Does adding Lidocaine to intrathecal Bupivacaine affect hemodynamic parameters during hip fracture surgery?

Running title:

Adding Lidocaine to intrathecal Bupivacaine for hip fracture surgery

Abstract:

Background

Hip fracture is one of the most common problems in elderly that needs surgical repair. As, the majority of these patients have chronic diseases, they are at increased risk of peri-operative mortality and morbidity. The purpose of this study was to evaluate spinal anesthesia with bupivacaine vs bupivacaine in combination with lidocaine in terms of hemodynamic changes in patients undergoing hip fracture surgery**.**

Materials and methods: This double-blind clinical trial was conducted on 292 patients undergoing surgery for hip fracture under spinal anesthesia. Patients were allocated into two groups of B (10 mg of hyperbaric 0.5% Bupivacaine) and BL (5 mg hyperbaric Bupivacaine 0.5% plus 50 mg Lidocaine 5%). Sensory and motor block and hemodynamic changes were consecutively measured before spinal anesthesia (T0), immediately after spinal injection (T1), every 5 minutes for half an hour (T2- T7), and at 45 minutes (T8) and 60 minutes (T9) after injection.

Results:

Patients in the two groups were homogeneous in demographic characteristics including age, sex, BMI, ASA Class, baseline blood pressure and heart rate. The onsets of sensory and motor blocks in group BL were faster than group B (P=0.0001). Also, the durations of sensory and motor blocks in group B were significantly longer than group BL (P=0.0001). The BL group had a significantly lower systolic blood pressure in all periods ($P<0.05$). Although the heart rate in the BL group was lower than group B at all time points, this difference was only significant during T2-T3 (P=0.033 and P=0.0001, respectively). Group BL had significantly more episodes of hypotension, bradycardia, nausea and vomiting (P=0.0001, P=0.023, P=0.003, and P=0.033, respectively).

Conclusion:

According to our findings, using Lidocaine 50 mg in combination with Bupivacaine 5 mg, compared with Bupivacaine 10 mg alone for spinal anesthesia in hip fracture fixation surgeries was associated with more hypotension and bradycardia. As a result, combination of Bupivacaine with Lidocaine at this dose is not recommended for induction of anesthesia in these patients.

Keywords: Bupivacaine ; Lidocaine; hemodynamics; pelvic surgery; hypotension; bradycardia

Introduction

Hip fracture is a relatively common, age dependent disease with a growing prevalence that needs surgical repair (1, 2). It is estimated that over 6 million people will suffer from one type of hip fracture in 2050 (3). Surgery as the key management in patients with hip fractures necessitates anesthesia. However, considering the high prevalence of cardiovascular and lung diseases in elderly, patients are commonly at increased risk of perioperative mortality and morbidity and complications (4-6). Postoperative outcomes can be affected by several factors such as comorbidities, surgery and anesthesia type. Both methods of anesthesia including general and regional are used for hip fractures. Comparing the general and regional methods have shown that general anesthesia may control the duration, depth of anesthesia, and hemodynamic status better than the regional rout (7, 8); however, abnormal reactions to anesthetic drugs, increased pulmonary complications, severe hypotension, nausea and vomiting can be mentioned as the complications of general anesthesia (9).

Although hypotension, headache, and neurological disorders are intraoperative complications of spinal anesthesia, it can improve the outcomes by preventing the intubation and pneumonia, reducing bleeding, deep vein thrombosis, pulmonary embolism, and improving postoperative analgesia (10-12). Therefore, spinal anesthesia is an effective method for perioperative analgesia which provides fewer drugs consumption and morbidity reduction in many cases and is a safe alternative for general anesthesia in many surgeries (1, 2). Spinal anesthesia is the accepted method for surgical repair of hip fracture, but it is associated with the risk of hemodynamic involvement (4, 13). Hypotension and bradycardia are the common complications of spinal anesthesia due to sympathetic block that is harmful especially in patients with coronary artery disease.

