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Analgesic efficacy of intrathecal fentanyl during the period of highest analgesic demand after cesarean section

A randomized controlled study

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Abstract

Cesarean section (CS) is one of the most common surgical procedures in female patients. We aimed to evaluate the postoperative analgesic efficacy of intrathecal fentanyl during the period of greatest postoperative analgesic demand after CS. This period was defined by detailed analysis of patient-controlled analgesia (PCA) usage.

This double-blind, placebo-controlled, parallel-group randomized trial included 60 parturients who were scheduled for elective CS. Participants received spinal anesthesia with bupivacaine supplemented with normal saline (control group) or with fentanyl 25 μg (fentanyl group). To evaluate primary endpoints, we measured total pethidine consumption over the period of greatest PCA pethidine requirement. For verification of secondary endpoints, we recorded intravenous PCA requirement in other time windows, duration of effective analgesia, pain scores assessed by visual analog scale, opioid side effects, hemodynamic changes, neonatal Apgar scores, and intraoperative pain.

Detailed analysis of hour-by-hour PCA opioid requirements showed that the greatest demand for analgesics among patients in the control group occurred during the first 12 hours after surgery. Patients in the fentanyl group had significantly reduced opioid consumption compared with the controls during this period and had a prolonged duration of effective analgesia. The groups were similar in visual analog scale, incidence of analgesia-related side effects (nausea/vomiting, pruritus, oversedation, and respiratory depression), and neonatal Apgar scores. Mild respiratory depression occurred in 1 patient in each group. Fewer patients experienced intraoperative pain in the fentanyl group (3% vs 23%; relative risk 6.8, 95% confidence interval 0.9–51.6).

The requirement for postoperative analgesics is greatest during the first 12 hours after induction of anesthesia in patients undergoing CS. The addition of intrathecal fentanyl to spinal anesthesia is effective for intraoperative analgesia and decreases opioid consumption during the period of the highest analgesic demand after CS, without an increase in maternal or neonatal side effects. We recommend using intrathecal fentanyl for CS in medical centers not using morphine or other opioids intrathecally at present.

Abbreviations: ASA = American Society of Anaesthesiologists (Physical Status classification system), C = control group, CS = cesarean section, F = fentanyl group, PCA = patient-controlled analgesia, PONV = nausea and vomiting, SD = standard deviation, VAS = visual analog scale.

Keywords: cesarean section, fentanyl, intrathecal, opioids, postoperative pain, spinal anesthesia

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1. Introduction

Effective pain management after cesarean section (CS) represents a unique challenge. Robust mother–infant interaction during the early postdelivery period is thought to be of considerable psychological importance to the new mother and to make substantial contribution to optimal development of the infant.[1] Therefore, post-CS analgesia must provide adequate pain control while allowing the mother to remain active and available to tend to the needs of her newborn baby. It is important for healthcare professionals to address the problems associated with insufficient analgesia while adhering to the modern standards of perioperative care, which include accelerated postoperative recovery and rapid discharge.[2] These goals must be met without compromising the quality of care, which includes patient satisfaction.[3] In light of this, a clear definition of the period of the greatest postoperative analgesic requirement should be a priority.

Multimodal analgesia represents an attempt to meet the above-mentioned goals and has thus become a widely used approach to post-CS pain management. The use of intrathecal opioids is a crucial component of this approach, and low-dose morphine has been the gold standard and the most widely recommended agent in this class.[4] However, this hydrophilic opioid has a late onset of

action that often precludes any intraoperative analgesic effect,[5,6] and also a high frequency of side effects,[7] including nausea and vomiting, pruritus, and rarely, potentially serious late respiratory depression.[8] For these reasons, a large segment of the world's medical centers currently refrains from the use of intrathecal morphine.[9–12] Therefore, in the search for optimal analgesic methods, the question regarding the potential risks and advantages of an opioid with lipophilic properties also arises. Fentanyl is one of the most commonly used intrathecal lipophilic opioids. It is characterized by a rapid onset and relatively short duration of action. These pharmacological properties may lead to improvement of intraoperative analgesia and enhanced duration of postoperative analgesia.[5] Given that the duration of action of fentanyl is short, the primary objective of this study was to evaluate the effectiveness of intrathecal fentanyl in the period of highest postoperative demand for analgesics after CS. However, this period has never been clearly defined. Therefore, a thorough analysis of postoperative patient-controlled analgesia (PCA) usage was performed to describe the pain profile of patients after CS and to determine the duration of the period of the highest analgesic requirement.

