



## Systematic review of spinal anaesthesia using bupivacaine for ambulatory knee arthroscopy

G. S. Nair, A. Abrishami, J. Lermite and F. Chung\*

Department of Anesthesia, Toronto Western Hospital, University Health Network, University of Toronto, McL 2-405, 399 Bathurst Street, Toronto, Ontario, Canada M5T 2S8

\*Corresponding author. E-mail: frances.chung@uhn.on.ca

The use of lidocaine in spinal anaesthesia is associated with transient neurological syndrome (TNS). Bupivacaine has a lower incidence of TNS as an alternative but it may have a prolonged action. This study systematically reviews the literature about the recovery profile of patients undergoing spinal anaesthesia, using bupivacaine for arthroscopic knee surgery. We identified 17 eligible randomized clinical trials (RCTs) (1268 patients). All the articles in this review, except one, used hyperbaric bupivacaine. Five trials compared different doses of bupivacaine (range 3–15 mg). Large doses of bupivacaine (10 and 15 mg) were associated with delayed recovery, and supine positioning was associated with a high incidence of failure. With unilateral positioning, a dose as low as 4–5 mg seems to be sufficient. Five trials comparing bupivacaine or levobupivacaine with ropivacaine showed no significant difference in the time to home discharge. When bupivacaine was combined with fentanyl in two trials, marginal delay in recovery was found [time to discharge (min); weighted mean difference (WMD) 14.1, 95% CI 11.9–40.1] and increased nausea and pruritus but had reduced postoperative pain. Unilateral and bilateral spinal anaesthesia were assessed in two trials, and the latter group was associated with early recovery and discharge [time to discharge (min); WMD –41.6, 95% CI –63.6 to –19.6]. The results of our systematic review suggest that 4–5 mg of hyperbaric bupivacaine can effectively produce spinal anaesthesia for knee arthroscopy with unilateral positioning. Ropivacaine or the addition of adjuvants did not improve the recovery time. There is a need for tighter RCTs with more consistent endpoints.

*Br J Anaesth* 2009; **102**: 307–15

**Keywords:** anaesthetic techniques, subarachnoid; anaesthetics local, bupivacaine; anaesthetic techniques, regional, knee; surgery, orthopaedic

The use of lidocaine in spinal anaesthesia has declined over the years and has become virtually nonexistent because of the high incidence of transient neurological syndrome (TNS). The abandonment of lidocaine in spinal anaesthesia, however, has been a setback for ambulatory anaesthesia, where early recovery is vital. Bupivacaine, the most common alternative to lidocaine, has a low incidence of TNS (0–1%)<sup>32 33 36</sup> but delays home discharge in ambulatory surgical patients if used in the usual doses.<sup>49</sup> Knee arthroscopy is a common procedure in the ambulatory setting. The incidence of TNS is increased with knee arthroscopy<sup>49 53</sup> because of the patient positioning<sup>35</sup> and ambulatory setting.<sup>26</sup> These factors make it necessary to evaluate the role of bupivacaine as an alternative anaesthetic agent to lidocaine for spinal anaesthesia in knee arthroscopy. The aim of this systematic review is to determine the optimal dosing of bupivacaine and to investigate the effect of other strategies such as unilateral patient

positioning, using alternative agents or adding adjuvants on the efficacy of the medication in this setting.

### Methods

#### Search strategy

This systematic review was carried out using the methods established by the Cochrane Collaboration.<sup>34</sup> We searched the Cochrane Central Register of Controlled Trials (CENTRAL) and the Database of Abstracts of Reviews of Effects (DARE) in The Cochrane Library (Issue 3, 2007) and conducted electronic searches utilizing MEDLINE from January 1950 to December 2007, EMBASE from January 1974 to December 2007, and CINAHL from January 1982 to December 2007. Both text-word and index-word terms were used; the text-word terms included in our search

strategies included: ‘bupivacaine’, ‘spin\$', ‘an?esthesia’, ‘ambulatory’, ‘out?patient’, ‘day?case’, ‘surg\$', ‘knee’, ‘arthroscop\$’. We also exploded the following index-word terms: ‘ambulatory surgical procedures’, ‘anesthesia, spinal’, ‘bupivacaine’, and ‘arthroscopy’. We hand-searched reference lists from the already retrieved articles to identify further trials. In addition, contact was made with the principal authors and experts in the field to identify additional published or unpublished data relevant to the review.

