CASE REPORT

Bradycardia and Severe Bispectral Index Drop Following Femoral Nerve Block by Dexmedetomidine due to Accidental Vascular Puncture: A Case Report

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A 25-year-old Afghan male was presented to the emergency department with femoral shaft fracture following fall from the height. The patient was subjected to femoral nerve block and general anesthesia. First try for performing nerve block led to vascular puncture. Therefore, the needle was removed and re-inserted 1 cm lateral to first puncture site and DEX injected slowly with aspiration check after every 5 mL to avoid intravascular injection. Immediately after injection, heart rate dropped to 40, blood pressure decreased to 85/50 mmHg and the BIS dropped to 30. Because of not spontaneous resolving the situation atropine and ephedrine were ordered that resulted to regain hemodynamic stability.

It is likely that vascular puncture during peripheral nerve block can lead to some adverse events that need to be monitored precisely.

Keywords: dexmedetomidine; anesthesia; bradycardia; hypotension; alpha-2 adrenoceptor agonist

Alpha-2 receptors are pre-synaptic ones that cause negative feedback mechanism decreasing the release of epinephrine and norepinephrine from the synaptic vesicles [1-2]. Dexmedetomidine (DEX) is an alpha-2 adrenoceptor agonist with favorable pharmacokinetic and pharmacodynamic. DEX affinity to Alpha-2 adrenoceptor is 8 ~ 10 times higher than that of other like Clonidine [3]. In 1999, the US Food and Drug Administration (FDA) approved DEX as a short term sedative and analgesic. Then, in 2008, FDA approved its use as an adjuvant sedative with anesthesia for surgical or non-surgical indications. In terms of safety, some reports described side effects of bradycardia, hypotension, and dry mouth with this agent. In terms of efficacy, DEX has hypnotic, sedative, anxiolytic, sympatholytic, and analgesic effects without significant respiratory depression and therefore it is used in various situations [4-15]. Recently, some reports have described the potential of DEX as a promising agent for peripheral nerve block but it's possible side effects are not well described [16-19]. In this paper, we are reporting a case of bradycardia and hypotension following peripheral nerve block with DEX that are usually reported via intravenous injection. This was an excuse for summarizing the literature about the efficacy and safety of DEX as an adjuvant component of anesthesia and pain management.

Case Description

A 25-year-old Afghan male (BMI=22.5 Kg/m2) was presented to the emergency department of Imam Hosein Hospital, Tehran, Iran with femoral shaft fracture following fall from the height. After performing the primary and secondary survey in emergency department and ruling out the other injuries, he was candidated for orthopedic surgery. He had no any positive past medical or family history. The patient was subjected to femoral nerve block and general anesthesia. In the operating room he was awake, alert, and calm. He had 90 beats/min heart rate, 135/85 mmHg blood pressure, 12/min respiratory rate and 99% O2 saturation in room air. His bispectral index (BIS) was 90. Premedication was done by 50 µg fentanyl and the case was monitored by cardiac monitoring, pulse oximetry, non-invasive blood pressure monitoring and BIS. The patient's femoral nerve block was done with a 22-gauge needle in supine position that led to vascular puncture. Therefore, the needle was removed and re-inserted 1 cm lateral to first puncture site. The needle was re-positioned to optimize biceps femoris contraction with <0.5 milliamp. The patient's received DEX (1µg/kg dilute in 20 ml distilled water). DEX was injected slowly with aspiration check after every 5 mL to avoid intravascular injection. Immediately after injection the heart rate dropped to 40, blood pressure decreased to 85/50 mmHg and the BIS dropped to 30. Because of not spontaneous resolving the situation atropine (0.5mg×2) + 10mg ephedrine were ordered that resulted to regain hemodynamic stability. Thereafter, induction was done by 40 mg propofol and 30 mg atracurium, and a maintenance dose of 30 µg/kg/h propofol. Throughout the surgery that lasted about three hours, patient just received the one-third of propofol maintenance dose for anesthesia, and the patient BIS was kept at 40-60 without increasing dose. After finishing the surgery, patient was reversed by neostigmine and atropine.

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The awakening was normal with no incidents or late awakening.

Discussion

DEX is an alpha-2 adrenoceptor agonist that was approved by FDA in 1999 and plays an important role in anesthesia. Centrally, it acts on locus ceruleus of the brain stem inhibiting the sympathetic output of brain stem and increasing firing of inhibitory neurons. In addition, it acts on the dorsal horn of spinal cord grey matter by modulating the release of substance p and interrupting the spinal neuron-glia cross talk [20].

