Postoperative Pain Management After Cesarean Section – A prospective Before-and-After Cohort Study on the Implementation of the Intraoperative Recommendation of the PROSPECT Guidelines

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Background

Inadequate pain relief remains a challenge after Cesarean section (CS) (O'carroll, Emrich) and may significantly impair postoperative recovery (Roofhooft, Ciechanowicz). A recent Danish single-center study (n=100) conducted at our institution revealed that 66% of elective CS patients experienced severe pain (NRS ≥ 7) during the first 24 hours, with the highest pain scores occurring within the initial 12 hours (Duch).

To optimize our current postoperative pain management for CS patients at our site, we have implemented recommendations for pain management from the PROSPECT guideline for procedure-specific postoperative pain management after CS (Figure 1) (Roofhooft, Roofhooft update), as recommended by the European Society of Regional Anaesthesia & Pain Therapy (ESRA).

The PROSPECT guidelines outline four key recommendations for clinical practice: 1) preoperative management, 2) intraoperative management after delivery, 3) postoperative care, and 4) surgical technique (Figure 1). At our center, we have already been adhering to the guidelines concerning postoperative care and surgical technique. We have now implemented the second recommendation, focusing on the intraoperative management after delivery, and implemented wound infiltration in combination with an ilio-inguinal field block, before closing the incision after CS (Roofhooft update). This approach is particularly relevant when intrathecal morphine (recommendation one) is not used, as is the case at our center, due to considerations regarding potential side effects (Roofhooft, Macones).

Studies reports that truncal nerve blocks provide analgesia for between 6 and 12 hours after CS (Hansen). This is particularly relevant in our setting, where patients report the most intense pain during the 6–12 hour period after CS (Duch), coinciding with the first mobilization and initiation of breastfeeding.

We have implemented an ilio-inguinal field block, placed using a landmark technique by the surgeon in combination with wound infiltration, at the end of surgery. This technique has demonstrated good pain scores after CS (Gharae) and provides an accessible approach for intraoperative pain management.

Additionally, following the PROSPECT guideline (Roofhooft), we have implemented intravenous dexamethasone (8mg), administered immediately after birth of the baby during CS. Studies of the CS population show that dexamethasone improves pain scores, prolongs the analgesic effects of local anesthetics, and reduces opioid consumption (Singh/Jeetinder/Neha).

We designed a before-and-after study with the aim of investigating whether our new practice of adding wound infiltration, an ilio-inguinal field block, and intravenous dexamethasone intraoperatively reduces the incidence of postoperative pain in the early period following CS.

Methods

Ethics and approvals

This study complies with the Helsinki declaration. Participation was voluntary, and informed consent was obtained from each patient during the inclusion process. Consent could be withdrawn at any time. Approval for data collection, handling, and storage were granted by the data protection authority for the Capital Region of Denmark (Region Hovedstaden) with case number P-2023-90. The Research Ethics Committee for the Capital Region of Denmark (Region Hovedstaden) waived the need for approval due to Danish legislation (Case number F-23004686). The study protocol will be available on clinicaltrials.gov.

Study design

A prospective, single-center before- and after cohort study. This study evaluates the quality of pain management after CS in our clinical unit following the implementation of intra-operative elements of an established treatment approach (PROSPECT) and is based on patient-reported outcomes and clinical data from electronic health records. The study is not an intervention study. We evaluate the routinely used protocols in our center before and after modification of the standard protocol.

Setting

Our Danish hospital in the Capital Region handles approximately 4,000 births including 400 elective CS annually (Danish birth registry).

We have a sample size of 100 historical CS patients with prospective data collection from before the implementation. The patients were included in a study testing the feasibility of electronic text messages for questionnaires on pain from December 2022 to June 2023 (Duch). In this study we plan to include elective CS patients after the implementation in a period between January 2025 and April 2025.

The setting, eligibility criteria, data collection and patient reported outcomes is the same for both groups before and after changing our standard pain management protocol.

Data collection

All data are entered directly into the closed and secure system, REDCap (Harris). Questionnaires are sent to the patient at 6, 12, 18, 24, and 48 hours after the CS. The questionnaires are delivered to the patient's smartphone as a text message with a link to a questionnaire in REDCap. Time-limits for responses are set at 3 hours after sending questionnaires. Baseline and perioperative data will be extracted from health records.