### *Study selection criteria*

Three reviewers (G.S.N., A.A., and J.L.) independently assessed titles, abstracts, or both of the hits retrieved from the electronic database and hand searches for possible inclusion according to the pre-defined selection criteria. Discrepancies were resolved by the fourth author (F.C.). Studies were eligible for inclusion if they were randomized clinical trials (RCTs) with parallel-group design, that evaluated the use of bupivacaine for spinal anaesthesia during elective knee arthroscopic surgery in ambulatory settings. Observational studies (e.g. non-randomized trials, case series) were not considered for review. There was no language restriction but all trials included in the review were published in English.

### *Data extraction*

We extracted the following information about each study: method of randomization, number and characteristics of study participants, trial design, treatment regimens, time to onset of spinal block, duration of specific positioning after placing the block, incidence of unilateral and bilateral spinal block, time to recovery, time to voiding, time to home discharge, incidence of complications and failures. Data were extracted from each trial by two reviewers (G.S.N. and A.A.), checked for consistency and accuracy, and then entered into a computer database for analysis. The authors of included trials were contacted for the missing data.

### *Assessment of study methodological quality*

Methodological quality was defined as the confidence that the design, conduct, and report restrict bias in the intervention comparison (Cochrane Handbook) as evaluated independently by the reviewers (G.S.N., A.A., and J.L.). Disagreements were resolved by the fourth author (F.C.). We assessed each study for the method of randomization, and of concealment of study intervention allocation, the degree of blinding, and the completeness of follow-up. Randomization method was considered adequate if it was generated by a table of random numbers, or computer-generated. Quasi-randomized trials (research design that does not ensure true randomization) were not included and assessed in this review. Allocation concealment was

graded adequate if the allocation of patients is carried out by independent staffs who are not involved in the study, using methods such as serially numbered opaque-sealed envelopes, on-site locked computer, etc. Blinding was adequate if the patient, care givers, and outcome assessors are blinded to the treatment. Follow-up was adequate if the numbers and reasons for dropouts and withdrawals in all intervention groups are described or if it is specified that there were no dropouts or withdrawals.

### *Data analysis*

Statistical methods of RevMan analyses (Review Manager, version 2.4, The Nordic Cochrane Centre, Copenhagen, Denmark) were used for analysing the data. In this review, pooling of the data was possible among the results of studies comparing bupivacaine with ropivacaine and studies evaluating the role of adjuvants and different positioning. Pooled treatment effects were estimated using both fixed- and random-effect methods. However, in the text, we have reported only the fixed-effect model, as the two analyses came into a similar conclusion in the sensitivity analyses. However, with regard to the different doses of bupivacaine, the available trials have reported the outcomes in variable formats. For example, time to discharge or voiding is reported as mean (SD) in some trials and as median with range or inter-quartiles in others. This factor along with the evident clinical heterogeneity (e.g. different design) among the trials led us not to proceed to meta-analysis in this group of studies. The results of these trials, however, were reported in the review for descriptive and qualitative analyses. For continuous variables, for example, time to voiding, we calculated the weighted mean difference (WMD) with corresponding 95% confidence intervals (CIs). No dichotomous data were pooled in this systematic review. The  $I^2$  statistic was used to measure inconsistency among the study results.  $I^2 = [(Q - df) / Q] \times 100\%$ , where  $Q$  is the  $\chi^2$  statistic and  $df$  is its degrees of freedom (*Cochrane Handbook*). This describes the percentage of the variability in effect estimates that is attributable to heterogeneity rather than to sampling error (chance). A value  $>50\%$  may be considered substantial heterogeneity. Subgroup analyses and assessment of publication bias (funnel plot) were not possible because of the limited number of studies used for pooling of the data. We analysed data with both fixed- and random-effect model for sensitivity analyses.