Bupivacaine is a long-acting local anesthetic that can induce anesthesia for 2.5 to 3 hours by using a single dose (13-14). To minimize the hemodynamic effects caused by this drug, different methods have been used including administering pre-loading with saline; unilateral spinal; on time administration of the vasopressors; low-dose local anesthetic; and addition of opioid or magnesium sulfate into the local anesthetic (1, 13,15-19).

Lidocaine is a moderate acting local anesthetic with a rapid onset of effect which can be used in ambulatory surgery (14). Recent studies have shown that adding intrathecal Lidocaine to Bupivacaine could decrease the duration of Bupivacaine effect by increasing its' clearance and leaded to faster recovery (20-22). In addition, this combination leaded to faster spinal recovery compared to the single dose of Bupivacaine. Addition of Lidocaine caused vasodilation in the spinal cord that increased the clearance of intrathecal Bupivacaine.

Although it is estimated that the techniques of combining drugs increased the potential of using spinal anesthesia in patients, studies have shown controversial results (23). Previous investigations have mentioned that by reducing the dose of Bupivacaine and adding compounds such as opioids, not only sufficient sub-arachnoid anesthesia was acquired, but also the harmful effects of Bupivacaine on hemodynamic status was declined. It reduced the incidence of hypotension compared with the full dose of Bupivacaine during spinal anesthesia (1, 24).

In this study, the effects of reduced dose of Bupivacaine and addition of a combination of Lidocaine and Epinephrine on hemodynamic complications such as hypotension and bradycardia were investigated.

Materials and methods

This double-blind clinical trial was conducted at the Anesthesia Research Center, Poursina Hospital, Guilan University of Medical Sciences on 292 patients undergoing surgery for hip fracture under spinal anesthesia. The approval was obtained from the ethics committee of Guilan University of Medical Sciences (1920452612, 2014/12/10) and the study was registered on IRCT (IRCT2014102713456N2).

The inclusion criteria were: patients aged 60-70 years with ASA class I - II, without any history of addiction or contraindication for spinal anesthesia (high intracranial pressure, coagulopathy, skin infection at the injection site, allergy to local anesthetic). Inadequate sensory and motor blocks, the need for general anesthesia during surgery, intraoperative bleeding and hemodynamic instability were defined as the exclusion criteria.

The sample size was determined based on a previous study by EI-Adawy (20) according the following formula: (α=0.05, β=0.20, z_1-α/2=1.96, z_1-β=1.28,

S_1=2.5,

S_2=3.2, μ_1-μ_2 =1.14)

$$n = \frac{\left((z_1 - \frac{\alpha}{2}) + (z_1 - \beta)\right)^2 ({S_1}^2 + {S_2}^2)}{(\mu_1 - \mu_2)^2}$$

With the probable drop rate of 10%, the sample size of 146 patients for each group was indicated.

A total of 292 eligible patients were allocated in two Group of B (10 mg of hyperbaric Bupivacaine 0.5% + Epinephrine) and BL (5 mg hyperbaric bupivacaine 0.5% plus 50 mg

Lidocaine 5% + Epinephrine) using randomized fixed quadripartite blocks. Participants had an equal probability of being assigned to each of the two groups.

Type of surgery, anesthetic technique, and the techniques to evaluate patients during and after surgery were explained and informed consents were obtained on the day before surgery.

To blind the study in Group B, 2 ml hyperbaric Bupivacaine 0.5% equivalent to 10 mg of Bupivacaine+Epinephrine 1/200000 was administered. Also, in group BL, 1 ml hyperbaric Bupivacaine 0.5% with 1 ml Lidocaine 5% equivalent to 50 mg Lidocaine+ Epinephrine 1/200000 was used. The volume for injection in both groups was 2 ml.

The medications were used by an anesthesiologist who performed neuroaxial blocking and appropriate action if the complications occurred.

Neither the patients nor the evaluator were aware of the type of injected anesthetic. In the operating room, all patients were monitored by 3-Lead electrocardiogram, pulse oximetry and noninvasive blood pressure measurement (SAADAT Digital Monitoring). After inserting an 18 gauge intravenous cannula, 5-7 ml / kg normal saline solution was injected during 15-30 mins, then spinal anesthesia was performed in sitting position by a skilled anesthesiologist using a 25-guage Quinke needle (B.Brown Company) through L3-L4 or L4-L5 intervertebral space at the speed of 0.2 cc/ seconds.

