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Efficacy of low-dose versus conventional-dose bupivacaine in spinal anesthesia induction: A narrative review article

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ABSTRACT

Spinal anesthesia is gaining popularity and more frequent use due to its efficacy, patient satisfaction, lower complication rates, and good durability. Nerve blocks reduce the complications and risks associated with general anesthesia and lessen the patient's need for postoperative care compared to general anesthesia, leading to earlier patient discharge. One spinal procedure involves administering low doses for anesthesia induction. This review article explored this approach by incorporating studies reporting the administration of lower doses of the local anesthetic bupivacaine. Findings indicate that lower and conventional doses of bupivacaine have comparable sensory and motor block impacts and induction times. However, the recovery time at lower doses is faster, and patients are discharged sooner from the postanaesthetic care unit. Complications associated with spinal anesthesia are significantly decreased at lower doses of bupivacaine administration. Thus, lower doses can be used to induce spinal anesthesia successfully with minimal adverse effects.

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Introduction

Spinal anesthesia constitutes an integral part of contemporary anesthesia practices thanks to its success, predictability, increased patient satisfaction, and low complication rate. The term spinal anesthesia refers to the injection of a local anesthetic into or around the central nervous system. It is a technique in which a local anesthetic is infused directly into the intrathecal space (subarachnoid space). Spinal anesthesia has a reduced complication rate compared to general anesthesia, which is associated with breathing issues and the risk of aspiration. The dose of local anesthetic is the key predictor of the effectiveness of a sensory nerve block suited for surgery, notwithstanding the influence of other variables. Reference books recommend bupivacaine in doses between 4 and 20 mg, depending on the surgery type [1-3]. Numerous studies have been conducted to determine the optimal dose of bupivacaine, with results varying significantly between 5 and 25 mg [4-6]. Lower doses of bupivacaine are aimed at reducing the side effects of this procedure. Hypotension, nausea, intraoperative and postoperative vomiting, and bladder dysfunction

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are some of the complications of spinal anesthesia. Lower doses lead to fewer side effects, greater hemodynamic stability, and earlier discharge [4].

Main Body

Literature Search Strategy

We examined several databases and search engines, including PubMed, Google Scholar, Medline, Medscape, and the Web of Science, using medical subject headings (MeSH). The search process was performed using the keywords anesthesia, spinal, anesthetics, local/administration & dosage, and bupivacaine/administration & dosage. Abstracts and full texts of related articles published in English were reviewed without a time limit. After irrelevant articles were deleted, the remaining records were carefully reviewed.

Spinal administration and dosage

A variety of drugs, including short-acting and intermediate-acting medications, are used for spinal anesthesia. Bupivacaine (marcaine) is the most widely used drug. Bupivacaine is a potent local anesthetic with unique characteristics from the amide group of local anesthetics. The typical dose of bupivacaine varies between 4 and 20 mg, depending on the required block-level [2, 3].

Bupivacaine in low doses is conventionally used along with narcotics. Various adjuvants such as narcotics and non-narcotics have been tested to improve postoperative anesthesia and prolong postoperative analgesia. Research has shown that adding a narcotic to local anesthesia increases the success of spinal anesthesia. It also allows using low-dose local anesthetics and increases the duration and quality of anesthesia without any effect on the motor block. Morphine is employed more commonly than fentanyl and sufentanil, given its long duration of action. Its hydrophilic nature leads to a slow release and long-lasting effects [7]. Intrathecal morphine (ITM) provides approximately 18 to 24 hours of postoperative analgesia. Depending on the indication, intrathecal morphine is conventionally administered to adults in 0.15 to 0.3 mg doses. In contrast, intrathecal fentanyl (10 to 20 μg) and intrathecal fentanyl (2.5 to 5 μg) are often administered to induce adequate analgesia intraoperatively [8]. Fentanyl and sufentanil have a faster onset of action (5 to 20 minutes) than morphine due to their hydrophobic nature [3]. Several studies have examined the effect of different doses of intrathecal fentanyl with bupivacaine, finding that none of the patients who received more than 6.25 μg of fentanyl needed narcotics intraoperatively. They conclude that an intrathecal dose of fentanyl between 6.25 and 50 μg provides adequate postoperative analgesia without affecting the sensory block onset and the motor block duration of the bupivacaine [9-11].