## **Results**

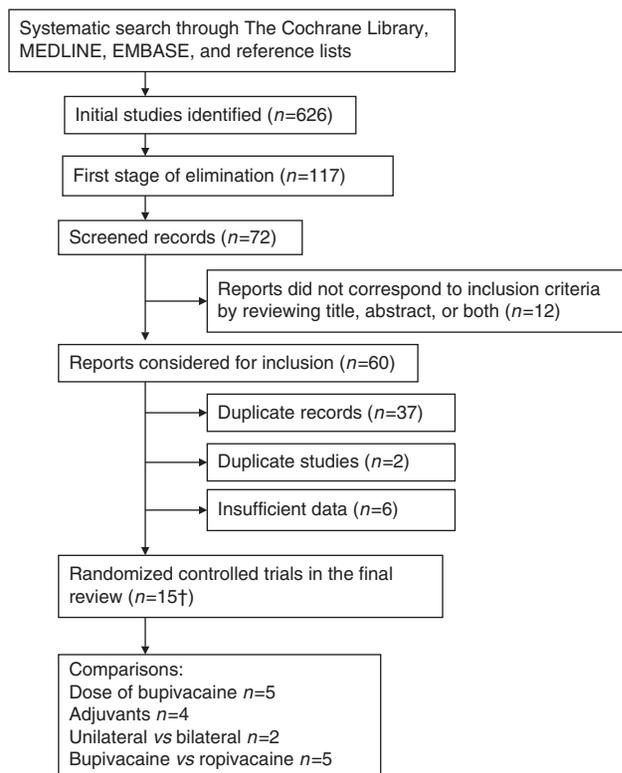
The literature search performed in December 2007 identified 626 articles of potential relevance. The study selection process eliminated 437 articles by a review of the abstracts and titles. Another 117 articles were excluded after a review of their methodology and results sections. This process left us with 72 articles on spinal anaesthesia

with bupivacaine for arthroscopic knee surgeries in ambulatory care (Fig. 1). The study was designed to include only randomized controlled trials. After eliminating duplicate articles (studies that are published in more than one journal or cited more than once in the same database) and non-randomized trials, only 15 articles (a total of 1248 patients)<sup>6 8 9 11 13 16 22–24 28 31 37 39 51 58</sup> remained. The authors of the articles with insufficient data were contacted to get more information on the data. All of the trials are included in the review and are fully referenced.

The average age of the patients was 41 yr (range 18–83). The average sample size was 33 patients (range 15–50). All the articles in this review, except one,<sup>13</sup> used hyperbaric bupivacaine. The RCTs were then divided into four groups. The first group was trials comparing different doses of bupivacaine,<sup>6 11 16 37 58</sup> the second group those comparing the effects of adding adjuvants,<sup>8 31 39 51</sup> the third group those comparing bupivacaine with ropivacaine,<sup>9 13 16 22 28</sup> and the fourth group comparing different patient positions after administering spinal anaesthesia.<sup>23 24</sup>

### Methodological quality of the trials

Eleven of the total 16 trials met all the factors of methodological quality and they have reported adequate methods for randomization, allocation, concealment, blinding, and completeness of follow-up. The remaining five trials<sup>9 22 23 51 58</sup>



**Fig 1** Flow chart of screened, excluded, and analysed papers. †The total number of the trials is not the sum of studies for each comparison. There is one study<sup>16</sup> which includes two types of comparison.

were associated with moderate risk of bias because they were not clear in the method of randomization, allocation, concealment, and blinding.

