Original research

Lower Dosing of Bupivacaine Spinal Anesthesia Is Not Associated With Improved Perioperative Outcomes After Total Joint Arthroplasty

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A B S T R A C T

Background: The choice of anesthesia plays a significant role in the success of total joint arthroplasty (TJA). Isobaric bupivacaine spinal anesthesia is often used. However, dosing of bupivacaine has not been extensively studied and is usually at the discretion of the treating anesthesiologist and surgeon. The goal of this study was to determine what, if any, effect the dose of bupivacaine spinal anesthesia had on perioperative outcomes in TJA.
Methods: A total of 761 TJAs performed with bupivacaine spinal anesthesia by arthroplasty surgeons were retrospectively reviewed. Perioperative outcomes evaluated were operation duration, estimated blood loss, length of stay (LOS) in the postanesthesia care unit, hospital LOS, discharge disposition, episodes of intraoperative hypotension, postoperative nausea and vomiting, and missed physical therapy sessions because of postoperative symptoms of hypotension. A Student's t-test was used for continuous variables, and a chi-squared test was used for categorical variables.
Results: Of the 761 patients, 499 (65.6%) received 15 mg isobaric bupivacaine while 262 (34.4%) received <15 mg (range = 7.5-14.5 mg, median = 12.5 mg). With the numbers available in this cohort, lower doses of bupivacaine were not associated with any significant differences between groups for any of the studied perioperative outcomes, including proportion of patients discharged home or LOS.
Conclusion: Dosage of bupivacaine spinal anesthetic did not affect perioperative outcomes. Bupivacaine may not have a dose-related response curve in this regard, and if seeking to perform same-day or outpatient TJA, other agents may need to be considered, rather than smaller doses of bupivacaine.
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Introduction

Primary total hip arthroplasty (THA) and primary total knee arthroplasty (TKA) are two of the most prevalent orthopedic procedures in the United States. These standardized surgical techniques have improved the outcomes and quality of life for patients with debilitating degenerative conditions such as osteoarthritis, rheumatoid arthritis, femoral head and neck fractures, and posttraumatic arthritis after previous knee injuries. It is projected that the demand for primary THA and primary TKA will increase 71% to 635,000 procedures and 85% to 1.26 million procedures, respectively, by 2030 [1]. THA and TKA have both been associated with intense pain in the perioperative period, which can adversely affect patient recovery by increasing the frequency of complications, length of stay (LOS),

utilization of postoperative opioid medications, and cost [2,3]. As a result, many studies have been performed with the goal of finding the most effective anesthetic technique that maximizes pain control and minimizes complications. Historically, general anesthesia (GA) has been used to induce rapid and lasting surgical analgesia; however, recent literature suggests that a neuraxial mode of administration such as spinal anesthesia (SA) is efficacious and can reduce the incidence of surgical site infections, adverse venous thromboembolic events, perioperative blood loss, and need for transfusion [4-8]. Paziuk et al. reported fewer postoperative complications, shorter hospital LOS, and fewer discharges to an extended care facility in patients who received SA for total joint arthroplasty (TJA), primarily TKA [9]. In addition, SA is preferred at some institutions over GA because of its low cost, reliability, rapid onset, and ideal duration of action for arthroscopy and arthroplasty. These findings suggest that SA not only provides a functional benefit to patients perioperatively but may also serve to preserve health-care resources and minimize unnecessary expenses [10-12].

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Over the last few decades, fast-track protocols have been introduced for TJA to reduce hospital LOS without a concurrent increase in complications or readmissions [13]. By protocolizing perioperative care and emphasizing early mobilization, patients are now able to leave the surgical setting more quickly than in the past. The use of SA is often a crucial aspect of these novel protocols. However, the dosing and drug of choice for SA remain debatable.

Standard of care and individual preference of both anesthesiologists and orthopedic surgeons for spinal anesthetics in fast-track TJA at our institution has historically been isobaric bupivacaine. Intermediate, shorter acting local anesthetics such as lidocaine and mepivacaine are used in ambulatory settings; however, the risk of developing transient neurological symptoms has been shown to occur more frequently with these agents, and insufficient duration of anesthesia has limited their use in the arthroplasty setting [14-16]. Bupivacaine's safety profile, low cost, and lack of adverse neurological events make it an appealing medication for these relatively common procedures. However, the long duration of action of bupivacaine and its side effects of increased risk of urinary retention, prolonged hospitalization, and hypotension [17] have made accurate dosing difficult. Pushes for lower dosing have yielded inconsistent results for certain procedures [18,19]. The disadvantages of smaller doses, namely, late-onset sensory block, short duration of action, intraoperative pain and extremity movement during surgery, and sometimes severe postoperative hypotension, have slowed advances in this area, and as such, there remains a debate over optimal dosing, despite one study showing that for TKA with operative times around 100 minutes, only 5 mg of bupivacaine is effective [20]. Hyperbaric bupivacaine is another alternative, but is not commonly used in our institution for orthopedic procedures, and is more often used in the obstetric setting, although a recent Cochrane review shows that the choice of isobaric vs hyperbaric bupivacaine is also debatable in that setting [21].

