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# Efficacy and tolerability of intravenous morphine patient-controlled analgesia (PCA) in women undergoing cesarean delivery

## Skuteczność i tolerancja morfiny podawanej dożylnie metodą PCA (analgezja kontrolowana przez pacjenta) u pacjentek po cięciach cesarskich

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### Abstract

***Objectives:*** *The aim of the study was to evaluate analgesic efficacy and tolerability of patient-controlled analgesia (PCA) with intravenous morphine.*

***Material and methods:*** *Our observational study included 50 women who underwent a Misgav-Ladach or modified Misgav-Ladach cesarean section. Automated PCA infusion device (Medima S-PCA Syringe Pump, Medima, Krakow, Poland) was used for postoperative pain control. Time of morphine administration or initiation of intravenous patient-controlled analgesia (IV PCA) with morphine was recorded, as well as post-operative pain at rest assessed by a visual analogue scale (VAS). All patients were followed up for 24 hours after discharge from the operating room, taking into account patient records, worst pain score at rest, number of IV PCA attempts, and drug consumption.*

***Results:*** *Median of total morphine doses used during the postoperative period was 42.9mg (IQR 35.6–48.5), with median infusion time of 687.0 min. (IQR 531.0–757.5). Pain severity and total drug consumption improved after the first 3 hours following cesarean delivery ($p<0.01$). Mean number of PCA attempts per patient was 33 (IQR: 24–37), with median of 11 placebo attempts (IQR: 3–27).*

***Conclusions:*** *Patient-controlled analgesia with morphine is an efficient and acceptable analgesic method in women undergoing cesarean section.*

Key words: **patient-controlled analgesia** / **PCA** / **intravenous morphine** / / **cesarean section** /

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## Streszczenie

***Cel pracy:*** *Celem badania była ocena skuteczności leczenia bólu morfiną podawaną dożylnie metodą PCA oraz jej tolerancji u pacjentek po cięciach cesarskich.*

***Materiał i metodyka:*** *Do badania włączono 50 pacjentek, które przeszły cięcie cesarskie sposobem Misgav-Ladah lub jego modyfikację. Do pooperacyjnego zwalczania bólu użyto morfiny podawanej w automatycznej pompie infuzyjnej (Medima S-PCA Syringe, Medima, Kraków, Polska). Moment podłączenia morfiny i.v. w pompie PCA, czas podaży leku oraz pooperacyjną ocenę bólu przy użyciu wizualnej analogowej skali wzrokowej (VAS) były odnotowywane.*

*Wszystkie pacjentki były pod obserwacją przez 24 godziny od zakończenia cięcia cesarskiego a w dokumentacji odnotowywano największy ból w spoczynku, liczbę prób podaży leku przez pacjentkę oraz ogólną ilość podanego analgetyku.*

***Wyniki:*** *Mediana całkowitej podanej dawki morfiny w okresie pooperacyjnym wyniosła 42,9mcg (IQR-rozstęp kwartylny – 35,6-48,5), mediana czasu podaży dożylnej wyniósł 687,0 min. Nasilenie bólu oraz dawka podanej morfiny zmniejszyły się po 3 godzinach od cięcia cesarskiego (p<0,01). Średnia ilość podanych dawek morfiny wyniosła 33, natomiast mediana ilości podań bez leku wyniosła 11.*

***Wnioski:*** *Analgezja morfiną przy użyciu pompy PCA to skuteczna i dopuszczalna metoda uśmierzania bólu u pacjentek po cięciach cesarskich.*

Słowa kluczowe: **analgezja kontrolowana przez pacjenta** / **PCA** / **morfina dożylnie** / / **cięcie cesarskie** /

## Introduction

Effective analgesia after cesarean section is critical to allow for mother-child bonding, early postoperative ambulation and discharge, resulting in greater patient satisfaction. Use of regional anesthesia for cesarean section has provided an option for rendering post-operative analgesia with neuraxial opioids. Also, it is associated with a decline in anesthesia-related maternal mortality [1].

The most common methods of pain management after cesarean section include continuous epidural or spinal analgesia, intramuscular subcutaneous and intravenous administration of opioid analgesics, continuous wound infiltration, ketamine and non-steroid anti-inflammatory drugs [2].

