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Case Report

Accidental Intrathecal Injection of Nilperidol® in Spinal Anesthesia. Case Report

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ABSTRACT

Some factors have been identified as contributing to medical errors such as labels, appearance, and location of ampoules. This report relates how droperidol associated with fentanyl (Nilperidol®) was given by mistake, intrathecally, during spinal anesthesia, to a 72-year-old man, who was a candidate for rectosigmoidectomy with ileostomy. When checking the ampoules used in spinal anesthesia, an error in the administration of droperidol along with fentanyl was noted. When preparing for general anesthesia, severe arterial hypotension occurred, which did not respond to the ephedrine injection. The use of norepinephrine was required but it was removed before extubation in the operating room. Upon entering PACU, he reported grade 8 pains and morphine was administered. The patient remained in the PACU for 2 hours and was referred to the infirmary without complaints, remaining conscious throughout the period. The patient was followed up by the Anesthesia Service until hospital discharge, which occurred after three days, without complaints or complications related to anesthesia. There was not any nervous disturbance observed within the week of follow up.

Keywords: Accidental injection, Intrathecal opioids injection, Spinal anesthesia, Droperidol.

Introduction

The subarachnoid space is an important anatomical site for drugs injection not only for performing spinal anesthesia but also for various medical specialties. In a recent review on inadvertent intrathecal injections and best practice management, 23 agents and their clinical manifestations and outcomes were cited [1].

Droperidol is a high-potency, rapid-acting butyrophenone like haloperidol that has been used in the Brazil since 1960. Fentanyl was opioid synthesized in the 1950s with potent analgesic activity and few adverse effects when compared to morphine. Nilperidol® manufactured in Brazil by Cristália Chemical Products Pharmaceuticals Ltd and presents the combination of a narcotic analgesic, fentanyl citrate (50 µg/ml), and a neuroleptic, droperidol (2.5 mg/ml), with the ampoule totaling 2 ml.

Droperidol has already been used in the epidural space with excellent results and few side effects [2, 3]. Although there are reports on a wide variety of medication errors in spinal anesthesia, accidental intrathecal use of drug containing the combination of fentanyl and droperidol (Nilperidol®), an association of a neuroleptic and opioid, has not been described previously.

Case Report

A type II diabetic, 72-yr-old man (75 kg) was scheduled for rectosigmoidectomy with ileostomy. Patient had no history of hypertension, cardiac arrhythmia, or hyperlipidemia. His hemoglobin was 12.0 g/dL, 39% hematocrit, 5,030,000/mm^3 red cells, and platelets 307,000/mm^3. Prothrombin time (13.9 seconds) and prothrombin activity (100%), with normal values. Creatinine 0.82 mg/dl, glucose 99 mg/dl, and potassium 5.3 mEq/l. The estimated glomerular

filtration was greater than 90 ml/min/ 1.73 m^2. ECG and chest X-ray unchanged. We obtained informed consent and discussed throughout the anesthetic technique with the patient and family.

Anesthetic technique with spinal anesthesia associated with general anesthesia has been proposed. Routine monitoring (electrocardiogram, pulse oximetry, and noninvasive blood pressure measurement) was placed and an intravenous line was established (18G). The initial vital signs assessments were of blood pressure (BP) 135x94 mmHg, heart rate (HR) 77 bpm and saturation 99% in room air the before induction of spinal and general anesthesia.

After sedation with midazolam (3 mg) intravenously and cleaning the skin with chlorhexidine and spinal puncture was performed with the patient in the sitting position, by the median line in the L_3-L_4 interspaces using 27 Quincke needle. After appearance of cerebrospinal fluid (CSF) 12.5 mg of 0.5% hyperbaric bupivacaine, 80 µg morphine and inadvertent intrathecal injection of 20 µg fentanyl and 0.10 mg droperidol (0.4 ml Nilperidol®) were administered at a speed of 1 $mL.15s^{-1}$.

Patients were immediately placed in the supine position to start general anesthesia. We noticed immediately after the injection when collecting the used ampoules (Figures 1, 2).

Immediately after spinal anesthesia, hypotension occurred (93x63 mmHg) with normal heart rate (79 bpm), injected IV 20 mg ephedrine. General anesthesia with denitrogenating was started, anesthetic induction with 2.5 mg alfentanil, 150 mg propofol and 10 mg cisatracurium, ventilation and tracheal intubation by laryngoscopy under direct visualization, without any complications.

However, after induction, there was a disproportionate hypotension to the anesthesia performed. Several doses of ephedrine were injected, however the blood pressure remained low and refractory to vasopressor medication (60x30 mmHg). Norepinephrine started at 0.04 µg/kg/min. Anesthetic plan maintained exclusively with propofol in a target TCI pump 3 µg ml, and supplementary doses of 5 mg of cisatracurium. Norepinephrine preserved hemodynamic stability having been reduced to the dose 0.02 µg/kg/min after the 2nd hour of surgery.

There was no oxygen desaturation or CO_2 retention during the entire procedure. The surgery lasted 3 hours. After this time, flumazenil 2.5 mg, atropine 1 mg, neostigmine 2 mg, dypirone 2 g and ondansetron 8 mg were administered with immediate extubation, and the norepinephrine was removed. The patient was stable with BP 106x70 mmHg, HR 68 bpm and oxygen saturation of 99%. Extubation was realized succefully. After extubation, the patient remained awake, responding to verbal requests, on spontaneous ventilation and without residual lower limb blockade. The patient received 2,400 ml of Ringer with Lactate and had 200 ml of diuresis. Anesthetic time was 3:30 hours.

