

## Research Article

# NALOXONE IN THE MANAGEMENT OF HARMFUL SIDE EFFECTS OF MORPHINE ADMINISTERED AS AN ADJUVANT IN SPINAL ANESTHESIA

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### ABSTRACT

**Objective:** Appreciate the effectiveness of antidote to pain killers in the treatment of the side effects of morphine administered intrathecally and its impact on post-operative pain. **Patients and method:** The study was a prospective, randomized, single-blind "case - control" study that took place over 1 year (November 1, 2023 - December 1, 2024). It focused on cesarean patients under spinal anesthesia. Were included: parturient ASA 1 and 2 eligible for a cesarean section under spinal anesthesia and having a size greater than 150 cm. All patients benefited from the same anesthetic protocol. The "case" population received 40 µg of naloxone systematically on IVD at the end of the intervention (M0). This dose was repeated only once in the sixtieth minute (M60) in the presence of adverse effects. Side effects were researched and the level of pain assessed during the first 24 hours after cesarean. The socio demographic, clinical parameters, the side effects of morphine, post-operative pain as well as patient satisfaction were studied. **Results:** 200 patients were selected. 100 received naloxone and the other 100 were controls. Their average age was 25.8 years. There was a regression of 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.

**Keywords:** Spinal anesthesia, naloxone, side effects of morphine. Painkillers, antidote.

### INTRODUCTION

Spinal anesthesia is the technique of choice applicable to most gynecological and trauma procedures. The practice of spinal anesthesia for caesarean section was 90% [1,2]. Advances in pharmacology, devices and techniques have contributed to increasing the safety of anesthesia and improving patient satisfaction. This post-operative period is characterized by numerous symptoms, defined as "malaise syndrome" [3,4]. In order to improve patient comfort in the postoperative period, our study aims to prevent and/or treat the side effects of morphine during spinal anesthesia for caesarean section. For us, it was a question of administering Naloxone (antidote to morphine) to prevent these side effects postoperatively while avoiding lifting the analgesic effect of morphine.

### PATIENTS AND METHOD

This was a prospective randomized single-blind "case-control" study that took place over 1 year (November 1, 2023-December 1, 2024). It focused on caesarean patients under spinal anesthesia. Were included: ASA 1 and 2 parturients eligible for caesarean section under spinal anesthesia and having a height greater than 150 cm. All patients received the same anesthetic protocol. The "case" population received 40 µg of naloxone systematically by IVD at the end of the procedure (M0). This dose was repeated once at the sixtieth minute (M60) in the presence of adverse effects. The side effects were sought and the level of pain assessed during the first 24 hours after the cesarean section. Sociodemographic and clinical parameters, side effects of morphine, postoperative pain and patient satisfaction were studied. The aim was to collect information on the adverse

effects (pruritus, nausea and vomiting) and the level of pain: at the end of the intervention (M0); one hour after surgery (M60); between the first hour and the twelfth postoperative hour (H1-H12); and between the twelfth and twenty-fourth postoperative hour (H12-H24) in both populations. The parameters studied were: Epidemiological: age, profession, school level. Clinical: anesthetic data, adverse effects and pain intensity (ENS) at M0, at M60, between H1 and H12, between H12 and H24 postoperatively, The level of patient satisfaction. The data was processed with Microsoft Word 2010 and Epi Info 3.5.4 software. The quantitative variables were expressed as a mean together with their dispersion indices and the qualitative data in proportions. The comparison of the qualitative variables was made with the statistical tests of Chi Deux, of Fisher.

### RESULTS

The mean age was 28.83 +/-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. Naloxone in the treatment of side effects of morphine in spinal anesthesia. Total Age (years) [15 - 25] 27 36 53 (21%) [25 - 35] 71 82 164 (52.66%) > 35 41 32 76 (24.33%) ASA 1 111 128 239 (79.67%) 2 39 22 61 (20.33%) Indications Circular cord 23 20 43 (14.33%) Large newborn 17 22 39 (13%) High blood pressure 9 5 14 (9.33%) Poor presentation 18 23 41 (13.66%) Preeclampsia 11 16 27 (9%) Acute fetal distress 38 34 72 (24%) Other 34 30 64 (21.33%) 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