The use of intravenous patient-controlled analgesia (IV-PCA) in obstetrics was first described in 1976 and since then has been widely used [3]. Patient-controlled analgesia (PCA) is a means for the patient to self-administer analgesics (pain medications) intravenously by using a computerized pump, which introduces specific doses into an intravenous line. The purpose of PCA is to improve pain control. Standard PCA uses more frequent but smaller doses of analgesia, thus providing even levels of medication within the circulation. Although there are numerous ways of counteracting post-cesarean section pain, none has been proven to be significantly superior [4-6].

The aim of our study was to evaluate analgesic efficacy and tolerability of PCA with intravenously administered morphine. Our secondary goal was to assess average drug consumption and cost effectiveness of such treatment.

## Material and methods

### *Study population*

A total of 50 women were included in this observational study. All subjects signed an informed consent. All participants underwent a routinely performed Misgav-Ladach or modified Misgav-Ladach cesarean section [7].

### *Postoperative care*

Time of morphine administration or initiation of IV PCA with morphine was recorded by the attending nurse or physician. In the recovery room, post-operative pain at rest was assessed by a visual analogue scale (VAS). Apart from cardio-respiratory vital signs, the patients were assessed hourly by ward nurses for the next 12 hours, then two-hourly for the next 12 hours, on the following: pain score at rest on VAS, total drug consumption, nausea, vomiting, pruritus and number of boluses (including placebo). Naloxone was readily available for administration in the event patients suffered from respiratory depression (respiratory rate <8). Nausea and vomiting would be treated with IV metoclopramide at patient's request. Antihistamines, such as chlorpheniramine, would be prescribed to women who requested treatment for itching. All patients would be followed up for 24 hours after discharge from the operating room by a dedicated pain service team, comprising an anesthetist and a pain nurse. The team would review patient records, collecting and analyzing data on the worst pain score at rest, number of IV PCA attempts, and drug consumption.

Automated patient-controlled analgesia infusion device (Medima S-PCA Syringe Pump, Medima, Krakow, Poland) was used for postoperative pain control. Parameters were set according to the available literature data [8]. Briefly, a loading dose of 3.0mg was administered with boluses of 1.0mg with a 6-minute lockout time. The subjects were also informed about an option of clinical bolus of 3.0mg that could be administered by the physician in case of insufficient pain relief. The maximum dose was set at 22.0 mg/h.

All data on the post-operative analgesia course were automatically stored by the device and analyzed afterwards. Analgesic efficacy was additionally assessed with the VAS form 2, 6 and 12 hours postoperatively.

### *Statistical analysis*

Statistical software package SPSS 20.0 (SPSS Inc., Chicago, Illinois, US) was used for data analyses.

**Table I.** Patient characteristics.

| Parameters | |
|---|---|
| Age, years median (IQR) | 31.5 (28.8 – 34.0) |
| Weight, kg median (IQR) | 77.3 (77.0 – 88.0) |
| Height, cm median (IQR) | 168.0 (163.8 – 170.3) |
| GA, weeks median (IQR) | 39.0 (37.0 – 39.0) |
| Parity: Nulliparous, n (%)<br>Multiparous, n (%) | 23 (46.0)<br>27 (54.0) |
| Subsequent cesarean section, n (%) | 14 (28.0) |
| Drainage, n (%) | 9 (18.0) |

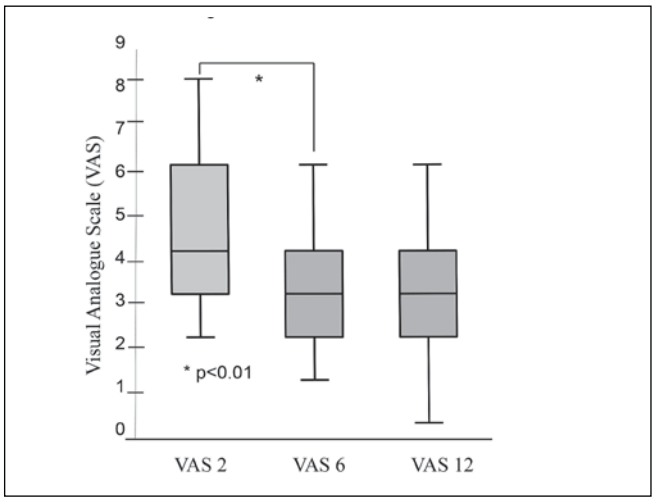


**Figure 1.** Whiskers Box Plot for Visual Analogue Scale (VAS) measured at 2, 6 and 12 hours following cesarean section.