Development and validation of questions:

The questions for the patient reported outcomes were developed with inspiration from international consensus regarding obstetric recovery, including the incorporation of the Obs-QoR-10 score (Sultan). Patients, maternity staff, anesthetists, and obstetricians was consulted to determine the key areas of focus during the first postoperative days after a cesarean section. Based on this, independent questions were developed and validated by using standardized methods for designing and conducting surveys (Eysenbach, Burns). The questions were created to be analyzed individually and not to aggregated into a single score. A validated pain score (Numeric rating scale, NRS 0-10) was incorporated to ensure reliability. Subsequently, the questionnaires were programmed in the REDCap database (Harris) and designed to present well on a smartphone screen. Finally, the questionnaires were set-up to be sent out as a text message via an external server (Sure-SMS, Denmark) with links to the questionnaires in REDCap. The questionnaires consist of 10 short questions that can be answered on the phone in less than three minutes. With an addition of the Obstetric Quality of Recovery questionnaire 24 hours after CS, that consist of 10 short questions.

Anesthesia, surgery, postoperative analgesia, and recovery plan for elective CS

At our center, hyperbaric bupivacaine combined with fentanyl are used for spinal anesthesia for CS.
The surgical procedure is performed using the Joel-Cohen method with blunt dissection of tissue layers. The uterus is either repaired extra-abdominally or in situ. Standardized postoperative pain management consist of fixed doses of paracetamol and NSAIDs, supplemented with oral morphine on request. Breastfeeding (if not declined by the mother) are initiated immediately after the birth, either in the operating room or shortly thereafter. Early mobilization within six hours post-CS is encouraged. The urinary catheter is removed after the first mobilization. The general aim for discharge to home are within 48 hours.

The description above indicates that our site follows the PROSPECT guideline, regarding surgical technique and postoperative pain management as shown in Figure 1 (Roofhooft update). In addition, we have recently incorporated the PROSPECT recommendations for intraoperative pain management, with intravenous dexamethasone 8 mg administered right after delivery, wound infiltration, and an ilio-inguinal field block.

A total of 40 ml of ropivacaine 3.75 mg/ml is administered as a local anaesthetic for wound infiltration (single shot) and an ilio-inguinal field block, using a landmark technique intended to target areas associated with the iliohypogastric nerve, as well as the anterior rectus muscle fascia, rectus sheath, and subcutaneous tissue (Gharae).

Figure 1. Box 1 from the PROSPECT guidelines (Roofhooft update):

Box 1 Updated recommendations for pain management in patients undergoing elective caesarean section.

Pre-operatively

- Intrathecal long-acting opioid (e.g. morphine 50–100 μg or diamorphine up to 300 μg). Epidural morphine 2–3 mg or diamorphine up to 2–3 mg may be used as an alternative, for example, when an epidural catheter is used as part of a combined spinal–epidural technique
- Oral paracetamol

Intra-operative after delivery

- Intravenous paracetamol if not administered pre-operatively
- Intravenous non-steroidal anti-inflammatory drugs at the end of surgery
- Intravenous dexamethasone
- If intrathecal morphine is not used, local anaesthetic wound infiltration (single shot) and/or continuous wound infusion and/or fascial plane blocks such as transversus abdominis plane blocks, erector spinae plane blocks and quadratus lumborum blocks

Postoperative

- Oral or intravenous paracetamol
- Oral or intravenous non-steroidal anti-inflammatory drugs
- Opioid for rescue or when other recommended strategies are not possible (e.g. contraindications to regional anaesthesia)
- Analgesic adjuncts include transcutaneous electrical nerve stimulation

Surgical technique

- Joel-Cohen incision
- Non-closure of peritoneum
- Abdominal binders

Participants

Elective CS Patients will be approached for inclusion in the postoperative care unit shortly after the CS and included as continuously as possible in the inclusion period.

Inclusion criteria

Patients who undergo planned cesarean section under spinal anesthesia.
Patients who speak and read Danish and can provide informed consent to participate.
Patients who have a mobile phone that can receive a text message with a link to a questionnaire that can be accessed on an online website on the phone.
Age ≥ 18 years

Exclusion criteria

The study excludes patients with daily opioid use.

Multiple pregnancies (gemelli or more).
Insulin-treated diabetes.
Chronic pain patients.
Unplanned CS.

Outcomes

Primary outcome:

- Pain at movement at 6 hours after CS (Moving from lying to sitting position), NRS 0-10

Secondary outcomes

- Pain at movement at 12 hours after CS (Moving from lying to sitting position), NRS 0-10
- Severe pain (NRS ≥ 7), at any time within the first 24 hours after CS. NRS 0-10
- Opioid consumption during the first 24 hours after CS. (oral morphine equivalents, mg)
- Pain at movement at 18, 24 after CS (Moving from lying to sitting position). NRS 0-10
- Severe pain (NRS ≥ 7), at 6, 12, 18, 24 hours after CS. NRS 0-10
- Pain at rest at 6, 12, 18, 24 hours after CS. NRS 0-10.
- Satisfaction with pain-treatment during the first 24 hours after CS. Rated from 0-10