The literature suggests that DEX shows synergism with regional anesthesia and facilitates postoperative pain control [1]. The addition of DEX and sufentanil showed better analgesic effect and greater patient satisfaction without other clinically relevant side effects for patients undergoing hysterectomy during the first 72 hours after abdominal hysterectomy [21]. In a randomized placebo controlled trial, Hoy et al. found that the percentage of patients requiring further sedation was less in the DEX group than placebo group [22]. Another randomized, double-blind study was conducted on 60 adult patients; 30 patients received clonidine 1 μg/kg while the other 30 patients received DEX 1 μg/kg added to 40 ml 0.5% preservative-free lignocaine. DEX significantly facilitated onset, prolonged recovery of sensory and motor block and also prolonged duration of analgesia as compared to clonidine. Patient satisfaction was also better with DEX [23]. In a randomized, triple-masked, placebo-controlled trial, the authors compared the efficacy of perineural and IV DEX in prolonging the analgesic duration of single injection interscalene brachial plexus block (ISB) for outpatient shoulder surgery. They found that both DEX routes reduced the pain and opioid consumption up to 8 h postoperatively (P<0.001) and did not prolong the duration of motor blockade [24]. A meta-analysis of six RCTs showed that for pediatric anesthesia, DEX provided a significantly longer postoperative analgesia [25]. Another meta-analysis of five RCTs showed that sensory block duration was prolonged by 150 min [95% confidence interval (CI): 96, 205, P<0.00001] with intrathecal DEX [26]. Agarwal et al. conducted a prospective, randomized, double-blind, placebo-controlled trial, where they added DEX (100 μg) as an adjuvant to bupivacaine (30 ml of 0.325% bupivacaine + 1 ml normal saline) for supraclavicular brachial plexus block. DEX significantly shortened the onset time and prolonged the duration of sensory and motor blocks and duration of analgesia [27]. A third meta-analysis including sixteen RCTs, (n=1092 participants), neuraxial DEX significantly decreased postoperative pain intensity and prolonged analgesic duration [20].

There are some concerns about DEX safety such as hypotension and bradycardia [28-29]. Bradycardia was reported frequently in the literature [30-35]. In spinal anesthesia, intravenous and intrathecal DEX significantly increased the risk of bradycardia requiring atropine (meta-analysis of eight studies; n=412) [36]. In a meta-analysis of sixteen RCTs, (n=1092 participants), neuraxial DEX increased the risk of bradycardia (OR, 2.68; 95% CI, 1.18 to 6.10; P= 0.02). However, no evidence showed that neuraxial DEX increased the risk of other adverse events, such as hypotension [20]. In the randomized, double-blind, placebo-controlled trial, by Agarwal et al. DEX (100 μg) was added as an adjuvant to bupivacaine (30 ml of 0.325% bupivacaine + 1 ml normal saline) for supraclavicular brachial plexus block. Bradycardia was observed in one patient in the group SD [27]. But bradycardia and hypotension following peripheral nerve block with DEX, as happened in our patient, was rarely reported.

The suggested mechanism for bradycardia and hypotension is the sympatholytic effect due to reducing norepinephrine release [37]. While, the central hypotensive effect from DEX is dependent on endothelial nitric oxide synthesis [38]. In a randomized controlled trial, the incidence of bradycardia and hypotension was higher in the DEX group, but both usually resolve without intervention [22]. A Cochrane review on Alpha-2 agonists showed a doubled (111%) increase in the incidence of bradycardia (RR 2.11; 95% CI 1.39 to 3.20, n=1587 participants) [5].

The rate of bradycardia and hypotension is not consistent in the literature. The incidence of these adverse events varied according to the route of administration, dose, and the underlying condition of the patients and it was reported from 4 to 100 percent [19,39-44]. A randomized controlled trial was conducted to test the hypothesis that adding dexmedetomidine to ropivacaine prolongs axillary brachial plexus block. Group R received 40 ml of 0.33% ropivacaine plus 1 ml of 0.9% NaCl; Group DR1 received 40 ml of 0.33% ropivacaine plus 1 ml of dexmedetomidine (50 μg); and Group DR2 received 40 ml of 0.33% ropivacaine plus 1 ml of dexmedetomidine (100 μg). In the DR1 group, bradycardia was observed in 8 patients, and four of them were treated with atropine. In the DR2 group, bradycardia was observed in all patients, and 9 of them were treated with atropine. None of the patients in the control group (R) experienced bradycardia [45]. In a randomized double blind trial of intrathecal DEX as an adjuvant to ropivacaine for postoperative analgesia duration of the motor and sensory block, bradycardia occurred with an incidence rate of 6.6% in patients of DEX group [46].

DEX-induced hypotension can be managed by decreasing the dose or by discontinuing the infusion. However, for bradycardia, some cases might resolve spontaneously while the majority of cases require atropine or vasoactive agents to resolve [31,36,47-49]. The addition of atropine to DEX dose for prophylaxis against bradycardia was not recommended for all patients [50].

Conclusion

The authors believe that the first vascular puncture in this case played a role in fast systematic absorption of drug that led to bradycardia, hypotension and BIS drop but a minimal dose of propofol for maintenance helped in keeping the BIS between 40-60. It is likely that vascular puncture during peripheral nerve block can lead to some adverse events that need to be monitored precisely. Such adverse events are more important with drugs like bupivacaine that have serious cardiovascular adverse effects and even could cause cardiac arrest. Therefore the safety concerns in terms of hypotension and bradycardia with DEX should be considered and managed in future research.

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