After spinal anesthesia, the patient was immediately placed in a supine position and supplemental oxygen was administered via a face mask at a rate of 5-8 L/min. The sensory block, and maximum sensory block level were assessed with the patient's ability to distinct the sharpness created by the tip of the needle (pin prick method) (25). The motor block level was assessed by examining the skeletal muscle strength criteria by modified Bromage scale (0=no paralysis, 1= only able to move the knee and feet, 2=only able to move feet, 3=inability to move the leg or knee).

Evaluations of patients were performed with one-minute interval to achieve maximum blocks and every 15 minutes until the return of sensory and motor blocks. The onset times of sensory and motor blocks were defined as the time from administering intrathecal anesthesia to peak sensory and motor blocks, respectively.

The duration between the end of intrathecal injection to decreased pinprink sense below S1 and the duration between the ends of intrathecal injection to free feet movement were indicated as the durations of sensory and motor blocks, respectively.

Blood pressure and heart rate were consecutively measured as a base before spinal anesthesia (T0), immediately after spinal injection (T1), every 5 minutes to half an hour (T2- T7) and every 15 minutes until the end of surgery.

In this study, systolic blood pressure less than 90 mmHg was defined as hypotension. With systolic blood pressure less than 90 mm Hg, 10 mg intravenous ephedrine (up to maximum dose of 30 mg) and in case of bradycardia with heart rate less than 60 beats/minutes, 0.5 mg intravenous atropine was administered. In case of nausea and vomiting, 0.1 mg / kg intravenous metoclopramide was injected.

Statistical analysis:

Data analysis was done using SPSS software version 17. Data were reported by descriptive statistics (number, percent, mean, and standard deviation) and analyzed with chi-square test and T-test. For intragroup comparison of variables after surgery, ANCOVA was used. A $P<0.05$ was considered as statistically significance and 95% confidence interval was noted.

Results

A total of 292 patients were enrolled in the study. Eleven patients in group BL and 13 patients in group B were excluded and 135 and 133 patients, respectively, were assessed. The results showed that 7 and 9 patients in group BL and B were excluded due to inappropriate block. Prolonged surgery and need for general anesthesia resulted in exclusion of 3 and 2 patients in group BL and B, respectively. Also, excessive bleeding and hemodynamic instability resulted in exclusion of 1 and 2 patients in group BL and B, respectively.

Patients were homogeneous in demographic characteristics including age, sex, BMI, baseline blood pressure and heart rate in the two groups (P=0.272, P=0.53, P=0.4, P=0.08 and P=0.439, respectively) (Table 1). The onset time of sensory and motor block in group BL was significantly faster than Group B (P=0.0001 and P=0.0001, respectively). Also, the duration of sensory and motor block in group B was significantly longer than group BL (P=0.0001). (Table 2)

Comparing the mean systolic and diastolic blood pressure as well as the mean arterial blood pressure by using t-test in all periods except T0, showed that BL group had lower blood pressure than those in group B ($P<0.05$) (Table3). Although the heart rate in the group BL was lower than Group B at all time points, this difference was only significant during T2-T3 (P=0.033 and P=0.0001, respectively) (Table 4).

The BL Group had more episodes of hypotension, bradycardia, nausea and vomiting (P=0.0001, P=0.023, P=0.003, and P=0.033, respectively). Also, the use of ephedrine in the group BL was significantly higher than group B (P=0.0001) (Table 5).

Discussion

Hip fractures are one of the most common problems in elderly especially in females. The incidence increases with age. As, the majority of these patients have chronic diseases, they are at increased risk of peri-operative mortality and morbidity. Its' annual mortality rate is 20-25 % and is 4 times more in comparison with the general population(8).