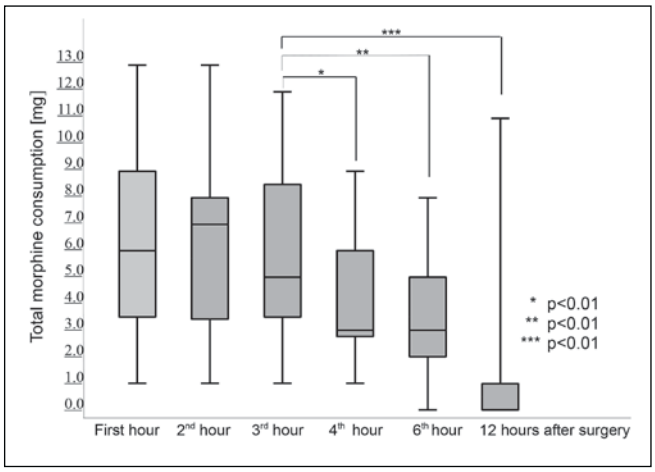


**Figure 2.** Whiskers Box Plot for total morphine consumption measured at 1, 2, 3, 4, 6 and 12 hours following cesarean section.

## Results

Patient characteristics are presented in Table I.

There was only 1 case of itching, with 4 cases of nausea and 3 of postoperative vomiting.

Median of total morphine doses used in the postoperative period was 42.9mg (IQR 35.6 – 48.5), with median infusion time of 687.0 minutes (IQR 531.0 – 757.5).

Total morphine consumption measured at 1, 2 and 3 hours after cesarean section was not significantly different (6.0mg, 7.0mg, and 5.0mg respectively, $p>0.05$). Morphine consumption measured 3 hours after cesarean section differed significantly from consumption measured 4, 6 and 12 hours after the procedure (5.0mg vs. 3.0mg vs. 3.0mg respectively, $p<0.01$).

A Kruskal-Wallis analysis showed that pain severity as measured by VAS and total drug consumption improves after the third hour following cesarean section ($p<0.01$) (Figures 1 and 2). Median number of PCA attempts was 33 (IQR: 24 – 37), with median 11 placebo attempts (IQR: 3 – 27).

## Discussion

The findings of our study demonstrate that higher morphine demand is observed within the first 3 hours postoperatively. Interestingly, 99% of the patients did not require drugs 12 hours after surgery.

Several studies showed that intravenous morphine PCA after cesarean section provides optimal pain control [9-10]. Our study focused on morphine alone, whereas other studies compared morphine with other or same-class medications [9-12]. An observational study of 75 women undergoing elective cesarean section under epidural anesthesia demonstrated that self-administered intravenous morphine offers good pain relief with low incidence of adverse events. It was also shown that two other opioids provide similar efficacy and safety [11,12]. One clinical trial involving 42 patients showed that PCA after cesarean delivery is superior to intramuscularly administered opioids, providing an effective and safe means of managing post-cesarean pain [13].

In our study, median morphine consumption was 42.9mg and median infusion time of 687 minutes. An observational study of 52 women who underwent cesarean delivery with postoperative pain control with intravenous morphine PCA showed similar results, with mean morphine consumption of 50mg [14].

Additionally, these authors suggested that postoperative pain severity significantly improved during the first 6 hours after surgery. This is consistent with our results showing significant pain reduction after the first 3 hours following surgery.

The presented data show that incidence of adverse events such as nausea, vomiting and itching is very low on intravenous morphine PCA. A prospective, double-blind study of 48 women randomized to receive intravenous PCA with meptazinol or morphine following elective cesarean section demonstrated similar results [15].

In our study, optimal pain control was proven by the VAS analysis, number of PCA attempts, number of additionally requested doses, and overall drug consumption. Our data support the hypothesis that PCA provides satisfactory analgesia after cesarean section. A previously cited study also showed that meptazinol and morphine delivered via intravenous PCA provide optimal pain control that can be measured by total drug consumption over a 24h period, pain (visual analogue scores), and sedation scores [15].

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A randomized, double-blind study comparing a combination of morphine and alfentanil with morphine alone for PCA after cesarean section under spinal anesthesia showed that there were no differences between the groups in terms of PCA usage or VAS pain scores measured at 2, 4, 6 and 24 hours, what is consistent with our findings. Similarly to previously published data, the incidence of side-effects in the morphine group in that study was low [16].

Various authors of recently published data based on a decision-tree model compared treatment with epidural analgesia (EDA) with PCA (morphine). Effects and costs of treatment were established, proving EDA to be more effective in terms of pain-free days but more expensive. The additional cost for each pain-free day was 5652 Euros [17].