Secondary objectives here included assessment of the safety of intrathecal fentanyl 25 μg during the first 24 hours after CS. Because this spinal opioid was administered before surgery, we also included as a secondary objective the evaluation of its intraoperative analgesic effect. However, in this study, we primarily focused on the postoperative period because the intraoperative analgesic effect of intrathecal fentanyl is relatively well-established in the literature,[7,13–15] and its re-measurement here is therefore a control.

2. Methods

2.1. Study design and population

Between June 2009 and April 2010, 60 ASA grade I or II parturients aged 18 to 45 years, who were scheduled for elective CS under spinal anesthesia at gestation >36 weeks, were included in this prospective, randomized, double-blind, placebo-controlled, parallel-group study. The study was approved by the Ethics Committee of the Medical University of Warsaw, Poland (KB/60/2009). All patients gave written, informed consent for participation in the trial. Detailed written and oral explanations regarding the aims and methods of the study were provided during preoperative visit the day before the surgery. The trial was performed at the Department of Obstetrics and Gynaecology, Medical University of Warsaw, Poland, and was conducted in accordance with the principles set forth in The Declaration of Helsinki and national regulations.

2.2. Anesthesia

Lumbar puncture was performed at the 3 to 4 lumbar interspace using a 27-G spinal needle. A dose of hyperbaric bupivacaine 0.5% was administered according to patient's height (from 7.5 to 15 mg) commensurate with the protocol used in our department (Table 1).

The spinal anesthetic was supplemented with 0.5 mL normal saline (control group) or with 25 μg of fentanyl (fentanyl group). The fentanyl dose of 25 μg was chosen based on the recommendations in the review of Hamber and Viscomi.[5] Participant randomization was based on a computer-generated permuted-block randomization list (block size = 60, allocation ratio 1:1). Patients were randomized to either control (C) or fentanyl (F) groups by use of sealed, sequentially numbered envelopes. The envelopes were opened before induction of anesthesia by the randomizing researcher, who prepared and provided spinal solutions in unlabeled syringes and who did not participate in the subsequent stages of the study. Patients, the attending anesthetist, and postoperative staff were blinded to group allocation. Sensory block was assessed bilaterally by loss of cold sensation. The surgery began as soon as the block reached the sixth thoracic dermatome (T6). Hypotension (systolic blood pressure <100 mm Hg) was treated with 5 to 10 mg of intravenous ephedrine. In all CS was performed via a Pfannenstiel incision and transverse incision of the lower segment of the uterus. Neonatal Apgar scores were assessed at 1, 3, and 5 minutes after birth.

Table 1

Protocol for hyperbaric bupivacaine administration.

Height, cm	Dose, mL	Dose, mg
<150	1.5	7.5
150–155	1.5–1.7	7.5–8.5
156–162	1.8–1.9	9.5–10
163–165	2.0–2.1	10–10.5
166–172	2.2–2.5	11–12.5
>172	2.5–3.0	12.5–15

The standard pain control regimen for all patients included intravenous infusion of 1 g paracetamol every 6 hours and 100 mg ketoprofen every 12 hours. The first dose of both drugs was administered 2 hours after induction of spinal anesthesia. In addition, intravenous pethidine (meperidine) was delivered via PCA (demand dose, 10 mg; lockout interval, 10 minutes; 4-hour limit, 1.5 mg/kg; no continuous infusion, clinician bolus 10 mg). Patients were instructed to use the pump as needed.

Intraoperative and postoperative monitoring of vital signs included heart rate, noninvasive arterial blood pressure, respiratory rate, and oxygen saturation. Patients were also carefully observed for side effects of opioid therapy.

2.3. Outcome measures

The selected parameters were evaluated during the intraoperative period and in the first 24 hours after surgery. Episodes of intraoperative discomfort were recorded and additional analgesics were given as needed (ketamine 10 mg intravenous [i.v.] before the delivery and fentanyl 100 μg after delivery). During the postoperative period, the time from induction of spinal anesthesia to the first use PCA (effective analgesia) and the total pethidine consumption during each postoperative hour were recorded. Pain intensity was assessed according to the visual analog scale (VAS; 0 = no pain, 10 = worst imaginable pain). Vital signs and VAS scores on movement (i.e., when breathing deeply or coughing) were recorded upon arrival at the postoperative unit, and at 2, 4, 6, 8, 12, 16, 20, and 24 hours after induction of spinal anesthesia.

