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Naloxone for managing adverse effects of intrathecal morphine in spinal anesthesia**La naloxone pour la prise en charge des effets indésirables de la morphine intrathécale au cours de la rachianesthésie.****Bensafir Salim, Boucherit Aslane, Tidjane Anisse, Ourabah Anissa.**

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Abstract**Objective:** To assess the effectiveness of naloxone in preventing side effects of intrathecal morphine and its impact on postoperative pain.**Patients and methods:** This was a prospective, randomized, single-blind case-control study conducted over 1 year (November 1, 2023 - December 1, 2024). It focused on patients undergoing cesarean section under spinal anesthesia. Inclusion criteria were: ASA 1 and 2 patients eligible for cesarean section under spinal anesthesia with height greater than 150 cm. All patients received the same anesthetic protocol. The "case" group received 40 µg of naloxone systematically by intravenous bolus at the end of the procedure (M0). This dose was repeated only once at the sixtieth minute (M60) in the presence of adverse effects. Side effects were monitored and pain level was assessed during the first 24 hours after cesarean section. Sociodemographic and clinical parameters, morphine side effects, postoperative pain, and patient satisfaction were studied.**Results:** 300 patients were selected. 150 received naloxone and 150 were controls. Their mean age was 25.8 years. There was a reduction in pruritus ($p = 0.001$) without significant change in analgesia in the population who received naloxone. There was no significant difference in the occurrence of postoperative nausea and vomiting ($p > 0.05$). The "case" patients were more satisfied with the anesthetic protocol than the "control" patients ($p = 0.0023$).**Conclusion :** Naloxone could improve the comfort of patients receiving spinal anesthesia using morphine as an adjuvant.**Résumé****Objectif :** Évaluer l'efficacité de la naloxone dans la prévention des effets indésirables de la morphine intrathécale et son impact sur la douleur postopératoire.**Patients et méthodes :** Il s'agissait d'une étude prospective, randomisée, en simple aveugle de type cas-témoins menée sur 1 an (du 1er novembre 2023 au 1er décembre 2024). Elle portait sur des patientes bénéficiant d'une césarienne sous rachianesthésie. Les critères d'inclusion étaient : patientes ASA 1 et 2 éligibles pour une césarienne sous rachianesthésie avec une taille supérieure à 150 cm. Toutes les patientes ont reçu le même protocole anesthésique. Le groupe « cas » a reçu systématiquement 40 µg de naloxone en bolus intraveineux à la fin de l'intervention (M0). Cette dose a été répétée une seule fois à la soixantième minute (M60) en présence d'effets indésirables. Les effets secondaires ont été surveillés et le niveau de douleur a été évalué pendant les premières 24 heures après la césarienne. Les paramètres sociodémographiques et cliniques, les effets indésirables de la morphine, la douleur postopératoire et la satisfaction des patientes ont été étudiés.**Résultats :** 300 patientes ont été sélectionnées. 150 ont reçu de la naloxone et 150 constituaient le groupe témoin. Leur âge moyen était de 25,8 ans. Il y a eu une réduction du prurit ($p = 0,001$) sans modification significative de l'analgesie dans la population ayant reçu de la naloxone. Il n'y avait pas de différence significative dans la survenue de nausées et vomissements postopératoires.Soumis le 04/10/25Accepté le 13/12/25Mots clés :

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($p > 0,05$). Les patientes du groupe « cas » étaient plus satisfaites du protocole anesthésique que les patientes « témoins » ($p = 0,0023$).

Conclusion : La naloxone pourrait améliorer le confort des patients bénéficiant d'une rachianesthésie avec la morphine comme adjuvant.

Introduction

Spinal anaesthesia remains the technique of choice for most gynaecological and orthopaedic trauma procedures, and its use in caesarean section has been reported in up to 90% of cases [1,2]. Advances in pharmacology, equipment, and anaesthetic techniques have significantly enhanced patient safety and satisfaction. Nevertheless, the postoperative period is often marked by a constellation of symptoms collectively referred to as postoperative discomfort [3,4]. Optimising patient comfort during this critical phase requires effective strategies to prevent and manage adverse effects associated with anaesthetic agents. In this context, our study focuses on mitigating the side effects of intrathecal morphine administered during spinal anaesthesia for caesarean section. Specifically, we investigated the use of naloxone, an opioid antagonist, to prevent these complications while preserving the analgesic benefits of morphine.

