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Postoperative Analgesia and Cesarean Section under General Anesthesia: Multicenter Study

Ghislain Edjo Nkilly[1*], Raphael Okoue Ondo[1], Pascal Christian Nze Obiang[2], Stéphane Oliveira[3], Jean-Marcel Mandji-Lawson[3], Romain Tchoua[1]

[1]Department of Anesthesia and Intensive Care, Omar Bongo Ondimba Army Training Hospital (HIAOBO), Libreville, Gabon
[2]Department of Anesthesia and Intensive Care, Jeanne Ebori Fondation, Libreville, Gabon
[3]Department of Anesthesia and Intensive Care, Akanda Army Training Hospital, Libreville, Gabon
Email: *edjonkillyghislain@yahoo.fr

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Abstract

Background: Neuraxial anesthesia with intrathecal morphine is the reference technique in cesarean section anesthesia for the management of postoperative analgesia. If there is a contraindication to this, general anesthesia is required. The objective of the study was to evaluate the analgesic effectiveness of 4 analgesic techniques performed during cesarean section under general anesthesia in two centers with different anesthetic practices (North Franche Comté Hospital and Omar Bongo Ondimba Army Training Hospital). **Method:** This is a retrospective and descriptive study over 2 years, from January 1, 2019 to December 31, 2020. It involved evaluating the analgesic effectiveness and tolerance of morphine in the epidural catheter, wound infiltration, intravenous analgesia and Transversus Abdominous Plane block (TAP block) from the post-anesthesia care unit (PACU) until the 4th post-operative day. **Results:** Of the 354 cesarean sections performed, 84 (11.14%) received general anesthesia. The average age was 32.27 years. Acute fetal distress was the first indication for cesarean section (45.2%), followed by hemorrhagic placenta previa (10.7%) and prolapse of the cord (8.33%). Morphine in the epidural catheter was the most used (47.6%) followed by parietal infiltration (36.9%), intravenous analgesia (13.1%) and TAP block (2.38%). The analgesic effectiveness was comparable between the techniques from postoperative day 0 to day 4. No difference in side effects. Postoperative morphine consumption was significantly reduced ($p = 0.011$) in the infiltration (9 mg) and TAP block (9mg) groups compared to the epidural catheter (16 mg) and intravenous analgesia (17 mg). No difference in 02 rehabilitation criteria (ambulation, first bowel movement). No difference in the occurrence of chronic pain. **Conclusion:** In the event of a cesarean section under general anesthesia, there are effective and well-tolerated alternatives to neuraxial anesthesia, particularly regional anes-

thesia techniques (nerve blocks), particularly in countries with low availability of morphine.

Keywords

Cesarean, General Anesthesia, Morphine, Parietal Infiltration, Epidural Catheter, Transversus Abdominis Plane Block, Intravenous Analgesia

1. Introduction

Cesarean section rates have increased particularly in developed countries [1] [2]. According to the World Health Organization, 18 million cesarean sections are performed each year [2]. The increase in the global trend of the cesarean section presents a significant challenge to postoperative pain management globally. Caesarean section is associated with moderate-to-severe postoperative pain in a significant proportion of women, which may delay recovery and return to activities of daily living; impair mother-child bonding; impact maternal psychological well-being; and may complicate breastfeeding [3]. Furthermore, inadequate postoperative pain relief may lead to hyperalgesia and persistent postoperative pain [4]. Pain after caesarean section is often under-treated due to unfounded fears that analgesic drugs or interventions might induce maternal and neonatal side-effects and because the severity of post-caesarean section pain is often underestimated [5]. In the last decade, attention has shifted to reducing opioid use and to implementing protocols for enhanced recovery after caesarean section. The prevalence of postoperative pain after cesarean section remains high, ranging from 25.5% to 80% [6] [7] [8] [9] [10].

Most recommendations on analgesia after cesarean section have been made for cesarean sections performed under spinal anesthesia during which local and locoregional anesthesia techniques are strongly recommended [5].

The use of general anesthesia for cesarean delivery has declined in the last decades due to the widespread utilization of neuraxial techniques and the understanding that neuraxial anesthesia can be provided even in urgent circumstances.