Opioid side effects were also recorded during the postoperative period, including nausea and vomiting (PONV), pruritus, oversedation, and respiratory depression. Oversedation was defined as delayed or no recovery of consciousness to loud auditory stimulus (Ramsay Sedation Scale score 5 and 6). Respiratory depression was considered when the respiratory rate was <8/min or arterial oxygen saturation was <90.

2.4. Statistical analyses

The primary endpoint was total pethidine consumption in the period of greatest requirement postoperatively. As the duration of this period has not been defined, an additional primary endpoint was to estimate its duration based on analysis of PCA usage, which was performed solely in the control group. Secondary endpoints were total pethidine consumption in other time windows, duration of effective analgesia, VAS score, opioid side effects, hemodynamic changes, Apgar scores, and intraoperative pain.

To determine a priori the sample size of each group that enables primary endpoint verification with test power 0.8 and significance level 0.05, we used pilot data (10 patients in each group) and the power.t.test function of the R2.3.1 program (www.r-project.org) with setup for a 2-sided, 2-sample test. At the beginning of the study, the period of greatest PCA pethidine requirement was not defined. However, based on the systematic review of Dahl et al,[7] who evaluated analgesia by intrathecal fentanyl in CS at postoperative times ranging from 2 to 13 hours, we decided to adopt the longest duration of action recorded in the literature as our analysis period. This period was also similar in length to a pivotal period of highest analgesic demand after CS that we could see in our previous study.[6] The difference between the 2 treatment groups in mean PCA-pethidine consumption within a 13-hour period in the pilot study (171 mg [83.7] vs 120 mg [32.7] for groups C and F, respectively) allowed us to calculate delta = 51, pooled SD = 63.5, and a required sample size of 26 patients in each group. A total of 60 patients were recruited to this study to compensate for possible dropouts.

Sample size was also calculated for some of the secondary endpoints. The required number of patients in each group was estimated to be 20 for effective analgesia duration (delta = 2.29, pooled SD = 2.49; results from pilot study) and 17 for VAS (assuming a difference of one VAS point between the study groups, pooled SD = 1).

For additional intraoperative analgesia, we computed Cohen effect size, assuming that 5% of patients in group F and 35% in group C would require additional analgesia. Our assumption was based on findings from a literature search, presented later in the "Discussion" section, which state that the incidence of insufficient intraoperative analgesia in CS drops from 10% to 70% to almost none when intrathecal fentanyl is added. Further, we used the equation: "$\lambda/(\text{effect size})^2 = \text{sample size}$," where λ = the noncentrality parameter, and is equal to 7.849 for accepted levels of significance and power. This gave a total sample size (sum of both groups) of 52 patients.

We based our clinical decision rule on the primary endpoint, because given that fentanyl is short-acting, it was not clear that it can influence the period when analgesics are most needed. Our secondary endpoints enabled wider understanding of treatment effects, but by themselves could not confirm treatment efficiency. They provided only supportive information (e.g., VAS, a complementary measure) or exploratory information (e.g., total pethidine consumption in the other time windows, duration of effective analgesia, hemodynamic changes, Apgar scores, and intraoperative pain). The intraoperative pain endpoint alone could fulfil criteria of being clinically beneficial, but was necessarily measured outside the period of main interest of this trial, and as mentioned previously, has been well-studied. The character of these secondary endpoints did not require correction for multiplicity of analyses.[16]

Furthermore, we did not adjust significance levels in the analyses of safety data, because it is generally considered more important to avoid false-negative conclusion about safety findings than to avoid false-positive conclusions.[16] However, the Bonferroni correction for multiple testing was applied to the analysis of the hour-by-hour pethidine consumption in the early postoperative period, resulting in a significance threshold of 0.008. For the rest of tests P value <0.05 was considered significant.

Data were assessed for normality using the Shapiro–Wilk test. Independent-samples t tests were undertaken for parametric data and the Mann–Whitney U test for nonparametric data. Differences in frequency and proportions were examined using a chi-square test. A correlation table (Spearman rank correlation coefficient with Bonferroni correction) was calculated to determine the degree of data independence of the data on PCA usage broken into 3-hour intervals. Statistical analyses were conducted using the R environment (R Development Core Team 2011).