The purpose of this investigation was to analyze different doses of isobaric bupivacaine SA in patients undergoing primary TJA to determine if there was an association between dosage and a variety of perioperative and intraoperative measures. We hypothesized that a lower dose would correlate with an improvement in perioperative outcomes. Our primary endpoint was hospital LOS. Secondary outcomes included other dose-related side effects, such as postoperative nausea or vomiting (PONV) and hypotension. We also evaluated intraoperative statistics, postoperative issues such as missing PT sessions, and hospital discharge disposition.

Material and methods

After approval was obtained from the local institutional review board, a retrospective chart review was performed to evaluate intraoperative and perioperative metrics in patients undergoing primary TJA between 3 surgeons at a single institution between January 2017 and December 2018.

Patient selection

All patients who underwent elective TJA at a single institution between January 1, 2017, and December 31, 2018, were included in the initial patient cohort. Patients who underwent arthroplasty for trauma were excluded, as were patients who received GA instead of SA, and patients receiving SA with any agent other than bupivacaine. Revision arthroplasty cases were also excluded from this analysis. There were no exclusions based on sex, medical comorbidities, or age. Preoperative characteristics including age, sex, body mass index (BMI), American Society of Anesthesiologists score, and preoperative diagnosis were documented. No formal power analysis was performed before the study as we included all primary

TJAs carried out with bupivacaine SA at our institution over that time period.

Bupivacaine dosing

The dose of bupivacaine spinal anesthetic received was recorded for every patient. The historic standard dose of bupivacaine at our institution is 15 mg, but over the study period, the arthroplasty surgeons at out institution expressed an ongoing preference for smaller doses to be used. The dose chosen for each patient was left to the discretion of the anesthesiologist, varied widely among individual providers, and was not chosen based on any protocol. Based on the amount of bupivacaine SA that patients received, they were separated into 2 groups for comparison: patients who received less than 15 mg (low dose) and those who received 15 mg (standard dose).

Perioperative multimodal protocol and operative standardization

All patients were given a multimodal pain regimen. Preoperatively, every patient was given acetaminophen, celecoxib, and gabapentin. Intraoperatively, patients were given tranexamic acid (1 g at incision and 1 g at closure) unless a medical contraindication existed and 10 mg of dexamethasone. Postoperatively, the oral medications were continued, and opiates were only used for breakthrough or severe pain. All patients were given the opportunity to get out of bed and ambulate with physical therapy on the day of surgery and twice a day for every postoperative day while hospitalized.

All primary THAs were performed via an anterior approach with the use of a standard operating room table. All TKAs in this cohort were performed with the use of a tourniquet.

Intraoperative and perioperative assessment

Intraoperative metrics included operative time and estimated blood loss (EBL). Preoperative blood pressure (systolic [SBP], diastolic, and mean arterial pressure [MAP]) were recorded in all patients and used to calculate intraoperative SBP and MAP thresholds. Intraoperative hypotension was defined as 3 consecutive BP readings during the procedure below 80% of the preoperative SBP or MAP. Patient's vital signs were continuously documented by the anesthesiologists throughout the duration of the cases, and a patient was noted to have intraoperative hypotension if his or her SBP was below the intraoperative threshold for 3 consecutive recordings. Bolus vasopressor use included phenylephrine and ephedrine, and the amounts of these medications were documented if they were needed in each case by the anesthesiologist. Infusion vasopressors were also documented in the same manner, although phenylephrine was the only medication used in this role in this cohort.