Exploratory:

- Patient reported: “Been out of bed during the last 6 hours”, asked at 6, 12, 18, 24 and 48 hours after CS. Yes/No.
- Patient reported: “Did pain impact how often you got out of bed during the last 6 hours?” Asked 6, 12, 18, 24, 48 hours after CS. From 0-10
- Patient reported: “Did pain impact how much you have breastfed or bottle-fed the infant in the last 6 hours?” Asked 6, 12, 18, 24, 48 hours after CS. Rated from 0-10
- Nausea after 6, 12, 18, 24, and 48 hours after CS. Rated from 0-10
- Dizziness after 6, 12, 18, 24, and 48 hours after CS. Rated from 0-10
- Itching after 6, 12, 18, 24, and 48 hours after CS. Rated from 0-10
- Location of pain at 6, 12, 18, 24, 48 hours after CS: Stomach/Shoulder/Other location.
- Obs-Qor-10 questionnaire, at 24 hours after CS (Ciechanowicz)
- Response rate for questionnaires 6, 12, 18, 24, and 48 hours after CS. (%)
- Opioid consumption during 25-48 hours after CS. (oral morphine equivalents, mg)
- Pain at movement at 48 hours after CS (Moving from lying to sitting position). NRS 0-10
- Pain at rest at 48 hours after CS. NRS 0-10.

Sample size considerations

The sample size estimation was based on our primary outcome: Pain during movement 6 hours after cesarean section (CS), measured using a numeric rating scale (NRS) from 0 to 10. A change of one point on

the NRS was deemed clinically relevant. In the "before" group (n = 78), the baseline mean for the primary outcome was NRS 6.76 (SD 1.90)**.** A power analysis performed using G*Power (Faul) with an alpha of 0.05 and a beta of 0.8 indicated that detecting a reduction to NRS 5.76 (SD 1.90) in the "after" group would require a minimum of 45 patients, with an allocation ratio of 2:1.To account for an anticipated non-response rate of approximately 33% for the 6-hour questionnaire, we aim to include 60 patients in the "after" group.

Baseline and perioperative data to be extracted from health records

- Age
- BMI
- ASA
- Indication for CS:
    - Maternal request/previous CS as sole indication
    - Obstetric or fetal indication
- Pregnancy related illness
    - Gestational diabetes, preeclampsia or other
- Number of prior CS
- Rescue nerve block or epidural
- Duration of surgery
- Extorization of uterus during CS
- Opioid consumption within the first 48 hours.
- Lengh of hospital stay, hours

Data Processing and statistics

All data will be handled in the secure REDCap database. Descriptive statistics will be used to analyze data. Continuous data will be summarized as median (interquartile range) or mean if the data is normally distributed, and categorical data as frequency (percentage).

To compare the primary and secondary outcomes between the two groups before and after the implementation, we will use a two-sample t-test for continuous variables if the data is normally distributed. For non-normally distributed data, a Wilcoxon rank-sum test will be applied. For categorical variables, a Chi-squared test will be used to compare the distribution of responses between the groups. A p-value of < 0,05 is considered significant.

We will try to minimize missing data as much as possible, by sending questionnaires directly to the participants mobile phones and including the patients face-to-face. The number of missing data will be accounted for when describing data.

References (alphabethecal)

Adesope O[1], Unyime Ituk, Ashraf S Habib. Local anaesthetic wound infiltration for postcaesarean section analgesia: A systematic review and meta-analysis. Eur J Anaesthesiol. . 2016 Oct;33(10):731-42. doi: 10.1097/EJA.0000000000000462.

Burns, Karen E A, Mark Duffett, Michelle E Kho, Maureen O Meade, Neill K J Adhikari, Tasnim Sinuff, and Deborah J Cook. 2008. "A Guide for the Design and Conduct of Self-Administered Surveys of Clinicians." CMAJ : Canadian Medical Association Journal = Journal de l'Association Medicale Canadienne 179 (3): 245–52. https://doi.org/10.1503/cmaj.080372.

Ciechanowicz, S, T Setty, E Robson, C Sathasivam, M Chazapis, J Dick, B Carvalho, and P Sultan. 2019. Development and Evaluation of an Obstetric Quality-of-Recovery Score (ObsQoR-11) after Elective Caesarean Delivery." British Journal of Anaesthesia 122 (1): 69–78. https://doi.org/10.1016/j.bja.2018.06.011.

Duch, P, Jørgensen C, Nedergaard H. Text message questionnaires for Patient-Reported Outcome Measures after Cesarean section-A feasibility study. Acta Anaesthesiol Scand. 2024 Oct;68(9):1254-1260. doi: 10.1111/aas.14477.