3. Results

3.1. Baseline patient characteristics

Sixty patients who were scheduled for elective CS were enrolled in this study. Fig. 1 presents the allocation of patients into the study groups. One patient in group F was excluded because of unsuccessful spinal blockade. Finally, 59 patients completed the study according to the protocol and none of them was lost to follow-up. No significant intergroup differences were identified with regard to individual characteristics (Table 2).

3.2. Primary outcome measures

Before the comparison of the study groups on postoperative opioid consumption, we aimed to identify the period of the greatest analgesic requirement in the group C alone by a detailed hour-by-hour analysis of PCA use among the patients in this group. However, due to high fluctuation, the hourly periods were accumulated into 3-hour intervals to obtain a unimodal plot to clarify the picture of postoperative PCA pethidine requirement (Fig. 2A).

The 2 periods (1–3 and 4–6 hours) of pronounced increase of pethidine consumption in group C are followed by 3 periods of gradual decline (7–9, 10–12, and 13–15 hours) and then a stabilization period (16–18, 19–21, and 22–24 hours) (Fig. 2A). The mean PCA use in the 3-hour intervals within the first 12 hours was strongly interdependent, and significant correlations between these periods were detected. Intervals 1 to 3, 4 to 6, 7 to 9, and 10 to 12 strongly correlated with at least 2 other intervals in the first 12-hour period and did not correlate with intervals from the 13 to 24 hour time window. None of the remaining 4 intervals—13 to 15, 16 to 18, 19 to 21, and 22 to 24 hours—was correlated with any

Table 2

Baseline patient characteristics.

Variable	Group C (n = 30)	Group F (n = 29)	P
Age, yrs	31.1 ± 4.4	31.6 ± 4.2	NS
Height, cm	166.4 ± 6.3	163.2 ± 6.1	NS
Weight, kg	79.3 ± 14.8	79.4 ± 20.5	NS
BMI	28.7 ± 6.0	29.9 ± 8.7	NS

Data are presented as mean ± SD; t test.
BMI = body mass index, NS = not significant.

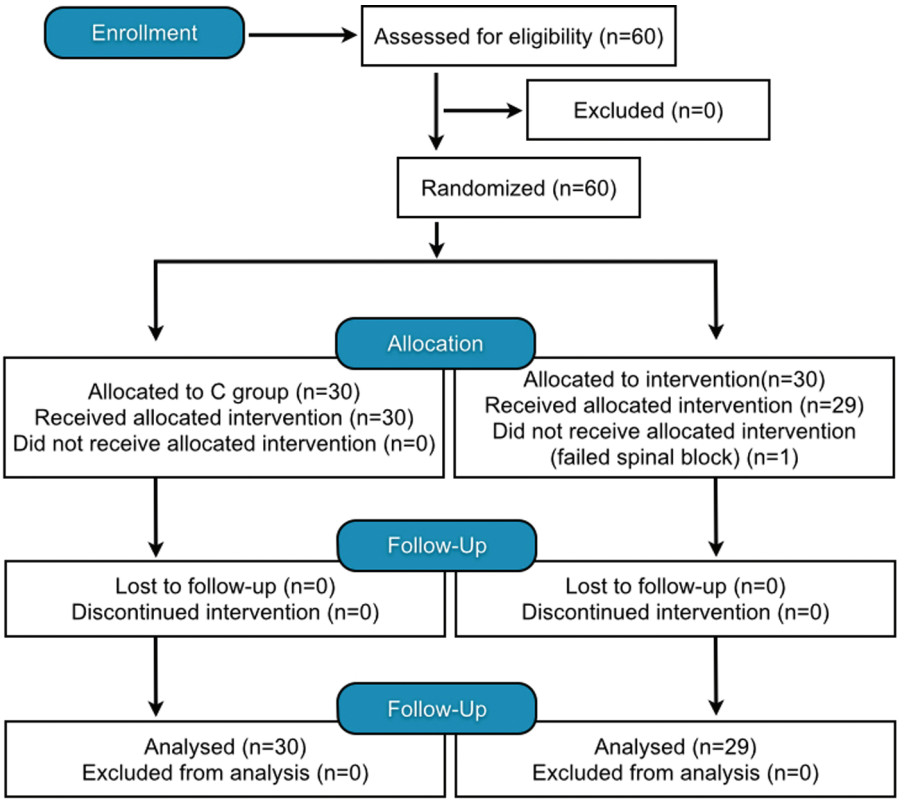

Figure 1. CONSORT study flow chart.