In the PACU, he maintained BP 129x80 mmHg, HR 60 bpm and oxygen saturation of 99% in room air (Figure 3). The patient reported grade 8 pains and 4 mg morphine were administered, relieving the pain (grade 3). The patient stayed in the PACU for 2 hours and was referred to the infirmary without any complaints, remaining consciousness, and hemodynamic stability throughout this period.

Figure 1: Ampoules used for spinal anesthesia.

Figure 2: Nilperidol® and Fentanyl ampoules.

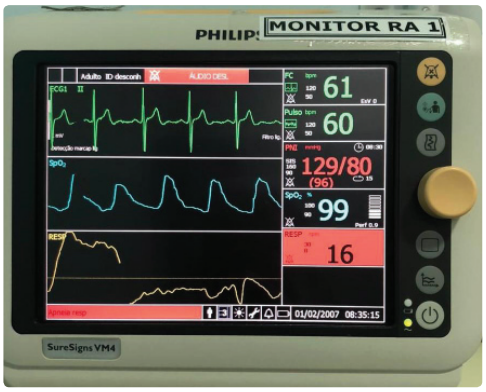

Figure 3: Vital signs in the PACU with atmospheric air.

The patient was discharged from the hospital after three days and followed up by the Anesthesia Service for one week without any complaints or complications related to anesthesia.

Discussion

Spinal anesthesia is one the most used for lower abdominal and lower limb surgery. Little is known about the effect of direct intrathecal administration of droperidol, although his associated compound fentanyl is well known for its effects. No case report

was found reporting the effects of inadvertent butyrophenone injection (droperidol, haloperidol, etc.) on spinal anesthesia. In the present case, the inadvertent injection of droperidol (0.10 mg) in spinal anesthesia resulted in severe hypotension only responsive to norepinephrine. The sedation could not be observed since the patient underwent general anesthesia.

Fentanyl is a lipophilic opioid and one of the most studied associated with local anesthetics for spinal anesthesia. Spinal anesthesia is often provided using a mixture of local anesthetic and opioids, which yield analgesic synergy. In a meta-analysis, it was demonstrated that the combination of low doses of local anesthetic with opioid ensured adequate intraoperative anesthesia and postoperative analgesia with reduction of adverse effects related to local anesthetic [4]. Combination of opioid (lipophilic + hydrophilic) demonstrates that this combination optimizes the analgesic effect with fewer side effects [5]. This was the reason for the proposal of spinal anesthesia to associate a hydrophilic opioid with a lipophilic opioid to the local anesthetic. Unfortunately, there was an accidental injection of droperidol.

Droperidol is a butyrophenone derivative and dopamine antagonist with high and preferential affinity for D2 receptors and a slightly lower affinity for α1A adrenergic receptors [6]. Droperidol when injected intravenously produces a slight increase in heart rate [7], and a decrease in mean blood pressure [7]. Caution should be used when droperidol is administered in hypovolemic patients.[6] The decrease in blood pressure can be exacerbated when administered with opioid [6].

The pharmacokinetics of droperidol were studied in 42 surgical patients using doses of 5, 10 and 15 mg intravenously in neuroleptanalgesia or associated with volatile anesthetics [8]. This study showed that in clinical practice, the pharmacokinetics of droperidol is considered linear within the recommended doses; its clearance and volume of distribution are not affected by the age and weight of adult patients [8]. In an evaluation of droperidol in 2006 based on several randomized, double-blind studies, the recommended dose of droperidol intravenously ranges from 0.625 to 2.5mg [6]. The most common adverse event associated with droperidol is sedation, which is dose dependent and more likely to occur in the early postoperative period [9, 10].

There is evidence that epidural butyrophenones may enhance opioid analgesics and reduce side effects. Droperidol was capable of potentiating both the analgesic and respiratory depressant effects of fentanyl [11]. Testing the anesthetic activity of droperidol in guinea pig proved to be equipotent with lidocaine [11]. A more recent prospective, randomized, observer-blinded clinical trial of epidural droperidol (2.5 mg) added to epidural fentanyl/bupivacaine improved postsurgical analgesia with less nausea and vomiting compared with epidural fentanyl/bupivacaine alone [2].

Using a mixture of haloperidol and epidural morphine in three patients, it showed that there was a decrease in the need or complete elimination of additional analgesics in the postoperative period [12]. Epidural injection of 2.5 mg droperidol did not result in any local or systemic side effects and significantly reduced the side effects of epidural morphine [3]. In the literature review for this Case Report, we found several articles on epidural injection of droperidol and haloperidol, and no reports of its use in spinal anesthesia.

Conclusion

Droperidol is a butyrophenone with anti-emetic, sedative and anti-anxiety properties. It is used in the management of chemotherapy-induced nausea and vomiting, and in conjunction with an opioid analgesic such as fentanyl to maintain the patient in calm state of neuroleptonalgesia with indifference to surroundings but still able to cooperate with the surgeon. In the present case, the accidental intrathecal injection of 0.10 mg of droperidol was presented by severe hypotension. Although it was safe it did not enhance analgesia, sensory or motor block in the immediate or late postoperative. There was not any nervous disturbance observed within the week of follow up.

Conflict of Interest

No financial sources supported this work. This paper has not been presented. No competing financial interests exist.

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