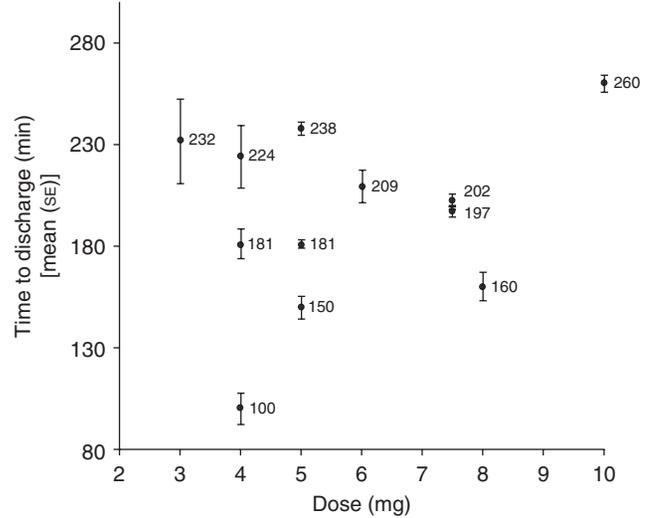
### Trials comparing different doses of bupivacaine

There were five trials<sup>6 11 16 37 58</sup> comparing different doses of bupivacaine ranging from 3 to 15 mg. The trials include a total of 387 patients. Three trials had two comparison groups<sup>16 37 58</sup> and two trials had more than two groups<sup>6 11</sup> (Table 1). Time to onset of block, time to voiding, home discharge, and failure rates were compared in the five trials. The definition used to describe the onset of block was heterogeneous between the trials. The criteria for home discharge used in the trials were based on standard criteria of stable cardiovascular and respiratory system, ability to void and walk with crunches, but were not uniform between trials. Failure was considered when general anaesthesia had to be given because of inadequate block. In some trials, values were reported as mean (SD), and in others as median (range). The authors of these trials were contacted for more relevant data, but the response rate was poor. Therefore, statistical pooling of the data was not feasible.

Studies comparing different doses of bupivacaine can be divided into two groups on the basis of the positioning of the patient during spinal anaesthesia,<sup>6 11 16 37 58</sup> as position affects the distribution of the drug in the subarachnoid space and hence affecting recovery. Unilateral position<sup>11 16 37 58</sup> results in the concentration of the drug, on the one hand, and hence the need for reduced dose. In one study,<sup>6</sup> doses of bupivacaine 5–15 mg were given, with patients in the supine position. The higher doses (10 and 15 mg) resulted in significant delay in time to voiding (>240 min) and time to home discharge (>260 min) without any significant changes in time to the onset of sensory block when compared with the 5 mg dose. However, the lower dose (5 mg) given in the supine position was associated with a high incidence of failure (>25%). On the other hand, three studies<sup>11 16 58</sup> (n=327 patients) compared different doses of bupivacaine from 3 to 8 mg, as unilateral spinal, and had variable time to recovery. We showed that the studies using the same dose of medication reported variable time to discharge (Fig. 2). On average, time to voiding ranged from 170 to 240 min and time to home discharge varied from 180 to 240 min. Valanne and colleagues<sup>58</sup> showed that 4 and 6 mg bupivacaine has a failure rate of 6.2% and 1.9%, respectively—statistically not significant. No failure of anaesthesia was reported in the other three trials using doses of 3–8 mg.<sup>11 16 37</sup> It was also shown that intermediate dose of bupivacaine (i.e. 6 or 7.5 mg) was associated with increased time to recovery when compared with lower doses. For example, in 90 patients,<sup>16</sup> bupivacaine 7.5 mg increased time to discharge by 40 min compared with 5 mg (P<0.05, Table 1). A similar pattern was reported in a

**Table 1** Studies on different doses of bupivacaine used for spinal anaesthesia in knee arthroscopy. Failure: required general anaesthesia for surgery because of inadequate spinal block. Values are mean (SD) or median (range). \*Statistically significant values ( $P < 0.05$ ). NA, data not available