Sensory Block

There is no statistically significant difference between the low-dose and conventional-dose groups regarding the highest level of sensory block and the time to reach the highest level of sensory block in the operated organ (Table 1) [12]. The mean value of the highest level of sensory block in both groups varies from T1 to T12, depending on the dose of bupivacaine and its concentration.

Nonetheless, most studies report the block level as T10, with an insignificant difference between the two groups [12-18]. In the study of Turhan et al., the time required for sensory block L2 regression is, on average, 149.85 minutes in the conventional-dose group and 105.62 minutes in the low-dose group, which is substantially shorter in the low-dose group (Table 1) [16]. The study by Unal et al. revealed that the time required for two-segment regression (SRT2) was lower in the low-dose than in the conventional-dose group (Table 1) [17]. The duration of the sensory block period at a dose of 5 mg bupivacaine is shown to be 252 minutes [19].

Motor Block

The Bromage Scale is typically built on to assess the motor block (score 3 for complete motor block, 1 and 2 for incomplete blocks, and 0 for no motor block) [20, 23]. Most participants scored 3 or higher in both groups. However, the number of individuals in the conventional-dose group was significantly higher [16, 17, 21]. The time required to reach a complete block is similar in both groups; nevertheless, the time required to eliminate the motor block is less in the low-dose group [12, 17, 22, 23].Other research findings, however, indicate that the time to reach the complete block in the conventional-dose group is faster than in the low-dose group, although the recovery time of motor block is still faster in the low-dose group [16, 24].

Postoperative outcome

Both groups are similar in terms of postoperative analgesia time [22]. There was no significant difference between the two groups regarding the time of first need for tranquilizer and the ability to walk [17]. Intrathecal injection of narcotics delays the time of first need for tranquilizer in the postoperative stage. While fentanyl at 0.25 μg/kg provides short-term postoperative analgesia, postoperative analgesia was longer at 0.5 μg/kg and 0.75 μg/kg doses [11]. In the study of Akcaboy et al., the block period was 110.8 minutes in the low-dose group and 158.5 minutes in the conventional-dose group (Table 1) [12].

Table 1: Description of the included studies. IB, isobaric bupivacaine; HB, hyperbaric bupivacaine; F, fentanyl; Morph, morphine; HD, high dose; MD, moderate dose; LD, low dose

The study	Sample size	Surgery Type	Studied groups	Anesthesia/analgesia supplements	Criteria of effectiveness	Time to motor recovery	Time to sensory recovery
Shahverdi and colleagues [40]	62	Transurethral Resection of Prostate	HB 0.5% 1 mg B + 20 mcg F; HB 0.5% 10 mg B	N/A	Time to reach T10 sensory level HD: 4.4 LD: 9.3	N/A	Time to sensory recovery: HD: 77.7 LD: 66.2
Akcaboy and colleagues [12]	45	total knee arthroplasty	IB 0.5% 5 mg B + 15 mg F; 10 mg B alone	continuous femoral nerve block	sensory block: HD: T10 LD: T8	N/A	Time to sensory recovery: HD: 110.8 LD: 158.5
Cenkowski and colleagues [14]	32	cesarean section	HB 0.75% 4.5 mg B + 15 mcg F; 9 mg B + 15 mcg F	150 mcg of morph	sensory block: HD: T6 LD: T6	HD: 132 LD: 54	Time to sensory recovery: HD: 153 LD: 103
TURHAN and colleagues [16]	52	outpatient arthroscopic meniscus repair	IB 0.5% 10 mg B; 5 mg B + single-shot femoral block with 0.25% bupivacaine	N/A	sensory block: HD: T10 LD: T10	HD: 178 LD: 115	Time to L2 regression of sensory block level HD: 149.85 LD: 105.62
Leo and colleagues [41]	60	cesarean section	HB 0.5% 7 mg B + 100 mcg Morph; HB 0.5% 8 mg + 100 mcg Morf ; HB 0.5% 9 mg B + 100 mcg Morph	IV hydroxyethyl starch 15 mL / kg at the time of initiation of combined spinal-epidural anesthesia.	sensory block: HD: T1 MD: T2 LD: T2	Time for recovery to Bromage score 2 HD: 132 MD: 106 LD: 111	Time to T10 regression of sensory block level HD: 137 MD: 140 LD: 132
Unal and colleagues [17]	45	Ambulatory Arthroscopic Knee Surgery	HB 0.5% 4 mg B; HB 0.5% 4 mg + 25 mcg F ; HB 0.5% 3 mg B + 15 mcg F	N/A	sensory block in all group: T10	N/A	N/A
Awad and colleagues [13]	49	otal knee arthroplasty	IB 10 mg B; IB 5 mg B	continuous femoral nerve block (CFNB) + sciatic nerve block (SNB)	sensory block after 20 min: HD: T10 LD: T10	N/A	Time to recovery of S2 dermatome HD: 207 LD: 145
Braga and colleagues [22]	66	caesarean section	HB 0.5% 10 mg B; HB 0.5% 10 mg B	clonidine 75g (0.5mL) + morphine 100g	sensory block: HD: T4 LD: T4	HD: 232.8 LD: 198.4	Time to sensory recovery: HD: 191.1 LD: 163.6
Agrawal and colleagues [42]	60	Caesarean S ection	HB 0.5% 12 mg B; HB 0.5% 7.5 mg + 25 mcg F	N/A	sensory block: HD: T6 LD: T5	N/A	Time to T10 regression of sensory block level HD: 114.25 LD: 148.50
Agrawal and colleagues [43]	32	caesarean section	IB 0.5% 10 mg B; IB 0.5% 5 mg + 25 mcg F	N/A	sensory block: HD: T3 LD: T5	N/A	N/A