other interval in the 24-hour period. Therefore, these intervals might be considered independent. Hence, the first 12-hour period was defined as the period of the greatest demand for additional analgesics. Intergroup comparison indicated that the PCA demand was significantly higher in group C during the first 12 hours than in group F ($P=0.002$).

3.3. Secondary outcome measures

In further calculations, 2 time windows (1–12 and 13–24 hours) were used for comparison within and between groups.

There was a significant disproportion between cumulative PCA use during the first 12 hours and in the remaining 12 hours ($\chi^2=9.5$, df=1, $P=0.002$) in group C, whereas no such disproportion was noted in group F ($\chi^2=0.86$, df=1, $P=0.35$). Detailed hour-by-hour differences in PCA dose between patients in groups C and F are shown in Table 3. During the first 4 hours after administration of spinal anesthesia, the mean consumption of pethidine was significantly lower in group F, and it remained lower during the period of 5 to 9 hours after induction of anesthesia, but the difference during this period was no longer statistically significant.

During the second time window (13–24 houres), the mean cumulative PCA pethidine consumption did not differ significantly between groups ($P=0.17$) (Table 4). However, the time to first PCA demand was significantly shorter in group C (Table 4). The average level of pain intensity (VAS) in the hours after spinal anesthesia was low and did not differ statistically between the groups (Fig. 2B, Table 4).

The number of patients experiencing PONV and pruritus in the postoperative period did not differ between groups (Table 5). Oversedation did not occur in any of the patients, and mean levels of oxygen saturation were similar. Two patients, 1 from each group, experienced symptoms that met the criteria for respiratory depression, but the respiration rate did not fall below 8/min in

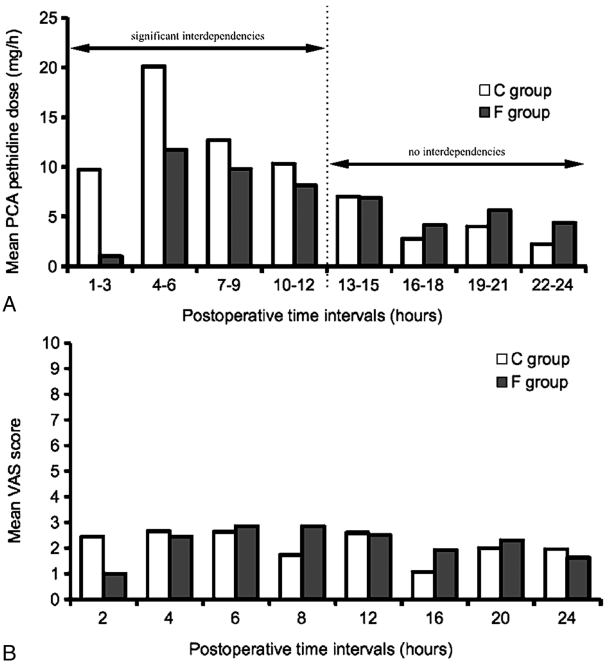

Figure 2. Mean postoperative PCA pethidine consumption (A) and VAS scores (B). PCA = patient-controlled analgesia, VAS = visual analog scale.

Table 3

Mean PCA pethidine consumption (mg/patient) during the first 6 hours after spinal anesthesia.

Hours	Group C	Group F	*P*
1	1	0	0.083
2	11	0	<0.001
3	17	3.1	<0.001
4	21.3	8.6	<0.001
5	21.6	13.8	0.061
6	17.3	12.7	0.13

Significance threshold of P value < 0.008 after Bonferroni correction for multiple testing was considered significant.

Data are presented as means; Mann–Whitney U test.

either patient. The oxygen saturation of the patient from group C fell to 86% to 89% between the 13 and 20 hours postoperatively, and the patient from group F had decreased oxygen saturation (81%) accompanied by moderate drowsiness in the second hour after spinal anesthesia. In both cases, patients remained hemodynamically stable during these incidents. Because both patients responded to the command for deep breathing, no naloxone administration was required.