The objective of the study was to analyze analgesic techniques in the management of post-cesarean pain under general anesthesia (GA) in two centers.

2. Material and Method

The study received approval from the ethics committee of the Omar Bongo Ondimba Army Training Hospital, Gabon military health service and Nord Franche Comte Hospital.

- Study design

This is a retrospective and descriptive study over 2 years, from January 1, 2019 to December 31, 2020. Study carried out in France (Nord Franche Comte Hospital) and in Gabon (Omar Bongo Ondimba army training hospital (HIAOBO)).

- Setting

Protocol: the techniques used were TAP block, morphine for epidural analgesia, parietal infiltration, and intravenous analgesia. In Gabon the most used techniques were intravenous analgesia, TAP block, in France all techniques were used. During the cesarean section, various analgesic techniques were carried out; however, all patients received an intravenous injection of paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs) or Tramadol. In the post-anesthesia care unit (PACU), patients who had received an epidural received 3 mg of morphine in PACU, intravenous analgesia was continued in the intravenous group. Postoperatively, in the event of insufficient analgesia, a titration of morphine (1 - 2 mg) or an addition of oral morphine derivatives was carried out. From Hour 10 post-operative (France) and day 1 post-operative (Gabon), the patients received an oral analgesia with level 1 and 2 analgesics (Paracetamol, NSAIDs, tramadol). The distribution of analgesic technique was not subject to randomization; it depended on practices and the degree of urgency of the cesarean section. We identified the files of patients who had undergone a cesarean section under general anesthesia. We divided them into 4 groups: TAP block group, parietal infiltration group, epidural morphine group and exclusive intravenous analgesia group.

- Participants

*Inclusion criteria: Patients who underwent a cesarean section under general anesthesia immediately or secondary to a conversion from epidural anesthesia were included.

*Non-inclusion criteria: cesarean section performed under regional anesthesia. Failed spinal anesthesia.

- Variables studied: for each analgesic technique were studied

The primary endpoint was the intensity of postoperative pain by Pain Score (Visual Analogue Scale (VAS)), in PACU, from Hour 8 to Hour 72 and on day 4.

The secondary endpoints were: Consumption of morphine equivalent postoperatively, side effects, two elements of postoperative rehabilitation: time to first get up and first bowel movement. The occurrence of chronic pain was also sought. Patients were contacted by telephone from the 2nd postoperative month to check for peri-scar pain.

The variables studied were obtained from medical records (sociodemographic variables, comorbidities), anesthetic records (anesthetic technique, drugs used, pain score in post anesthetic care unit) and hospitalization records (pain scores, side effects), rescue analgesia). All these variables were listed on a separate survey form in 2 periods (Post Anesthesia Care Unit) and hospitalization (Day 1 to Day 4). The patients were contacted by telephone from the 2nd month postoperatively to look for chronique pain.

- Data analysis

Data entry was done on WORD version 2010. The data was entered into an electronic XLSFORM form deployed using the KoboToolbox platform. The database thus formed was analyzed with the R 4.1.1 software (R Core Team, Vienna) in the RStudio 2021.09.0 environment.

- Bias

There is a risk of recruitment bias, analgesic techniques for cesarean section are not identical in the two countries, in Gabon, scar infiltration is non-existent, very little epidural analgesia, intravenous analgesia and TAP block are more common. In France, epidural analgesia is widely used. In addition, the failure of spinal anesthesia is a frequent reason for conversion to general anesthesia in Gabon.

- Study size

Given the retrospective nature and variability of the incidence of cesarean sections in the two centers, the calculation of the number of subjects necessary was not carried out.

- Quantitative variables

The quantitative variables were presented according to their means and standard deviations. The qualitative variables were presented according to their respective numbers and percentages.

- Statistical methods

We carried out a univariate and bivariate descriptive analysis. For the comparison of numerical variables, after checking normality by the Shapiro-Wilk test, non-parametric tests were used if necessary. Fisher's exact test was used for comparison of proportions.

3. Results

During the 2 years of study, 354 cesarean sections were performed, including 84 (11.14%) under general anesthesia. The average age was 32.27 years. The youngest patient was 21 years old and the oldest patient was 45 years old.