Hypotension and Bradycardia

Hypotension is a common complication of spinal anesthesia. This reduction can be minimized by reducing the anesthetic dose. Some studies consider hypotension as systolic blood pressure (SBP) decreased by 20 to 30 percent or reaching below 90 to 95 mmHg. Others define hypotension as when SBP drops to 20 percent to 30 percent relative to the base value. Hypotension was reported in all studies. The risk of hypotension in the low-dose bupivacaine group is 29% lower than in the conventional-dose group [6]. Biboulet et al. showed that the risk of hypotension in elderly patients using a 5 mg dose of intrathecal bupivacaine was 40% [25].

Some studies have reported no hypotension or a very low percentage of hypotension in the low-dose group [12, 21, 23]. This may be due to different doses of bupivacaine and fentanyl. In any case, hypotension in the low-dose group is significantly lower than in the conventional-dose group. Moreover, more hemodynamic stability is observed in the low-dose group [17, 24, 26].

It has been shown that epinephrine infusion can restore arterial SBP during spinal anesthesia and increase cardiac output. Yet, it does not affect diastolic pressure and, therefore, does not increase mean arterial pressure [27]. Additionally, no significant difference has been reported regarding bradycardia between the two groups [12, 21, 24].

Hypotension and Ejection Fraction

Spinal anesthesia is often considered a safe method for patients with heart disease, especially congestive heart failure, due to a minimal reduction in myocardial contraction and a slight reduction in cardiac output [28]. Ejection fraction and heart rate are two factors that affect cardiac output.

The ejection fraction depends on myocardial contraction and end-diastolic filling. Spinal anesthesia with sympathetic block leads to accumulated peripheral blood and reduced volumes of the diastolic end. Patients with low ejection fraction rely on preload, while spinal anesthesia further reduces stroke volume and cardiac output. Due to the increased activity of the sympathetic nervous system in patients with congestive heart failure, spinal anesthesia in these cases can reduce systemic vascular resistance (SVR) and blood pressure more than in patients with normal left ventricular function [29-31].

A spinal block might reduce the left ventricular end-diastolic volume by up to 19%. This change is the primary contributor to declined cardiac output, especially in patients with low ejection fractions. Low-dose spinal anesthesia in patients with low

cardiac index decreases the mean arterial pressure more than spinal anesthesia with the conventional dose. It is because low-dose local anesthetic blocks the sympathetic system less than the conventional dose [32]. It was also observed that the reduction of systolic, diastolic, and mean arterial pressure in patients with low ejection fraction (EF <40) was less than in patients with EF> 40%. Hence, it is safer and more successful to use lower doses of bupivacaine in these patients [21].