In the postoperative period, the amount of time spent in the postanesthesia care unit (PACU) was measured as the time after the patient left the room until the patient was deemed safe to be discharged out of the PACU (This is documented in a note in our institution's electronic medical record.). Depending on the time of day that the patient leaves the operating room, the patient either works with physical therapy on postoperative day 0 or during the morning of postoperative day 1. If a patient was unable to participate in physical therapy because of orthostatic hypotension or nausea, this was documented in the physical therapists' note. The number of missed therapy sessions was documented, along with how many times the patient required intravenous antiemetic medication for PONV. LOS in the hospital measured from the end of

surgery was recorded along with whether they were discharged home or to a rehabilitation facility.

Statistical analysis

A Student's t-test was used to compare continuous variables such as EBL, operative time, PACU LOS, and hospital LOS. Chi-squared tests were used to compare categorical values such as discharge (home vs rehab), occurrences of intraoperative hypotension, any missed physical therapy sessions, and incidences of PONV. Differences were considered statistically significant if $P < .05$.

Results

Study population

The data from 761 patients were analyzed, and all these patients underwent primary TJA between January 1, 2017, and December 31, 2018, by fellowship-trained arthroplasty surgeons at an academic medical center (Fig. 1). Four hundred ninety-nine patients received 15 mg of bupivacaine, and 262 patients received less than 15 mg (range = 7.5-14.5 mg, median = 12.5 mg, mean = 11.8 mg). The mean age of all participants was 66 years. The mean age of patients who received the standard dose of bupivacaine was 64.9 years ($\pm$11.8), and 67.7 years ($\pm$12.3) in those who received a lower dose ($P = .002$). Patients who received a lower dose spinal anesthetic had significantly lower BMIs than did those who received the standard dose (27.9 ± 5.17 vs 29.4 ± 5.62, respectively; $P = .0002$). Forty-three percent of patients who received the standard dose were male, vs 34% in the low-dose cohort ($P = .03$). There was no difference in American Society of Anesthesiologists classification between groups (2.2 ± 0.49 vs 2.3 ± 0.54). There was also no difference between groups in relation to proportion of THA and TKA (Fig. 1).

Intraoperative differences

Patients who received lower doses had shorter operative times (104.0 ± 25.5 minutes) than those in the standard group (111.9 ± 27.1 minutes) ($P = .001$) (Fig. 2). EBL was the same between groups (215.7 ± 164.4 ml vs 211.1 ± 89.9 ml; $P = .69$). Each group also had similar incidences of intraoperative hypotension (68.9% vs 67.9%; $P = .78$).

Perioperative differences

Neither group had a significantly longer hospital LOS (2.2 ± 1.1 days vs 2.0 ± 2.0 days; $P = .16$; Fig. 3). Most patients in both groups were discharged home instead of a rehabilitation facility (84.0% vs 83.2%; $P = .79$). There were also no differences in terms of missed physical therapy sessions (20% vs 16%; $P = .18$) and reports of postoperative nausea and vomiting (42% vs 38%; $P = .30$).

	Standard Dose		Low Dose		
	Mean	+/-	Mean	+/-	p value
Number of Patients	499		262		
Age (years)	64.9	11.9	67.7	12.3	**0.002**
BMI (kg/m²)	29.4	5.6	27.9	5.2	**0.0001**
Sex (% Male)	43		34		**0.03**
ASA score	2.2	0.50	2.3	0.5	0.09
THA (%)	240 (48)		137 (52)		
TKA (%)	259 (52)		125 (48)		0.27

Figure 1. Comparison of preoperative patient characteristics between the group of patients who received 15 mg of bupivacaine and those who received less than 15 mg. Bold values signify statistical significance.

	Standard Dose		Low Dose		
	Mean	+/-	Mean	+/-	p value
Operative Time (minutes)	111.9	27.1	104.0	25.5	**0.0001**
Estimated Blood Loss (ml)	215.7	164.4	211.3	89.9	0.68
Intraop Hypotension (%)	68.9		67.9		0.78

Figure 2. Comparison of intraoperative metrics between the group of patients who received 15 mg of bupivacaine and those who received less than 15 mg. Bold values signify statistical significance.

Post-hoc analysis

As stated previously, no a priori power analysis was performed, as we included all cases handled within the study timeframe. Upon post-hoc analysis for the primary endpoint of hospital LOS using these numbers, a study would have to include many more patients (approximately 1100, which were not available in the institutional review board–approved study period) to be adequately powered to detect a difference in LOS.

Discussion

SA is the preferred method for anesthesia in TJA at our institution and many places around the world. Bupivacaine is commonly used as the agent of choice. However, optimal dosing of bupivacaine has not been established. The current investigation used retrospectively collected data from patients who underwent elective TJA at a single institution during a 2-year period to compare a variety of perioperative and intraoperative measures.