Emrich et al. Risk Factors for Severe Pain and Impairment of Daily Life Activities after Cesarean Section—A Prospective Multi-Center Study of 11,932 Patients. J Clin Med. 2023 Nov 9;12(22):6999. doi: 10.3390

Eysenbach, Gunther. 2004. "Improving the Quality of Web Surveys: The Checklist for Reporting Results of Internet E-Surveys (CHERRIES)." J Med Internet Res 6 (3): e34. https://doi.org/10.2196/jmir.6.3.e34.

Faul, F., Erdfelder, E., Lang, A.-G., & Buchner, A. (2007). G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior Research Methods*, *39*, 175-191

Gharae, N, Roofthooft, E, FIletIccI, N, Devroe, S, Vanhove, Ph, Rex, S, Van de velde, M. Postoperative pain after cesarean section: an audit of practice after implementation of the PROSPECT recommendations. Acta Anaesth. Belg., 2021, 72, 109-113

Hansen, Christian K, Mette Dam, Gudny E Steingrimsdottir, Gunnar Hellmund Laier, Morten Lebech, Troels Dirch Poulsen, Vincent W S Chan, Morné Wolmarans, Thomas Fichtner Bendtsen, and Jens Børglum. 2019. "Ultrasound-Guided Transmuscular Quadratus Lumborum Block for Elective Cesarean Section Significantly Reduces Postoperative Opioid Consumption and Prolongs Time to First Opioid Request: A Double-Blind Randomized Trial." Regional Anesthesia and Pain Medicine, July.

https://doi.org/10.1136/rapm-2019-100540.

Harris, Paul A, Robert Taylor, Robert Thielke, Jonathon Payne, Nathaniel Gonzalez, and Jose G Conde. 2009. "Research Electronic Data Capture (REDCap)—A Metadata-Driven Methodology and Workflow Process for Providing Translational Research Informatics Support." Journal of Biomedical Informatics 42 (2): 377–81. https://doi.org/https://doi.org/10.1016/j.jbi.2008.08.010.

Macones GA, Caughey AB, Wood SL, Wrench IJ, Huang J, Norman M, Pettersson K, Fawcett WJ, Shalabi MM, Metcalfe A, Gramlich L, Nelson G, Wilson RD. Guidelines for postoperative care in cesarean delivery: Enhanced Recovery After Surgery (ERAS) Society recommendations (part 3). Am J Obstet Gynecol 2019; 221: 247.e1-247.e9. doi: 10.1016/j.ajog.2019.04.012

J E O'Carroll [1], L Zucco [2], E Warwick [3], G Arbane [2], S R Moonesinghe [4], K El-Boghdadly [2], N Guo [1], B Carvalho [1], P Sultan [1]; ObsQoR Collaborators. Quality of recovery following childbirth: a prospective, multicentre cohort study. Anaesthesia. 2023 Sep;78(9):1071-1080. doi: 10.1111/anae.16039.

Roofthooft, E, G P Joshi, N Rawal, and M Van de Velde. 2021. "PROSPECT Guideline for Elective Caesarean Section: Updated Systematic Review and Procedure-Specific Postoperative Pain Management Recommendations." Anaesthesia 76 (5): 665–80. https://doi.org/10.1111/anae.15339.

E. Roofthooft, G. P. Joshi, N. Rawal, M. Van de Velde, on behalf of the PROSPECT Working Group of the European Society of Regional Anaesthesia and Pain Therapy. PROSPECT guideline for elective caesarean section: an update. First published: 27 April 2023. https://doi.org/10.1111/anae.16034

N P Singh [1], D Monks [2], J K Makkar [3], A Palanisamy [2], P Sultan [4], P M Singh [2]. Efficacy of regional blocks or local anaesthetic infiltration for analgesia after caesarean delivery: a network meta-analysis of randomised controlled trials. Anaesthesia. . 2022 Apr;77(4):463-474. doi: 10.1111/anae.15645. Epub 2021 Dec 27.

Singh N P/Jeetinder K Makkar, Nidhi Bhatia, Preet Mohinder Singh. The analgesic effectiveness of ilioinguinal-iliohypogastric block for caesarean delivery: A meta-analysis and trial sequential analysis. Eur J Anaesthesiol. 2021 Aug 1;38(Suppl 2):S87-S96. doi: 10.1097/EJA.0000000000001379.

N P Singh/Jeetinder Kaur Makkar/Neha Yadav, Basavana Gouda Goudra, Preet Mohinder Singh. The analgesic efficacy of intravenous dexamethasone for post-caesarean pain: A systematic review with meta-

analysis and trial sequential analysis**.** Eur J Anaesthesiol. 2022 Jun 1;39(6):498-510. doi: 10.1097/EJA.0000000000001626. ´