Nausea and Vomiting

Numerous factors can cause nausea and vomiting after spinal anesthesia, including the arrival of drugs to the brain's nausea center, decreased blood pressure, or increased gastrointestinal motility due to sympathetic block and parasympathetic increase. Nausea and vomiting are common complications of spina bifida. However, only a small percentage of patients require treatment for nausea and vomiting [33]. Some studies have found no side effects of nausea and vomiting at low doses [12, 23].

As a result, there is no significant difference between spinal anesthesia at low doses and conventional doses in terms of nausea and vomiting. Nevertheless, nausea and vomiting can be reduced to an acceptable level by using a lower dose of narcotics [6, 19, 33].

Pruritus

One of the most common side effects of narcotics in cases of spinal injection is pruritus. Pruritus was the most common side effect after intrathecal injection in low-dose spinal anesthesia due to narcotic use as an adjuvant [33]. The chance of pruritus in the low-dose group was 15 times higher than in the conventional-dose group [24].

In Unal et al.'s study, where an intrathecal dose of 25 micrograms of fentanyl was employed, nearly half of the patients developed pruritus. Yet, only a very small percentage of patients needed pruritus treatment [17]. In another study with a dose of 10 micrograms of fentanyl, no pruritus was reported [23]. Moreover, it is demonstrated that no pruritus occurs if narcotics are not used [16].

Post-Dural Puncture Headache (PDPH)

A common complication of neuraxial anesthesia is PDPH. The cause can be CSF fluid loss. PDPH incidence rates may range from 0.2% to 24% [34]. No difference has been reported in PDPH incidence between the two groups across studies. Notably, none of the patients experienced PDPH in some studies [17, 33].

Urinary Retention

One of the side effects of using hydrophilic drugs is urinary retention, while lipophilic drugs are less likely to cause this complication [35-37]. The chance of urinary retention in spinal anesthesia is about 17% [38]. Low-dose first-time urination occurs earlier than cases with conventional doses [38]. In low-dose spinal anesthesia, the initial urine happens sooner than in conventional-dose anaesthetia [13, 16]. In the reviewed studies, urination occurred approximately within three hours in groups receiving 3 to 5 mg bupivacaine plus 25 mg fentanyl, and catheterization was not required [17,19].

Therefore, the use of low doses of local anesthetics diminishes the incidence of postoperative urinary retention and thus lowers the need for invasive catheterization of the bladder. This reduces the complications and problems of invasive bladder catheterization, including damage to the urethra, prostatitis, and patient discomfort.

Conclusion

This study indicated that the use of low doses of bupivacaine to induce adequate sensory and motor blocks is not significantly different from the use of conventional doses.

Nevertheless, low doses cause faster recovery of the block and reduce the patient's stay in the PACU. It also provides good analgesia for the patient. Using lower doses can significantly minimize the incidence of spinal anesthesia complications such as hemodynamic instability, nausea, vomiting, headache, and urine retention, which are prevalent with conventional doses. The complication of pruritus, which is mostly induced by narcotics, can also be reduced by decreasing narcotic dosages.

References

1. Tsen LC. Anesthesia for cesarean delivery. REFRESHER COURSES IN ANESTHESIOLOGY. 2005;33:235.
2. Benzon HT, Raja SN, Liu SS, et al. Dedication. In: Benzon HT, Raja SN, Liu SS, Fishman SM, Cohen SP, editors. Essentials of Pain Medicine: Elsevier; 2018. p. v.
3. Gropper MA. Miller's anesthesia. Philadelphia: Elsevier; 2020.
4. Finucane BT. Spinal anesthesia for cesarean delivery. The dosage dilemma. Reg Anesth. 1995;20:87-89.
5. Ben-David B, Miller G, Gavriel R, et al. Low-dose bupivacaine-fentanyl spinal anesthesia for cesarean delivery. Reg Anesth Pain Med. 2000;25:235-239.
6. Arzola C, Wieczorek PM. Efficacy of low-dose bupivacaine in spinal anaesthesia for Caesarean delivery: systematic review and meta-analysis. Br J Anaesth. 2011;107:308-318.
7. Stoelting RK. Intrathecal morphine—an underused combination for postoperative pain management. Anesthesia & Analgesia. 1989;68:707-709.
8. Dahl JB, Jeppesen IS, Jorgenseet al. Intraoperative and postoperative analgesic efficacy and adverse effects of intrathecal opioids in patients undergoing cesarean section with spinal anesthesia: a qualitative and quantitative systematic review of randomized controlled trials. Anesthesiology. 1999;91:1919-1927.
9. Shende D, Cooper GM, Bowden MI. The influence of intrathecal fentanyl on the characteristics of subarachnoid block for caesarean section. Anaesthesia. 1998;53:706-710.
10. Connelly NR, Dunn SM, Ingold V, et al. The use of fentanyl added to morphine-lidocaine-epinephrine spinal solution