Acute fetal distress was the first indication for cesarean section under general anesthesia with a frequency of 45.2% of our sample. This indication is followed by hemorrhagic placenta previa (10.7%) and prolapse of the cord (8.33%).

All our patients received acetaminophen, 92.9% of patients on nefopam, and 84.5% on ketoprofen for a minimum of 48 hours. The most useful opioid was tramadol in 36.9% of patients. Strong opioids were used in 59.5% of patients. In the group of other drugs we had: ketamine, intra venous lidocaine and phoroglucinol.

Epidural morphine was the most used technique. Table 1 summarizes the analgesia techniques used.

Table 1. Distribution according to analgesia technique.

Analgesia techniques used	N (%)
Epidural morphine	40 (47.6%)
Wound infiltration	31 (36.9%)
Intra venous only	11 (13.1%)
Transversus abdominous plane block	2 (2.38%)

The pain scores were variable. **Tables 2-4** summarize the pain scores according to the analgesic technique.

In the group of patients who received 2 mg of morphine in the epidural catheter, 72.5% of patients presented moderate to unbearable pain when entering in the PACU. After titration of morphine in PACU, the pain subsided. At Hour 16, 45% of patients still have moderate to intense pain. This figure increases to 22.5% at Hour 48 and less than 10% at Hour 72 (Table 2).

In the group of patients who had parietal infiltration with 20 ml of 0.2% Ropivacaine. 25.8% of patients presented moderate to severe pain. No unbearable pain. More than half of the patients had no pain and 22.6% had mild pain. 4 hours later in the maternity ward we had 3.2% of patients presenting with unbearable pain, 12.9 with intense pain and 12.9 with moderate pain. At 48 hours 84% of patients presented with mild pain (Table 3).

In the group of patients receiving intravenous analgesia only, 54.6% of patients had moderate to unbearable pain upon entering the PACU. At Hour 4, 36.4% of patients presented moderate to severe pain. At Hour 48, 9.1% of patients still had severe pain. At Hour 72, 18.2% of patients still had moderate pain (Table 4).

The two in the TAP Block group presented mild pain upon entering the PACU, then moderate pain at Hour 4 and one of them presented unbearable pain at Hour 12.

Postoperative nausea and vomiting were the most frequent complications (11.9% of patients). There were 10% in the epidural morphine group compared

Table 2. Morphine epidural pain score.

	No pain (%)	Mild pain (%) VSA between 1 and 3	Moderate pain (%) VSA between 3 and 5	Severe pain (%) VSA between 5 and 7	Unbearable pain (%) VSA greater than 7
PACU	7.5	20	17.5	37.5	17.5
Hour 4	10	60	20	7.5	2.5
Hour 8	7.5	55	32.5	2.5	2.5
Hour 12	10	50	35	2.5	2.5
Hour 16	7.5	47.5	40	5	0
Hour 20	5	55	35	2.5	2.5
Hour 24	7.5	65	25	2.5	0
Hour 36	5	72.5	20	2.5	0
Hour 60	2.5	87.5	7.5	2.5	0
Hour 72	2.5	87.5	10.5	0	0
Day 4	7.7	89.7	2.5	0	0
Day 5	10	90	0	0	0

Table 3. Wall infiltration pain score.

	No pain(%)	Mild pain (%)	Moderate pain (%)	Severe pain (%)	Unbearable pain (%)
PACU	51.6	22.6	16.1	9.7	0
Hour 4	22.6	48.4	12.9	12.9	3.2
Hour 8	16.1	84.5	22.6	6.5	0
Hour 12	9.7	58.1	29	3.2	0
Hour 16	0	74.2	22.6	3.2	0
Hour 20	0	77.4	22.5	3.2	0
Hour 24	0	67.7	29.0	3.2	0
Hour 36	0	83.9	12.9	3.2	0
Hour 60	0	83.9	12.9	3.2	0
Hour 72	0	90.3	6.5	3.2	0
Day 4	9.7	87.1	3.2	0	0
Day 5	12.9	87.1	0	0	0

Table 4. Pain score _Intravenous only.