Surgical reduction and fixation is the selected treatment in these patients. To now, the selected anesthesia technique in these patients has been remained unknown. Spinal anesthesia is an effective method in diverse surgical procedures. This technique can effectively reduce intraoperative bleeding, thromboembolic events, and postoperative nausea and vomiting. However, Hemodynamic complications due to spinal block, such as severe and prolonged hypotension in short to medium length procedures, are the main concerns that have been extensively studied (4, 12).

Our study showed that for spinal anesthesia, adding 50 mg Lidocaine to 5 mg Bupivacaine was associated with lower blood pressure and heart rate comparing to 10 mg of Bupivacaine. Group BL had more frequent hypotension and bradycardia compared to group B and significant higher ephedrine consumption in this group was noted.

In a previous study no significant difference in peri and post-operative hemodynamic status was reported between the Lidocaine-Bupivacaine and Bupivacaine groups (20). In contrast with our results, Yazicioglu et al. have mentioned that adding Lidocaine to Levobupivacaine did not cause significant hemodynamic changes (21). They administered 6 mg and 12 mg Lidocaine in combination with Bupivacaine. The difference in doses of administered medications could explain the different results. Therefore, hemodynamic stability in previous studies might be occurred as a result of compensatory homeostatic vasoconstrictive mechanisms of low dose Lidocaine.

Punj et al compared different doses of Bupivacaine and Lidocaine in patients undergoing hip surgery and mentioned consistent results. Patients receiving Lidocaine 5% had more episodes of hypotension and bradycardia, and needed more ephedrine and atropine compared to Bupivacaine 0.5% (26). Lee et al compared patients receiving 12 mg of Lidocaine with Bupivacaine to the group receiving 6 mg of Lidocaine or saline in combination with Bupivacaine. They showed that the first group had lower mean arterial pressures and heart rates(22). Their similar results noted higher incidence of hypotension and bradycardia by administering higher doses of Lidocaine.

Olofsson et al compared the effect of administering low dose of Bupivacaine-sufentanil with Bupivacaine in spinal anesthesia on hemodynamic parameters in patients undergoing hip fracture. They showed that the use of intrathecal opioid in combination with Bupivacaine caused better hemodynamic stability and lower hypotension creases (1).

Regarding the sensory and motor blocks, adding 50 mg Lidocaine to 5 mg Bupivacaine caused higher sensory peak and more rapid onset of sensory and motor blocks. Most of the patients in the group BL and group B had the sensory level at T7 and T8, respectively. In the study of EI-Adawy et al. adding 12 mg Lidocaine to Bupivacaine caused a higher sensory level (T6) and faster block onset compared to administering Bupivacaine alone or 6 mg Lidocaine plus Bupivacaine(20). The study by Jacobsen et al also mentioned consistent results. They noted that adding 6 mg of Lidocaine to 10 mg Bupivacaine caused higher block peak compared to the control group, but this difference was not statistically significant (23). However, Chohedri et al indicated that adding 0.6 ml Lidocaine 1% to 7.5 mg Bupivacaine didn't cause significant difference between the two groups (27). Their results were inconsistent with our study and the study by Jacobsen et al. The difference might have been caused by administering lower doses of Lidocaine in our study and Bupivacaine by Jacobsen et al. (23).

Since the baricity of the injected solution is one of the most important factors that could affect the level of sensory block in spinal analgesia, adding Lidocaine to Bupivacaine 0.5% caused indistinguishable baricity of injected solution into the spinal space and this could explain the higher sensory level in BL group patients (26).

Regarding the duration of the sensory and motor blocks, our study showed that the use of Lidocaine in combination with Bupivacaine shortened the duration of the block, resulting in a faster recovery. The cause of faster recovery following the addition of Lidocaine is unknown, but Lidocaine can cause vasodilation of spinal blood vessels and increase the Bupivacaine clearance from the spinal space.