Patients and methods

This was a prospective, randomized, single-blind case-control study conducted over a one-year period (November 1, 2023 to December 1, 2024). The study population consisted of parturients undergoing caesarean section under spinal anaesthesia.

Inclusion criteria were ASA physical status I or II, eligibility for caesarean section under spinal anaesthesia, and height greater than 150 cm. All patients received the same standardized anaesthetic protocol.

The case group received 40 µg of naloxone intravenously at the end of the procedure (M0). In the presence of adverse effects, this dose was repeated once at the sixtieth minute (M60).

Outcomes assessed included sociodemographic and clinical parameters, morphine-related side effects, postoperative pain, and patient satisfaction. Adverse effects (pruritus, nausea, vomiting) and pain intensity were evaluated at four time points:

- At the end of the intervention (M0)
- One hour after surgery (M60)
- Between the first and twelfth postoperative hour (H1–H12)
- Between the twelfth and twenty-fourth postoperative hour (H12–H24)

Parameters studied were:

- Epidemiological: age, occupation, educational level

- Clinical: anaesthetic data, adverse effects, pain intensity (Numeric Rating Scale, NRS) at M0, M60, H1–H12, and H12–H24, and patient satisfaction

Data analysis was performed using Microsoft Word 2010 and Epi Info 3.5.4 software. Quantitative variables were expressed as means with dispersion indices, while qualitative variables were presented as proportions. Comparisons of qualitative variables were carried out using chi-square and Fisher's exact tests.

Results

The mean age was 28.83 $\pm$ 6.41 years (extremes of 17 and 45 years) (Table I). About two-sixths (2/6) of the patients had undergone caesarean section at least once in the two populations. Acute fetal distress was the most common surgical indication and the ASA1 class was the most represented in both populations.

Tableau I : Répartition selon les données cliniques et les indications opératoires.

Paramètres	Cas	Témoin	Total (%)
Age (année)	15-25	27	36
	25-35	82	82
	> 35	41	32
ASA	1	111	128
	2	39	22
Indications	Circulaire du cordon	23	20
	Gros fœtus	17	22
	HTA	9	5
	Mauvaise présentation	18	23
	Prééclampsie	11	16
	Souffrance fœtale aigue	38	34
	Autres	34	30

At the end of the intervention (M0) There was no significant difference between the two groups concerning the occurrence of pruritus ($\chi^2 = 0.38$ $p = 0.53$) and postoperative nausea and vomiting (PONV) ($\chi^2 = 0.57$ $p = 0.45$). None of the patients in the two groups felt any pain. 60 Minutes after the procedure (M60) Patients who received the naloxone at M0 presented less pruritus than the controls with a significant difference (OR: 0.30; 95% (0.15-0.4); $p < 0.0001$). The occurrence of PONV between H12 and H24 was more observed in “cases” (OR: 0.7 with 95% (0.16-3.58); $p = 0.7$). Postoperative pain was identical in both groups except that one patient in the "Control" group presented with intense pain after the twelfth postoperative hour (OR: 1.68 with

95%(0.51-6.23); $p=0.36$). (Table II) The patients who received naloxone were more satisfied (83/100) with the anesthetic protocol than the "Control" patients

(68/100) with a significant difference (OR: 3.89 with 95% (1.62-9.33); $p=0.0023$).

Tableau II : Evolution de l'intensité de la douleur de M0-M24.

période		M0		M60		H1-H12		H12-H24	
catégorie		Cas	Témoin	Cas	Témoin	Cas	Témoin	Cas	Témoin
Echelle numérique simple	0	150	150	134	149	145	146	142	139
	1-3	0	0	11	1	1	0	2	4
	4-6	0	0	5	0	4	4	6	6
	>7	0	0	0	0	0	0	0	1