Study ID	Number of patients	Age (yr)	Dose (mg)	Sensory block	Time to onset (min)	Time to voiding (min)	Time to home discharge (min)	Number of patients with failure
Borghetti and colleagues <sup>11</sup>	90	37 (13)	4/6/8	T12 level	13 (5)/10 (4)/9 (4)*	NA	NA	0/0/0
Kirans and Upma <sup>37</sup>	40	NA	3/4	Peak level (NA)	12.5 (3.9)/10.2 (3.0)*	212 (95)/200 (66)	232 (90)/224 (67)	0/0
Cappelleri and colleagues <sup>16</sup>	91	47 (16)	5/7.5	T12 level	10 (9–13)/11 (10–116)	190 (181–247)/238 (221–276)*	238 (219–277)/197 (187–251)*	0/0
Valanne and colleagues <sup>38</sup>	106	45 (15)	4/6	NA	NA	172 (115–319)/203 (122–377)*	181 (115–319)/209 (147–377)*	3 (6.2%)/1 (1.9%)
Ben-David and colleagues <sup>6</sup>	60	41 (3)	5/7.5/15/10	Peak level T5	15 (1)/14 (1)/15 (1)/12 (1)	163 (8)/186 (14)/241 (14)/428 (34)*	181 (8)/202 (14)/260 (15)/471 (35)*	0/0/0/4 (26%)



**Fig 2** Recovery profile based on different doses of bupivacaine in the included trials. Each point indicates the mean (SE) of time to discharge (min) in one study.

comparison of bupivacaine 4 and 6 mg<sup>58</sup> (i.e. the delay in time to home discharge >20 min,  $P < 0.05$ ; Table 1). Trials also showed that the height of the maximum sensory block was similar among the different dosages. Time to onset of sensory block was slightly lower (i.e. 2–3 min lower) after higher doses of bupivacaine; however, it was not clinically significant (Table 1). The incidence of complications in the included studies is very low. There was no reported incidence of TNS in any of the included trials. The most common reported complication is post-dural puncture headache and its incidence is ~1%<sup>11</sup> to 4%<sup>58</sup> ( $P > 0.05$ ). The incidences of other complications such as nausea, vomiting, and urinary retention are between 0% and 1%. Data regarding intraoperative complications were not reported.

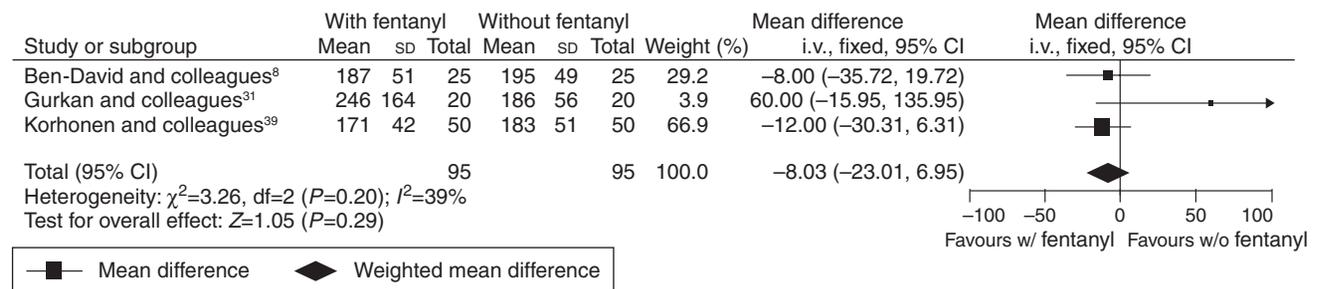
To summarize, hyperbaric bupivacaine showed a significantly prolonged recovery with high doses (e.g. 10 or 15 mg). In the supine position, a lower dose (5 mg) has a higher incidence of failure (25%). In the unilateral position, however, doses of bupivacaine as low as 4–5 mg can produce enough anaesthesia with no or very low incidence of failure. Increasing the dose of medication to 6–7.5 mg may result in delayed recovery without any significant changes in failure rate.