No clinically important hemodynamic changes were noted in either group during the intraoperative and postoperative period, and neonatal Apgar scores did not differ significantly between the 2 groups.

All patients developed sensory block ≥ the T6 dermatome. Those in group C experienced intraoperative pain more frequently and required additional analgesics (relative risk 6.8, 95% confidence interval [CI] 0.9–51.6) (Table 4). To avoid possible confounder caused by additional intravenous analgesics during CS (ketamine and fentanyl) on outcome measures, supplementary statistical analysis was performed. However, no change in significance was found in any part of the results.

4. Discussion

In this study, we defined the period of the greatest requirement for postoperative analgesics after CS. We assumed that this also defined the duration of the most painful period of postoperative recovery. Furthermore, we evaluated the impact of intrathecal fentanyl on the quality of intraoperative analgesia and during the period of the greatest demand for postoperative analgesia. Demand for parenteral opioids in the postoperative period is often used as a parameter for evaluating the analgesic efficacy of intrathecal opioids.[13,17] However, there are only a few studies regarding postoperative pain management after CS that have analyzed the demand for additional analgesia by determining exact PCA consumption. PCA was introduced more than 30 years ago and was designed to allow the patient to administer preset doses of an analgesic on demand.[18] Here, we first analyzed hourly PCA use by the control group alone, which allowed us to define the period of the greatest demand for postoperative analgesia after CS that was found to be 12 hours. It has been reported previously that plasma concentrations of opioids are directly related to subjective pain scores[19] and that the opioid dose required to achieve pain relief can be used as an estimate of pain intensity.[20] Therefore, we regarded the period of the greatest analgesic requirement as the most painful period and the most critical in postoperative pain management. Inadequate pain relief after CS remains an area of concern,[21] and high-intensity acute pain has been associated with an increased risk of chronic pain and postpartum depression.[22] Proper pain management during the immediate postoperative period could decrease these risks. Thorough understanding of the pain profile after CS is very important. We found several studies that reported similar patterns of postoperative analgesic requirement using PCA.[23,24] A slightly shorter (6 hours) period of the greatest demand for opioid analgesia has been reported,[23,25] but that result was not subject to statistical analysis. We did not find any other study that analyzed PCA use according to the method of hour-by-hour bolus counting that we used in the present study. The 12-hour period of the greatest analgesia demand identified in our result seemed to describe well the overall dynamics of the increase and decrease of pain intensity after CS. Thus, we can conclude that vigilant monitoring of pain intensity and proactive pain management should be mandated during this period. We do not wish to suggest that the other 12 hours are not important, but suggest that if, for some reason, it is not possible to assist parturients for an entire 24 hours after CS, at least 12 hours should be considered, especially since some authors report that in some countries, no standardized protocols for measuring postcesarean pain exist on a national level.[9]

In further analyses, including cross-group comparisons, we found that intrathecal fentanyl was associated with significant reductions in pethidine consumption during the first 12 hours after CS and with a slower increase in demand for opioids during the early postoperative period. We also found that intrathecal fentanyl extended the period of effective analgesia to 4 hours, as confirmed by the detailed analysis of the differences in demand for PCA pethidine between the 2 groups during the first hours after surgery. The extension of the duration of effective analgesia has been well-described before. Prolonged periods of effective analgesia, ranging from 40 to 120 minutes, have been observed for intrathecal fentanyl 6.25 to 12.5 μg in several studies,[13,15,26,27] although not in all.[28–30] Nonetheless, most of the research on higher doses has been in agreement, and a prolongation of effective analgesia averaging 3 to 5 hours, which

Table 4

Analgesic requirement in intraoperative and postoperative periods and mean postoperative pain score (VAS).

Variables	Group C (n = 30)	Group F (n = 29)	*P*
Mean cumulative PCA pethidine consumption (mg/1–12 h/patient)	158.3 ± 76.4	92.1 ± 41.1	0.002
Mean cumulative PCA pethidine consumption (mg/13–24 h/patient)	48.0 ± 26.4	63.1 ± 39.5	0.17
Time to first PCA demand, h*	2.5 ± 1.9	4.3 ± 1.4	<0.001
Mean post-operative VAS score	2.1 ± 1.2	2.2 ± 1.0	0.83
Additional intra-operative analgesia, number (%)	7 (23%)	1 (3%)	0.025

Data are presented as mean ± SD and number of parturients with their percentage rate in parentheses; t test or chi-square test.