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(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 (143/150) with the anesthetic protocol than the "Control" patients (126/150) with a significant difference (OR: 3.89 with 95% (1.62-9.33);  $p=0.0023$ ). Figure 1: Evolution of pruritus from M0 to H24 M0:  $\chi^2 = 0.38$   $p = 0.53$  M60: OR: 0.24; 95% (0.15-0.4);  $p < 0.0001$  Table II: Evolution of pain intensity from M0 to H24 Period M0 M60 H1-H12 H12-H24 Category Case Control Case Control Case Control Simple Numerical Scale (ENS) 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 1 M0: No patient felt pain M60: OR: 0.087 95 % (0.37-3.5);  $p=0.1$  H1-H12: OR: 1 95% (0.24-4.07);  $p=0.1$  H12-H24: OR: 1.78-95% (0.51-6.23);  $p=0.36$  44 46 62 50 50 96 100 97 0 20 40 60 80 100 120 0h 1h 12h 24h . Naloxone in the treatment of side effects of morphine in spinal anesthesia. Our sample is relatively small but representative because the survey was carried out by a single person during duty hours (08:00-18:00) in order to reduce bias both at the level of the patients and of the survey. Our spinal anesthesia protocol was the same for all patients. The dose of morphine (200 $\mu$ g) was identical in all patients. This dose does not require any particular post-operative monitoring, especially in young subjects, as evidenced by various studies [5, 6]. The benefit of morphine as an adjuvant in spinal anesthesia no longer needs to be demonstrated in our context due to the extension of postoperative analgesia and the reduction in expenses related to analgesics [7, 8]. However, this generated benefit is often accompanied by discomfort in the postoperative period as noted in the study by Abé *et al.*, [4]. Our study confirms the importance of these adverse effects in the first 24 hours after surgery at different kinetics. It was noted that nausea and vomiting were preponderant in the immediate postoperative period up to one hour later, while the pruritus persisted significantly until the 24th hour with a peak between the 12th and 24th hour in the postoperative period. (figures 1 and 2) With regard to pruritus, At the end of the intervention (M0) and before the injection of naloxone in the "case" population pruritus was present in the 2 populations (31.33%) but more lower than those found in other studies. A significant reduction in pruritus was noted in patients who received naloxone at M0 (28.66%) compared to 61% in "control" patients with a significant difference. Thus 40 $\mu$ g of naloxone by IVD in the immediate postoperative period (M0) reduced the occurrence of pruritus. This observation was made in the work of Choi JH in epidural anesthesia [9] where pruritus was significantly reduced in the population having received naloxone ( $p < 0.05$ ). From H1 to H12, the populations having received naloxone at M0 and M60 showed less pruritus (41.33%) than the control population (66.66%) with a statistically significant difference ( $p < 0.0001$ ). 13 7 7 3 18 6 1 4 0 2 4 6 8 10 12 14 16 18 20 0h 1h, pruritus was maximal and reinjection of a second dose reduced the occurrence of pruritus. This could be explained by the short duration of action of naloxone (approximately one hour) and the time interval to assess its impact which is 12 hours. To compensate for these effects, some authors recommend the continuous administration of naloxone [10]. From H12 to H24, the "case" population had less pruritus (33.33%) than the "control" population (64.66%) ( $p < 0.0001$ ). We also observed a regression of pruritus in both populations. This could be explained by the decrease in the effect of morphine, the duration of action being between 12 and 24 hours [11]. Concerning PONV Depending on whether the population studied received doses of naloxone or not, there was no significant difference in the occurrence of PONV ( $p > 0.05$ ). Indeed, several studies confirm the ineffectiveness of naloxone in the prevention of nausea and vomiting. Dexamethasone, serotonin

receptor antagonists are instead proposed [12]. Regarding postoperative pain at M0, we noted no pain (ENS=0) in the two populations as demonstrated by several previous studies. Indeed, morphine used as an adjuvant in spinal anesthesia provides postoperative analgesia for 12 to 24 hours [7,13]. At M60, 10.6% of the patients who received naloxone felt pain, whereas in the "control" population, only one felt mild pain. None of the patients presented with severe pain. The naloxone administered reduced the analgesic effect, showing mild and moderate pain. However, there was no statistically significant relationship between naloxone and occurrence of pain ( $p = 0.1$ ). This has been the subject of numerous studies with identical observations [14,15]. This observation was not made after the 2nd dose of naloxone. It could be concluded that naloxone reduces the analgesic effect during the 1st hour after its administration. However, this reduction is brief due to its short half-life. The action is maximal in 2 minutes after intravenous injection. Its duration of action is short, about 45 minutes. Since after the 2nd injection of naloxone, the side effects are not immediately sought but rather the following 12 hours.

## CONCLUSION

Side effects related to intrathecal morphine are frequent postoperatively. They are poorly lived. Their care remains difficult. The administration of naloxone in the immediate postoperative period partially improves patient comfort by reducing the occurrence of pruritus without lifting the sensory block but remains ineffective on nausea and vomiting. Additional large-scale work is needed to define the ideal protocol that would improve patient comfort postoperatively.

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