in patients undergoing cesarean section. Anesthesia and analgesia. 1994;78:918-920.
11. Belzarena SD. Clinical effects of intrathecally administered fentanyl in patients undergoing cesarean section. Anesth Analg. 1992;74:653-657.
12. Akcaboy Z, Akcaboy Y, Mutlu M, et al. Spinal anesthesia with low dose bupivacaine-fentanyl combination: a good alternative for day case TURP surgery in geriatric patients: 2AP2-4. European Journal of Anaesthesiology| EJA. 2012;29:34.
13. Awad IT, Cheung JJ, Al-Allaq Y, et al. Low-dose spinal bupivacaine for total knee arthroplasty facilitates recovery room discharge: a randomized controlled trial. Can J Anaesth. 2013;60:259-265.
14. Cenkowski MJ, Maguire D, Kowalski S, Al Gurashi FA, Funk D. Hemodynamic effects of low-dose bupivacaine spinal anesthesia for cesarean section: A randomized controlled trial. Saudi J Anaesth. 2019;13:208-214.
15. Korhonen AM, Valanne J, Jokela R, et al. Intrathecal hyperbaric bupivacaine 3 mg+ fentanyl 10 μg for outpatient knee arthroscopy with tourniquet. Acta anaesthesiologica scandinavica. 2003;47:342-346..
16. Turhan KS, Akmese R, Ozkan F, et al. Comparison of low-dose spinal anesthesia and single-shot femoral block combination with conventional dose spinal anesthesia in outpatient arthroscopic meniscus repair. Eur Rev Med Pharmacol Sci. 2015;19:1489-1497.
17. Unal D, Ozdogan L, Ornek HD, et al. Selective spinal anaesthesia with low-dose bupivacaine and bupivacaine + fentanyl in ambulatory arthroscopic knee surgery. J Pak Med Assoc. 2012;62:313-318.
18. Valanne JV, Korhonen A-M, Jokela RM,et al. Selective spinal anesthesia: a comparison of hyperbaric bupivacaine 4 mg versus 6 mg for outpatient knee arthroscopy. Anesthesia & Analgesia. 2001;93:1377-1379.
19. Florio P, Puzzutiello R, Filippeschi M, et al. Low-dose spinal anesthesia with hyperbaric bupivacaine with intrathecal fentanyl for operative hysteroscopy: a case series study. J Minim Invasive Gynecol. 2012;19:107-112.
20. Buggy DJ, Hall NA, Shah J, et al. Motor block during patient-controlled epidural analgesia with ropivacaine or ropivacaine/fentanyl after intrathecal bupivacaine for caesarean section. Br J Anaesth. 2000;85:468-470.
21. Sanatkar M, Sadeghi M, Esmaeili N, et al. The hemodynamic effects of spinal block with low dose of bupivacaine and sufentanil in patients with low myocardial ejection fraction. Acta Med Iran. 2013;51:438-443.
22. Braga AdFdA, Frias JAF, Braga FSdS, et al. Spinal anesthesia for elective ceasarean section: use of different doses of hyperbaric bupivacaine associated with morphine and clonidine. Acta cirurgica brasileira. 2013;28:26-32.
23. Tolia G, Kumar A, Jain A, et al Low dose intrathecal bupivacaine with fentanyl for cesarean delivery. Journal of Anaesthesiology Clinical Pharmacology. 2008;24:201-204.
24. Abate SM, Belihu AE. Efficacy of low dose bupivacaine with intrathecal fentanyl for cesarean section on maternal hemodynamic: Systemic review and meta-analysis. Saudi J Anaesth. 2019;13:340-351.
25. Biboulet P, Vacher E, Deschodt J, et al. Continuous Spinal Anesthesia:: Does Low-Dose Plain or Hyperbaric Bupivacaine Allow the Performance of Hip Surgery in the Elderly? Regional Anesthesia and Pain Medicine. 1993;18:170-175.