### Studies comparing the effect of adding adjuvants to bupivacaine

Four trials<sup>8 31 39 51</sup> (260 patients with mean age 39–42 yr) compared the effect of adding opioid adjuvants to bupivacaine for arthroscopic knee surgeries in the day-case setting (Table 2). Fentanyl was added to bupivacaine in all four trials, and morphine was added to bupivacaine as a third group in one.<sup>8</sup> Fentanyl was used in a dose of 10–25 µg along with varying doses of bupivacaine. One study<sup>8</sup>

**Table 2** Studies comparing bupivacaine plus adjuvants with plain bupivacaine. Values are mean (SD) or medians (range)

Study ID	Number of patients	Age	Adjuvant ( $\mu\text{g}$ )	Mean (SD) of time to voiding (min)	Mean (SD) of time to home discharge (min)
Gurkan and colleagues <sup>31</sup>	60	42	Morphine (50)	422 (161)	424 (162)
			Fentanyl (25)	244 (163)	246 (164)
			Saline	183 (54)	186 (56)
Korhonen and colleagues <sup>39</sup>	100	43 (14)	Fentanyl (10)	171 (111–279)	171 (111–279)
			None	183 (111–316)	183 (111–316)
Ben-David and colleagues <sup>8</sup>	50	39 (14)	Fentanyl (10)	169 (52)	187 (51)
			None	177 (53)	195 (49)
Roussel and Heindel <sup>51</sup>	50	35 (11)	Fentanyl (25)	NA	NA
			Saline		

**Fig 3** Meta-analysis of the discharge times comparing bupivacaine plus adjuvant vs plain bupivacaine. The horizontal line with box shows the respective odds ratio (95% CI) for individual studies, and the dark diamond represents the pooled WMD.

used a high dose of bupivacaine (12 mg) but the others used doses of 3–6 mg.<sup>31 39 51</sup> One trial was excluded from the statistical analysis because of insufficient data.<sup>8</sup> Pooling of data from three trials<sup>8 31 39</sup> showed no significant change in discharge time when fentanyl was added to bupivacaine for spinal anaesthesia (WMD -8.0, 95% CI -23.0 to 6.9,  $P=0.20$ , Fig. 3).

All the trials reported an increased incidence of side effects when fentanyl was used as an adjuvant. The most notable side effect was the incidence of pruritus of 48–75% in the fentanyl group compared with 0–4% in the bupivacaine-alone group. In spite of this high incidence of pruritus in the opioid group, only 15–23% of the patients needed treatment. Other side effects such as hypotension (<1%) and urinary retention (<1%) were equally distributed between the groups. The addition of morphine resulted in longer recovery time than plain bupivacaine or plain bupivacaine plus fentanyl.<sup>31</sup> On the other hand, qualitative analysis showed that the use of intrathecal opioids was associated with reduced pain scores and decreased analgesic requirement in the postoperative period. Overall, using intrathecal opioids for knee arthroscopy in ambulatory anaesthesia results in a prolongation of discharge by 14 min ( $P=0.21$ , Fig. 3) and a higher incidence of pruritus but has the benefit of reducing the postoperative pain scores.

#### Studies comparing bupivacaine with ropivacaine

There were five trials<sup>9 13 16 22 28</sup> that compared the different doses of bupivacaine or levobupivacaine with ropivacaine

for spinal anaesthesia in outpatient knee arthroscopies. In two of the trials,<sup>9 13</sup> levobupivacaine was compared with ropivacaine; in two others,<sup>22 28</sup> racemic bupivacaine was compared with ropivacaine; and one studied all three drugs in three different groups.<sup>16</sup> Pooling of data was not possible, as there is a significant heterogeneity in the data and there is variation in the isomer of bupivacaine used in these trials.

Descriptive analysis of data showed that there was no significant difference between bupivacaine or levobupivacaine, and ropivacaine with regard to time to voiding, time to discharge, and side effects (Table 3). However, in two trials,<sup>12 22</sup> there is a longer time to onset and shorter time to recovery from motor and sensory block with ropivacaine than with bupivacaine or levobupivacaine. But this did not change the time to home discharge. A trial<sup>28</sup> aimed at calculating the dose potency ratio of bupivacaine and ropivacaine concluded that bupivacaine was 1.5 times as potent as ropivacaine. Our search did not yield articles that compared bupivacaine and other local anaesthetics such as mepivacaine or chloroprocaine for knee arthroscopy. Overall, ropivacaine shows a similar profile to bupivacaine when used in knee arthroscopy in day-case setting.

