD. Regardless, based on our study findings and our 4 years of clinical experience, ITM appears to be an acceptable analgesic modality in patients having CD.

Human and animal rights

The authors declare that the work described has been carried out in accordance with the Declaration of Helsinki of the World Medical Association revised in 2013 for experiments involving humans as well as in accordance with the EU Directive 2010/63/EU for animal experiments.

Informed consent and patient details

The authors declare that this report does not contain any personal information that could lead to the identification of the patient(s).

The authors declare that they obtained written informed consent from the patients and/or volunteers included in the article. The authors also confirm that the personal details of the patients and/or volunteers have been removed.

Disclosure of interest

None.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contributions

- Nicolas Gautier: conceptualization, data curation, formal analysis, funding acquisition, investigation, methodology, project administration, resources, software, supervision, validation, visualization, writing - original draft, writing - review & editing
- Delphine Lejeune: investigation, methodology
- Lilas Al Zein: investigation, methodology
- Cédric Kesteloot: investigation, methodology
- Yannick Ciccarella: investigation, methodology
- Jean-François Brichant: investigation, methodology, writing - original draft, review & editing
- Lionel Bouvet: formal analysis, writing - original draft, review & editing
- Jirka Cops: writing - original draft, review & editing
- Admir Hadzic: formal analysis, writing - original draft, review & editing
- Philippe E Gautier: conceptualization, data curation, formal analysis, funding acquisition, investigation, methodology, project administration, resources, software, supervision, validation, visualization, writing - original draft, writing - review & editing.

Acknowledgments

The authors thank Edgard Engelman, MD (EW Data Analysis, Brussels, Belgium) for the data analysis and interpretation.

References

[1] Betran AP, Ye J, Moller A-B, Souza JP, Zhang J. Trends and projections of caesarean section rates: global and regional estimates. BMJ Global Health 2021;6e005671.
[2] Guglielminotti J, Landau R, Li G. Adverse events and factors associated with potentially avoidable use of general anesthesia in cesarean deliveries. Anesthesiology 2019;130:912–22.
[3] Sultan P, Halpern SH, Pushpanathan E, Patel S, Carvalho B. The effect of intrathecal morphine dose on outcomes after elective cesarean delivery: a meta-analysis. Anesth Analg 2016;123:154–64.
[4] Bollag L, Lim G, Sultan P, Habib AS, Landau R, Zakowski M, et al. Society for obstetric anesthesia and perinatology: consensus statement and recommendations for enhanced recovery after cesarean. Anesth Analg 2021;132:1362–77.
[5] Dahl JB, Jeppesen IS, Jørgensen H, Wetterslev J, Møiniche S. Intraoperative and postoperative analgesic efficacy and adverse effects of intrathecal opioids in

patients undergoing cesarean section with spinal anesthesia: a qualitative and quantitative systematic review of randomized controlled trials. Anesthesiology 1999;91:1919–27.
[6] Palmer CM, Emerson S, Volgoropolous D, Alves D. Dose-response relationship of intrathecal morphine for postcesarean analgesia. Anesthesiology 1999;90:437–44.
[7] Gehling M, Tryba M. Risks and side-effects of intrathecal morphine combined with spinal anaesthesia: a meta-analysis. Anaesthesia 2009;64:643–51.
[8] Mulder FEM, Hakvoort RA, de Bruin JP, Janszen EW, van der Post JAM, Roovers JWR. Long-term micturition problems of asymptomatic postpartum urinary retention: a prospective case-control study. Int Urogynecol J 2018;29:481–8.
[9] Liang CC, Chang SD, Chang YL, Chen SH, Chueh HY, Cheng PJ. Postpartum urinary retention after cesarean delivery. Int J Gynaecol Obstet 2007;99:229–32.
[10] Zahumensky J, Dolezal P, Braticak M, Baneszova R, Papcun P. The risk of urine bacterial colonisation in patients with a permanent catheter after caesarean section. J Obstet Gynaecol 2021;41:699–702.
[11] Zanfini BA, Paradisi G, Savone R, Catarci S, Quagliozzi L, De Waure C, et al. Bladder function after spinal anesthesia for cesarean section: an urodynamic evaluation. Eur Rev Med Pharmacol Sci 2012;16:1525–9.
[12] Engel O, Haikin Herzberger E, Yagur Y, Hershko Klement A, Fishman A, Constantini N, et al. Walking to a better future? Postoperative ambulation after cesarean delivery and complications: a prospective study. Int J Gynaecol Obstet 2022;157:391–6.
[13] Kuipers PW, Kamphuis ET, van Venrooij GE, van Roy JP, Ionescu TI, Knape JT, et al. Intrathecal opioids and lower urinary tract function: a urodynamic evaluation. Anesthesiology 2004;100:1497–503.
[14] Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. BMC Med Res Method 2005;5:13.
[15] Bjerregaard LS, Hornum U, Troldborg C, Bogoe S, Bagi P, Kehlet H. Postoperative urinary catheterization thresholds of 500 versus 800 ml after fast-track total hip and knee arthroplasty: a randomized, open-label, controlled trial. Anesthesiology 2016;124:1256–64.
[16] Black AS, Newcombe GN, Plummer JL, McLeod DH, Martin DK. Spinal anaesthesia for ambulatory arthroscopic surgery of the knee: a comparison of low-dose prilocaine and fentanyl with bupivacaine and fentanyl. Br J Anaesth 2011;106:183–8.
[17] Chapron K, Sleth JC, Capdevila X, Bringuier S, Dadure C. Hyperbaric prilocaine vs. Hyperbaric bupivacaine for spinal anaesthesia in women undergoing elective caesarean section: a comparative randomised double-blind study. Anaesthesia 2021;76:777–84.
[18] Goffard P, Leloup R, Vercruysse Y, Fils JF, Gautier PE, Kapessidou Y. Comparison of equipotent doses of intrathecal hyperbaric prilocaine 2% and hyperbaric bupivacaine 0.5% for elective caesarean section: a prospective, randomised, controlled, two-centre clinical trial. Eur J Anaesthesiol 2022;39:227–35.
[19] Herman RM, Wainberg MC, delGiudice PF, Willscher MK. The effect of a low dose of intrathecal morphine on impaired micturition reflexes in human subjects with spinal cord lesions. Anesthesiology 1988;69:313–8.
[20] Kamphuis ET, Kuipers PW, van Venrooij GE, Kalkman CJ. The effects of spinal anesthesia with lidocaine and sufentanil on lower urinary tract functions. Anesth Analg 2008;107:2073–8.
[21] Breen TW, Shapiro T, Glass B, Foster-Payne D, Oriol NE. Epidural anesthesia for labor in an ambulatory patient. Anesth Analg 1993;77:919–24.

Glossary

ASA: American Society of Anesthesiologists
CD: Cesarean delivery
ITM: Intrathecal morphine
PACU: Postanesthesia care unit
PMRV: Post-micturition residual volume
PS: Prilocaine-sufentanil group
PSM: Prilocaine-sufentanil-morphine group
TAP: Transverse abdominal plane
WHO: World Health Organization