PCA = patient-controlled analgesia, VAS = visual analog scale (1 to 10, where 10 is worst pain imaginable).

* For parturients who did not use the PCA, the maximal time (24 hours) was assumed.

Table 5

Opioid side effects in the postoperative period.

Variables	Group C (n = 30)	Group F (n = 29)	*P*
Nausea/vomiting	3 (10%)	2 (7%)	0.67
Pruritus	0 (0%)	3 (10.3%)	0.08
Sedation	0 (0%)	0 (0%)	ND
Respiratory depression	1 (3.5%)	1 (3.5%)	0.98

Data are presented as a number (percent); chi-square test.
ND = not done.

is in line with our result, has been reported for intrathecal fentanyl at doses of 15 to 25 μg.[7,17,26,28,31] Additionally, in our study, the analysis of the proportion of opioid consumption between the first and second time windows (1–12 and 13–24 hours) indicated that the temporal pattern of increased PCA use was mitigated by intrathecal fentanyl. Interestingly, when the whole 24-hour period after CS was considered, fentanyl 25 μg did not reduce the need for opioids. This result was close to significance ($P = 0.07$), and post hoc calculation revealed the power of 0.42. Thus, we could not make a strong statement about lack of significant difference and we did not include this into results. For the power of 0.8, we would require 146 patients, what was beyond possibilities of our trial. This is important limitation of this study. However, other studies have also shown no reduction in opioid consumption in 24-hour period.[7,26,31] We checked power for 2 other time windows (1–12 and 13–24 hours) and found its satisfactory levels of 0.87 and 1, respectively.

The PONV was rare (2/29; 7%) among the patients who received intrathecal fentanyl in our study. Similar results have been reported in other studies,[13,26,32] and some authors have attributed an antiemetic role to fentanyl.[7,15]

We observed a low incidence of pruritus among the women who received spinal anesthesia with local anesthetic alone, as has been reported in other studies.[13,31] The incidence of pruritus reached 10% among patients in the fentanyl group, which was also consistent with results of other studies that have reported rates of pruritus ranging from 10% to 24%.[13,31]

Possibly, the most dangerous side effect of opioid analgesia is respiratory depression. Reports of respiratory depression after spinal administration of lipophilic opioids in obstetrics have mostly implicated sufentanil.[33,34] However, some case studies have raised the possibility of respiratory depression after neuraxial administration of fentanyl as well.[35,36] Although the risk is thought to be extremely remote,[13,26,31] it must be assumed that it can occur, even if only in mild form. A recently described case of mild respiratory depression after administration of 15 μg of intrathecal fentanyl was similar to the case we encountered, and it also occurred about 2 hours after injection of spinal fentanyl.[37]

There was no relationship between intrathecal fentanyl administration and neonatal Apgar scores, and this finding is in agreement with those of other studies.[13–15,26,27,31]

Finally, we found that a substantial number of patients (7/30; 23%) in the control group needed additional intraoperative analgesics. Previous studies have reported insufficient intraoperative analgesia rates varying from 10% to 70%, when local anesthetics alone were used in CS.[13,14,26,27,31,38,39]

Moreover, many authors have reported improvement of intraoperative analgesia for CS after addition of intrathecal fentanyl at doses ranging from 2.5 to 60 μg, and for doses >10 μg, abolition of intraoperative visceral pain was observed in almost all cases.[7,13–15,27,28,31] Doses of <10 μg are considered sufficient by some authors[26] and insufficient by others.[28]

5. Conclusions

Our results indicate that the requirement for postoperative analgesia is greatest during the first 12 hours after induction of spinal anesthesia in patients undergoing CS. Therefore, pain intensity should be assessed regularly during this period and adequate pain relief provided. Supplementation of spinal anesthesia with intrathecal fentanyl provides effective intraoperative analgesia and decreases opioid consumption during the period of the highest analgesic demand after CS, without an increase in maternal or neonatal side effects. We recommend the use of intrathecal fentanyl for CS in medical centers that do not use intrathecal morphine or any other intrathecal opioid at present, provided that patients are monitored during the early postoperative period.

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