In this study, we observed that patients who received 15 mg of bupivacaine had longer operative times than patients who received lower doses. It is important to note here that no patients in either cohort required conversion to GA because of insufficient duration of SA, despite operative times being shorter in the lower dose cohort. The shorter operative times are likely due to the fact that the surgeon and anesthesia team were not blinded to patient selection, and operative difficulty is therefore a confounder. Less technically challenging cases in patients with more straight-forward anatomy were likely preferentially given lower doses of bupivacaine, as both the surgeon and anesthesiologist expected the case to be shorter in duration. This also explains the higher percentage of female patients and lower BMI in the low-dose cohort as well. In addition, the Hawthorne effect is likely at play here as well, as surgical teams may have changed their behavior and operated more expeditiously knowing that they were being observed [22]. Finally, anesthesiologists may have communicated to the surgeons to operate with more alacrity in those cases as well. However, even with those cases being handled more efficiently, that cohort still had just as much intraoperative and postoperative side effects as the cohort getting the standard dose and having longer surgeries.

In addition, regardless of dosing, patients who received bupivacaine had a lengthy hospital stay (2.2 vs 2.0 days), and a sizable portion of patients in each arm missed physical therapy visits while admitted (20% vs 16%). Postoperative mobilization is key to

	Standard Dose		Low Dose		
	Mean	+/-	Mean	+/-	p value
Hospital LOS (days)	2.2	1.1	2.0	1.3	0.16
Discharged home (%)	84		83		0.79
Missed PT (%)	20		16		0.18
PONV (%)	42		38		0.30

Figure 3. Comparison of perioperative metrics between the group of patients who received 15 mg of bupivacaine and those who received less than 15 mg.

accelerating discharge and ensuring patient safety by decreasing venous stasis. When a patient is unable to participate in PT post-operatively because of the hypotensive effects of a lingering SA, this can be discouraging and has been shown to lead to increased 30-day readmission rates [23].

With numbers available, there was no association found between bupivacaine dosage and EBL, episodes of intraoperative hypotension, discharge disposition, or frequency of PONV.

There are several limitations of the study. As mentioned previously, there was no standardized protocol for determining which patients received 15 mg of anesthetic and which received a smaller dose. Figure 1 elucidates that there are some baseline differences in the patients who received smaller doses of anesthetic, most notably those who had lower BMIs. A lower BMI is unsurprisingly associated with better outcomes after TJA, and it is likely that anesthesiologists felt that patients with lower BMIs would have sufficient coverage with a smaller dose of bupivacaine because of shorter predicted operative times. On a related note, it is possible that the lower BMI of these patients played a significant role in OR times being shorter, likely related to an easier surgical approach. Conversely, older patients tended to receive smaller doses of spinal anesthetic. However, even with the low-dose cohort having shorter surgeries and likely representing more straight-forward cases, there was no difference in LOS, PONV, hypotension, or missed PT. This suggests even these "easier" cases were still hampered by the side effects from their bupivacaine SA.

Contrary to our original hypothesis, lower dosing of bupivacaine for SA in TJA did not corroborate with improved perioperative outcomes, nor did it expedite discharge or allow patients to work with PT more reliably. Future studies should focus on developing a more standardized approach to determining who will receive a larger or smaller dose of this anesthetic and should randomize patients so that both groups are equal.

The average LOS in this cohort was about 2 days, which may suggest that surgeons seeking to perform same-day or accelerated discharge TJA may want to seek other anesthetic options. An alternative to lower doses of bupivacaine is to choose a different agent altogether. Recent research has shown promising results for shorter acting agents such as chloroprocaine, especially in select patients that can have their surgeries performed quickly [24].

Conclusions

These data suggest that for same-day or fast-track TJA, neuraxial anesthetic agents other than low-dose bupivacaine should be considered, even in select patients for whom a faster surgery is anticipated, to expedite patient recovery and discharge.

Conflicts of interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: C. L. Herndon is a board/committee member in AAOS. R. P. Shah is a paid consultant for Link Orthopaedics and is a board/committee member in US Food and Drug Administration. H. J. Cooper received royalties from Corin U.S.A. and research support from KCI; is in the speakers' bureau of KCI; is a paid consultant for Corin U.S.A., KCI Medical Canada Inc., KCI USA Inc., and Zimmer Biomet; is in the editorial or governing board of JOA and JBJS-America; and is a board/committee member in AAOS.

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