26. Qiu MT, Lin FQ, Fu SK, et al. Combination of low-dose bupivacaine and opioids provides satisfactory analgesia with less intraoperative hypotension for spinal anesthesia in cesarean section. CNS Neurosci Ther. 2012;18:426-432.
27. Akcaboy EY, Akcaboy ZN, Gogus N. Low dose levobupivacaine 0.5% with fentanyl in spinal anaesthesia for transurethral resection of prostate surgery. J Res Med Sci. 2011;16:68-73.
28. Wilkins K. Health care. Health Reports. 1999;10:47.
29. Beaupre LA, Jones CA, Saunders LD,et al. Best practices for elderly hip fracture patients. A systematic overview of the evidence. J Gen Intern Med. 2005;20:1019-1025.
30. Gullberg B, Johnell O, Kanis JA. World-wide projections for hip fracture. Osteoporos Int. 1997;7:407-413.
31. Ben-David B, Frankel R, Arzumonov T, et al. Minidose bupivacaine–fentanyl spinal anesthesia for surgical repair of hip fracture in the aged. The Journal of the American Society of Anesthesiologists. 2000;92:6.
32. Sen S, Aydin K, Discigil G. Hypotension induced by lateral decubitus or supine spinal anaesthesia in elderly with low ejection fraction undergone hip surgery. J Clin Monit Comput. 2007;21:103-107.
33. Anabah T, Olufolabi A, Boyd J, et al. Low-dose spinal anaesthesia provides effective labour analgesia and does not limit ambulation. Southern African Journal of Anaesthesia and Analgesia. 2015;21:19-22.
34. Liu SS, McDonald SB. Current issues in spinal anesthesia. Anesthesiology. 2001;94:888-906.
35. Ben-David B, Solomon E, Levin H, et al. Intrathecal fentanyl with small-dose dilute bupivacaine: better anesthesia without prolonging recovery. Anesthesia & Analgesia. 1997;85:560-565.
36. Choi S, Mahon P, Awad IT. Neuraxial anesthesia and bladder dysfunction in the perioperative period: a systematic review. Can J Anaesth. 2012;59:681-703.
37. Mulroy MF, Salinas FV, Larkin KL,et al. Ambulatory surgery patients may be discharged before voiding after short-acting spinal and epidural anesthesia. The Journal of the American Society of Anesthesiologists. 2002;97:315-319.
38. D O'Donnell B, Iohom G. Regional anesthesia techniques for ambulatory orthopedic surgery. Current Opinion in Anesthesiology. 2008;21:723-728.
39. Abdel-Aziz S, Adams MCB, Ahmed M, et al. List of Contributors. In: Benzon HT, Raja SN, Liu SS, Fishman SM, Cohen SP, editors. Essentials of Pain Medicine (Fourth Edition): Elsevier; 2018. p. xi-xvii.
40. Shahverdi M, Sabertanha A, Nikraftar F, et al. Spinal anesthesia with a low dose of hyperbaric bupivacaine plus fentanyl versus hyperbaric bupivacaine for transurethral resection of prostate surgery: Hemodynamic effects, duration of analgesia and motor block. Evidence Based Care. 2020;10:18-26.
41. Leo S, Sng BL, Lim Y, et al. A randomized comparison of low doses of hyperbaric bupivacaine in combined spinal-epidural anesthesia for cesarean delivery. Anesthesia & Analgesia. 2009;109:1600-1605.
42. Agrawal A, Agrawal S, Asthana V,et al. Comparison of intrathecal fentanyl and sufentanil in addition to bupivacaine for caesarean section under spinal anaesthesia. J Anaesth Clin Pharmacol. 2009;25:154-156.
43. Ben-David B, Miller G, Gavriel R, et al. Low-dose bupivacaine-fentanyl spinal anesthesia for cesarean delivery. Regional Anesthesia & Pain Medicine. 2000;25:235-239.