	No pain (%)	Mild pain (%)	Moderate pain (%)	Severe pain (%)	Unbearable pain (%)
PACU	0	100	0	0	0
Hour 4	0	63.5	27.3	9.1	0
Hour 8	9.1	81.5	9.1	0	0
Hour 12	9.1	54.5	18.2	18.2	0
Hour 16	9.1	81.5	9.1	0	0
Hour 20	0	90.9	9.1	0	0
Hour 24	9.1	63.6	27.3	0	0
Hour 36	9.1	81.8	0	9.1	0
Hour 60	9.1	81.8	0	9.1	0
Hour 72	18.2	63.6	18.2	0	0
Day 4	36.4	63.6	0	0	0
Day 5	36.4	63.6	0	0	0

to 19.4% for the parietal infiltration group. No patients showed signs of local anesthetic poisoning. Secondary outcomes are summarized in Table 5.

Chronic post-operative pain: six patients (7.14%) presented with chronic postoperative pain. Chronic postoperative pain was more frequent in patients on TAP block (50%, n = 2) after 3 months on average followed by patients on intravenous analgesia alone (9.1%) after 5.25 months and 6.5% for parietal

Table 5. Secondary endpoints.

	Intravenous only (n = 11)	Epidural morphine (n = 40)	Wound infiltration (n = 31)	Transversous abdominal plane bloc (n = 2)	p
Equivalent consumption of post-operative oral morphine (mg)	16.18 mg	17.53 mg	9 mg	9 mg	0.011
First bowel movement (hours)	69 h	73 h	70 h	55 h	0.4754
First rise (hours)	24 h	21 h	15 h	19 h	0.2176
Chronic pain number(%)	1 (1.9%)	2 (5%)	2 (6.5%)	1 (50%)	0.29

infiltrations after 2.38 months and 5% for the epidural group after 2.88 months (p value = 0.2898).

4. Discussion

The aim of the study was to analyze the effectiveness and tolerance of different analgesia techniques after cesarean section under general anesthesia.

1) Primary endpoint

With regard to the post-operative pain scores (Tables 2-4), the parietal infiltration was very effective despite poorly effective analgesia in the recovery room. There was a clear improvement over time until the 4th post-operative day, followed by epidural morphine and then intravenous analgesia.

Intravenous analgesia is quickly effective in the post-interventional monitoring room, then reduction in effectiveness over time, this reduction in effectiveness is related to ambulation, this analgesia is effective on rest pain and is not very effective on movement-related pain.

Our result is not isolated, the randomized study by Garmi [11] comparing scar infiltration and absence of infiltration found a superiority of infiltration on the post-operative pain score and the use of emergency analgesia. In 2009, A Cochrane database review [12] revealed that wound infiltration with local anesthesia was associated with decreased opioid consumption at 24 hours after cesarean delivery but did not reduce VAS scores Meta-analyses from 2016 [13] and 2021 concluded that wound infiltration with local anesthesia was associated with reductions in opioid consumption only among patients who did not receive intrathecal morphine.

Gaetano Riemma [14] compared scar infiltration and TAP block and did not find any differences in morphine consumption and postoperative pain scores at 24 and 48 hours postoperatively.

The Sina Grape Metaanalysis [15] on 7 randomized controlled studies (275 patients) concluded that there is moderate level evidence that TAP block and wound infiltration provide similar postoperative analgesia after caesarean section.

The meta-analysis by Pervez Sultan [16] on 42 studies (2906 patients) concluded that in the absence of a long-acting neuraxial opioid after cesarean delivery, single-dose TAP blocks and continuous infusion infiltrations are effective strategies on pain scores and to reduce opioid consumption, moreover both techniques were free of side effects such as nausea, vomiting, pruritus.

The Transversus Abdominus Plane block was effective, despite the small size of the group, studies confirm this data. The meta analysis of Abdallah [17] and Mishriky [18] show that TAP block improves postoperative analgesia after cesarean section in patients who did not receive spinal morphine but not in those who received intrathecal morphine.

2) Secondary endpoints

- Side effects

There was no significant difference between the different groups, although postoperative nausea vomiting (PONV) was the most represented (4 patients in the epidural morphine group and 6 patients in the parietal infiltration group). The whole difficulty is knowing what is the part of morphine in epidural and that linked to anesthetic drugs used during general anesthesia.