## Conclusions

In conclusion, patient-controlled analgesia with morphine is an efficient, acceptable and cost-effective analgesic method in women undergoing cesarean section.

**Oświadczenie autorów:**

1. Marta Andziak – autor koncepcji i założeń pracy, przygotowanie manuskryptu i piśmiennictwa – autor zgłaszający i odpowiedzialny za manuskrypt.
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3. Jarosław Beta – autor założeń pracy, współautor tekstu pracy i protokołu, korekta i aktualizacja literatury.
4. Tadeusz Issat – współautor tekstu pracy, analizy i interpretacji wyników, przygotowanie, korekta.
5. Artur J. Jakimiuk – ostateczna weryfikacja i akceptacja manuskryptu.

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## References

1. Ranasinghe JS, David Birnbach D. Current Status of Obstetric Anaesthesia: Improving Satisfaction and Safety. *Indian J Anaesth.* 2009, 53 (5), 608–617.
2. Russell R, Lucas N. Obstetric anaesthesia guidelines. Int J Obstet Anesth. 2014 23 (2),101-5. doi: 10.1016/j.ijoa.2013.10.011. *Epub* 2013 Nov 19.
3. Miaskowski C. Patient-controlled modalities for acute postoperative pain management. *J Perianesth Nurs.* 2005, 20 (4), 255–267.
4. Lim Y, Jha S, Sia AT, Rawal N. Morphine for post-caesarean section analgesia: intrathecal, epidural or intravenous? *Singapore Med J.* 2005, 46 (8), 392-396.
5. Van de Velde M. What is the best way to provide postoperative pain therapy after caesarean section? *Curr Opin Anesthesiol.* 2000, 13 (3), 267-270.
6. Cooper DW, Saleh U, Taylor M, [et al.]. Patient-controlled analgesia: epidural fentanyl and i.v. morphine compared after caesarean section. *Br J Anaesth.* 1999, 82 (3), 366-370.
7. Rzepka R, Żukowski M, Michalczyk M, [et al.]. The influence of patient-controlled epidural analgesia on labor progress and neonatal outcome. *Ginekol Pol.* 2012, 83, 92-98.
8. Momeni M, Crucitti M, De Kock M. Patient-controlled analgesia in the management of postoperative pain. *Drugs.* 2006, 66 (18), 2321-2337.
9. Cade L, Ashley J. Towards optimal analgesia after caesarean section: comparison of epidural and intravenous patient-controlled opioid analgesia. *Anaesth Intensive Care.* 1993, 21 (5), 696-699.
10. Capogna G, Celleno D, Sebastiani M, [et al.]. Continuous intravenous infusion with patient-controlled anesthesia for postoperative analgesia in cesarean section: morphine versus buprenorphine. *Minerva Anestesiol.* 1989, 55 (1-2), 33-38.
11. van der Vyver M, Halpern S, Joseph G. Patient-controlled epidural analgesia versus continuous infusion for labor analgesia: a meta-analysis. *Br J Anaesth.* 2002, 89 (3), 459-465.
12. Bamgbade OA, Khalaf WM, Ajai O, [et al.]. Obstetric anesthesia outcome in obese and non-obese parturients undergoing caesarean delivery: an observational study. *Int J Obstet Anesth.* 2009, 18 (3), 221-225.
13. Perez-Woods R, Grohar JC, Skaredoff M, [et al.]. Pain control after cesarean birth. Efficacy of patient-controlled analgesia vs. traditional therapy (IM morphine). *J Perinatol.* 1991, 11 (2), 174-181.
14. Anwari JS, Butt A, Alkhunein S. PCA after subarachnoid block for cesarean section. *Middle East J Anesthesiol.* 2004, 17 (5), 913-926.
15. James KS, Davidson IT, McGrady E. Patient-controlled analgesia following caesarean section: a comparison of morphine and meptazinol. *Int J Obstet Anesth.* 1997, 6 (2), 93-96.
16. Ngan Kee WD, Khaw KS, Wong EL. Randomized double-blind comparison of morphine vs. a morphine-alfentanil combination for patient-controlled analgesia. *Anesthesia.* 1999, 54 (7), 629-633.
17. Bartha E, Carlsson P, Kalman S. Evaluation of costs and effects of epidural analgesia and patient-controlled intravenous analgesia after major abdominal surgery. *Br J Anaesth.* 2006, 96 (1), 111-117.