Similar to our study, in the study by EI-Adawy et al, adding 6 mg Lidocaine to Bupivacaine shortened the duration of the sensory and motor blocks; but, adding 12 mg Lidocaine prolonged the sensory and motor blocks and delayed the recovery (20). The shorter length of the block in our study might have been due to the lower dose of used Bupivacaine despite using the higher dose of Lidocaine. In our study, 5 mg Bupivacaine was used compared to 7.5-10 mg in previous studies. Also, Jacobsen et al. and Chohedri et al. have mentioned that adding 6 mg of Lidocaine to Bupivacaine did not lead to significant shortening of the blocking time(23, 27). This can be caused by their high doses of Bupivacaine. However, Yazicioglu et al, added Lidocaine and mentioned shortened block and faster recovery which was similar with this study(21).

In terms of complications, patients in BL group had higher hypotension, bradycardia, nausea and vomiting compared to group B. Neuroaxial anesthesia causes the blockage of the peripheral (T1-L2) and cardiac (T1-T4) sympathetic fibers. Sympathectomy causes venous vasodilation (decreased venous return) and arterial vasodilation (decreased systemic vascular resistance) and reduced stroke volume. During the spinal anesthesia, hypotension occurs consequent to the decreased systemic vascular resistance or cardiac output. The amount of local anesthetic cephalad expansion in subarachnoid space determines the degree of sympathetic blockage and consequently, the amount of hypotension (4,12). When clinicians use the combination of lidocaine and bupivacaine, the change in the baricity of the injected solution can increase the level of sensory and sympathetic blockages and consequently hypotension (26). This can be indicated as the cause of decreased blood pressure in BL group compared with B group. In the study by Yazicioglu et al, adding Lidocaine to Levobupivacaine did not cause more nausea and vomiting than Levobupivacaine alone (21). They assessed the effect of lower dose of Lidocaine (6mg).

Several mechanisms cause nausea and vomiting by neuroaxial anesthesia that included direct exposure to chemoreceptive trigger zone in the brain with emetogenic drugs, hypotension due to generalized vasodilation and gastrointestinal hyperpristaltism secondary to unopposed parasympathetic activity (14). So, one cause of more nausea and vomiting in group BL than group B might be the greater incidence of hypotension in this group.

TNS was reported for the first time in 1993 after intrathecal injection of Lidocaine 5%. This phenomenon relates with sensory dysfunction as well as pain in the back and lower extremities that starts within 1 to 24 hours after operation. It lasts from a few hours to a few days (24,28). A study by Umbrain et al showed that injecting intrathecal Lidocaine was associated with changes in PGE2 in cerebrospinal fluid. They showed that PGE2 increased with increasing TNS and the spinal prostaglandin change was dose dependent (29). Zaric et al noted that these changes were not neurological dose-dependent (30). So, whether or not the incidence of TNS was a dose-dependent issue has yet remained unclear. In this study, TNS and PDPH were not checked after the operation and it might be a limitation of our study. It is recommended to evaluate the incidence of this complication and its relationship with the consumed Lidocaine dose in future studies. Furthermore, only one dose of Lidocaine (50 mg) was used in our study in combination with Bupivacaine. It is recommended that future studies use other doses of local anesthetics for hip fracture surgery to determine the most appropriate dose with the minimal complications. Although in most of the previous studies, the majority of patients with hip fractures were elderly women, since this study was conducted in patients with trauma, male sex was more frequent. Therefore, future studies on elderly patients with osteoporotic hip fracture can be recommended.

According to the researches, few studies have assessed the effect of Lidocaine-Bupivacaine on hemodynamic responses in patients undergoing hip fracture and the majority of studies have examined the effects of drug combinations on the properties of the blocks. Also, the sample size of our study was higher than previous studies and it can be declared as the strength of this study.

Conclusion

According to our findings using 50 mg of Lidocaine in combination with 5 mg of Bupivacaine, compared with 10 mg Bupivacaine alone for spinal anesthesia for hip fracture was much more associated with hypotension and bradycardia. As these patients were usually old and may have had multiple cardiovascular and pulmonary disorders, more unstable hemodynamic status was noted by Lidocaine plus Bupivacaine compared to Bupivacaine alone. As a result, using Bupivacaine with Lidocaine at this dose in these patients is not recommended for induction of anesthesia.

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