- Chronic pain

Approximately 7.14% of patients in our study population presented chronic pain with an average duration of onset of 3 months, a rate compatible with literature data which is 6% to 10%. although one would expect to have a higher rate because general anesthesia was described as a risk factor for chronic pain after cesarean section by NIKOLAJSEN *et al.* in 2004 [19]. There was no significant difference between the different groups ($p = 0.2898$). Among the risk factors for the occurrence of chronic pain after cesarean section found in most studies, there is insufficient analgesia in the first 48 hours postoperatively [20] [21].

The results of a metanalysis by El-Boghdadly *et al.* showed that QLB (Quadratus Lumborum block) and the TAP Block were superior to control in the absence of intrathecal morphine. However, when intrathecal morphine was administered, no difference was found between the truncal blocks and control [24]. Studies show that regional anesthesia techniques (particularly Quadratus Lumborum block (QLB) and Transversus Abdominis Plane Blocks (TAP Block)) considerably reduce the incidence of chronic pain after cesarean section [22] [23] The results of a metanalysis by El-Boghdadly *et al.* [24] showed that QLB and the TAP Block were superior to control in the absence of intrathecal morphine. However, when intrathecal morphine was administered, no difference was found between the truncal blocks and control.

Thus, the low rate of chronic pain in our series is the result of the different techniques used, knowing that spinal anesthesia with intrathecal morphine is the reference technique for reducing the risk of chronic pain after cesarean section [25].

- Rehabilitation elements

No significant difference on the rehabilitation elements (**Table 5**). The average time to first rise in our work was around 20 hours, which is greater than the

time limit of 6 - 8 hours currently recommended [26]. This figure is probably due to the degree of urgency because 24% of cesarean sections were code red due to obstetric pathologies endangering maternal and fetal prognosis (retroplacental hematoma, haemorrhagic placenta previa, severe preeclampsia). So the delay in ambulation is probably not due to pain but to anemia, post-ictal coma. There was no significant statistical difference between the groups although this delay in all groups remained well above that recommended. One might believe that general anesthesia is a risk factor for delayed ambulation after cesarean section. The average time to return to the stool was 71 hours, with no significant difference between the groups. The return to the stool was faster in the TAP block group is probably due to the small size of the sample (2 patients). The review of the literature by Ituk *et al.* [27] shows that the TAP block and wound infiltration improve rehabilitation after cesarean and can integrate an Enhanced Recovery After Surgery (ERAS) protocol.

- Opioid savings

There was a significant reduction in postoperative opioid consumption in favor of the groups receiving parietal infiltration and TAP block ($p = 0.011$) (**Table 5**). In the other groups, insufficient analgesia led to recourse to morphine titration. This data confirms studies on the effectiveness of regional anesthesia techniques.

- Limitations

Our study has several limitations: Retrospective study, the difference in size of each group, risk of selection bias: in fact, the surgical technique has not been standardized; moreover the distribution of the analgesia technique has not been randomized.

- Interpretation

Despite the small sample, our results can be compared to the literature.

- Generalisability

Our results are in agreement with other randomized studies and meta-analysis confirming good external validity.

5. Conclusion

The analgesic technique after cesarean section under GA which seems to provide the best analgesia, good opioid sparing and a low complication rate was parietal infiltration and TAP block. This is without increasing the rate of post-cesarean complications. Indeed, numerous studies report the effectiveness of regional techniques in cesarean section analgesia. Mekonnen's systematic review [28] and Ryu's meta-analysis [29] show the effectiveness of regional techniques, particularly parietal infiltration in cesarean section analgesia, even in the absence of neuraxial anesthesia as in our study. The difference in practice of the two centers did not play a major role in the analysis of the results. In the event of a contraindication to neuraxial anesthesia, alternative analgesic techniques are available with good effectiveness and tolerance.

Authors' Contributions

G. Edjo Nkilly: principal investigator, drafting the manuscript;
R. Okoue Ondo: inclusion and follow-up of patients;
PC. Nze Obiang: inclusion and follow-up of patients;
S. Oliveira: inclusion and follow-up of patients;
JM Mandji-Lawson: reading final manuscript;
R. Tchoua: reading and final approval of the manuscript.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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