M0 : Aucune patiente ne ressentait de douleur

M60 : OR : 0,087 (0,37-3,5) $p=0,1$

H01-H12 : OR=1 (0,24-4,07) $P=0,1$

H12-H24 : OR=1,78 (0,51-6,23) $P=0,36$

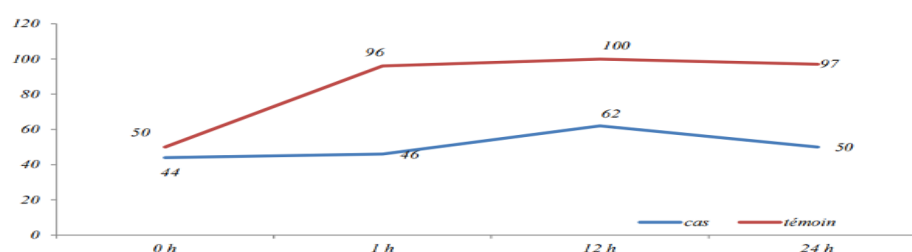


Figure 1 : Évolution des Prurits de M0 à H24

M0 : $\chi^2 = 0,38$ $p = 0,53$
M60 : OR : 0,24 ; 95%(0,15-0,4); $p < 0,0001$
H1-H12 : OR : 0,24 ; 95%(0,15-0,4); $p < 0,0001$
H12-H24 : OR: 0,27; 95%(0,16-0,4); $p < 0,0001$

Discussion

Our sample size was relatively small but representative, as the survey was conducted by a single investigator during duty hours (08:00–18:00), thereby reducing bias both at the patient level and in data collection. All patients received the same spinal anaesthesia protocol, with an identical intrathecal morphine dose of 200 μ g. This dose is generally considered safe and does not require specific postoperative monitoring in young subjects, as supported by previous studies [5,6].

The benefit of morphine as an adjuvant in spinal anaesthesia is well established in our context, particularly for its ability to prolong postoperative analgesia and reduce costs associated with additional analgesics [7,8]. However, this benefit is often accompanied by postoperative discomfort, as highlighted by Abé et al. [4]. Our study confirms the significance of these adverse effects within the first 24 hours after surgery, with distinct kinetics. Nausea and vomiting predominated in the immediate postoperative period up to one hour, whereas pruritus persisted

throughout the 24-hour period, peaking between the 12th and 24th hour (Figures 1 and 2).

At M0, before naloxone administration, pruritus was present in both groups (31.33%), though at lower rates than reported in other studies. A significant reduction was observed in patients who received naloxone at M0 (28.66%) compared to controls (61%). This finding is consistent with Choi JH's work in epidural anaesthesia, where naloxone significantly reduced pruritus ($p < 0.05$)

[9]. Between H1 and H12, pruritus was maximal, but reinjection of naloxone at M60 reduced its occurrence (41.33% vs. 66.66% in controls, $p < 0.0001$). This effect may be explained by the short duration of action of naloxone (approximately one hour) compared with the 12-hour interval used for assessment. Continuous administration of naloxone has been recommended by some authors to overcome this limitation [10]. From H12 to H24, pruritus remained lower in the case group (33.33%) compared to controls (64.66%, $p < 0.0001$), with regression noted in both groups, likely due to the

waning effect of morphine, whose duration of action ranges between 12 and 24 hours [11].

Regarding postoperative nausea and vomiting (PONV), no significant difference was observed between groups ($p > 0.05$). This aligns with previous studies reporting the ineffectiveness of naloxone in preventing PONV, with dexamethasone and serotonin receptor antagonists being more effective alternatives [12].

Postoperative pain assessment revealed no pain at M0 (NRS = 0) in both groups, consistent with prior studies demonstrating that intrathecal morphine provides analgesia for 12–24 hours [7,13]. At M60, 10.6% of patients in the naloxone group reported mild pain, compared with only one patient in the control group. No severe pain was observed. Although naloxone appeared to transiently reduce the analgesic effect of morphine, this difference was not statistically significant ($p = 0.1$), consistent with findings from other studies [14,15]. Importantly, this effect was not observed after the second dose of naloxone, likely due to its short half-life (approximately 45 minutes) and rapid onset (peak effect within 2 minutes). Overall, our findings suggest that low-dose naloxone effectively reduces pruritus without significantly compromising analgesia, though its short duration of action limits sustained benefit.

Conclusion

Postoperative side effects related to intrathecal morphine are common and often poorly tolerated, making their management challenging. Our study demonstrates that the administration of low-dose naloxone in the immediate postoperative period can partially improve patient comfort by significantly reducing the incidence of pruritus, without compromising the sensory block. However, naloxone proved ineffective in preventing postoperative nausea and vomiting. Further large-scale studies are warranted to establish the optimal protocol that balances effective analgesia with minimal adverse effects, thereby enhancing overall patient satisfaction in the postoperative period.

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