#### Trials comparing unilateral and bilateral spinal anaesthesia

Two trials<sup>23 24</sup> of 170 patients compared the effect of unilateral and bilateral spinal anaesthetic (Table 4). Unilateral spinal anaesthesia is defined as patient positioned with the

**Table 3** Studies comparing different local anaesthetics with bupivacaine. Bup, bupivacaine; Rop, ropivacaine; Ligno, lignocaine. Values are mean (sd) or median (range). NA, data not available

Study ID	Number of patients	Age	Doses of anaesthetics (mg)	Time to void (min)	Mean (sd) of time to home discharge (min)
Bigat and colleagues <sup>9</sup>	40	46 (12)	Bup: 7.5 Rop: 10	305 (174–720) 330 (162–670)	NA
Cappelleri and colleagues <sup>16</sup>	91	47 (16)	Bup: 5/7.5 Rop: 7.5	190 (181–247)/238 (221–276) 189 (126–154)	238 (219–277)/197 (187–251) 197 (177–218)
El-Halafawy <sup>22</sup>	60	46 (9)	Bup: 8 Rop: 8/12	178 (12.3) 175.4 (10.5)/171 (16.1)	162.2 (14.9) 160.5 (22.4)/159.2 (26.1)
Gautier and colleagues <sup>28</sup>	150	NA	Bup: 8 Rop: 8/10/12/14	200 (50) 165 (45)/174 (38)/199 (52)/233 (52)	NA
Breebaart and colleagues <sup>13</sup>	90	40	Ligno: 60 Bup: 10 Rop: 12	245 (65) 284 (57) 285 (65)	265 (70) 311 (56) 305 (73)

**Table 4** Studies comparing unilateral vs bilateral positioning for spinal anaesthesia using bupivacaine in knee arthroscopy. \*Failure: required general anaesthesia for surgery because of inadequate spinal block. BL, bilateral; UL, unilateral

Study ID	Number of patients	Mean (sd) of age	Doses of bupivacaine (mg)	Positioning duration (min)	Number of patients with unilateral sensory block <i>n</i> (%)	Mean (sd) of time to home discharge (min)	Number of patients with failure*
Fanelli and colleagues <sup>24</sup>	50 in BL 50 in UL	39 (13)	8 8	15 15	— 26 (55)	281 (83) 264 (95)	3 3
Esmagolu and colleagues <sup>23</sup>	35 in BL 35 in BL	36 (10)	15 7.5	10 10	— 30 (85.7)	252.87 (72.2) 195 (45.97)	None

operating side lateral for 10–15 min after the administration of the spinal anaesthetic. Bilateral spinal anaesthesia is defined as a patient positioned supine immediately after the administration of the spinal anaesthetic. The analysis of discharge time revealed that unilateral spinal anaesthesia was associated with an early recovery and discharge (Fig. 4). Patients who had received unilateral spinal anaesthesia were ready for discharge to home, on an average, 42 min earlier than patients who received bilateral spinal anaesthesia. In patients in whom unilateral spinal anaesthesia was attempted, 55–86% had pure unilateral sensory anaesthesia, and 75–95% had pure unilateral motor block. Unilateral spinal anaesthesia also resulted in a denser block (mean Bromage scale<sup>14</sup> score for motor block in bilateral patients was 0/1/2/3:0/2/0/45 compared with unilateral patients, 0/1/2/3:4/1/6/36) on the operating side. Unilateral spinal anaesthesia is also associated with a lower incidence of side effects such as hypotension (0–6% vs 9–28%,  $P < 0.05$ ). The incidence of bradycardia is 0–8% in the unilateral group and 5–10% in the bilateral group ( $P > 0.05$ ). There was no incidence of post-dural puncture headache and nausea. Eight per cent to 9% of patients in the unilateral group developed urinary retention compared with only 2–5% patients in bilateral spinal anaesthesia, but this was not significant ( $P > 0.05$ ).

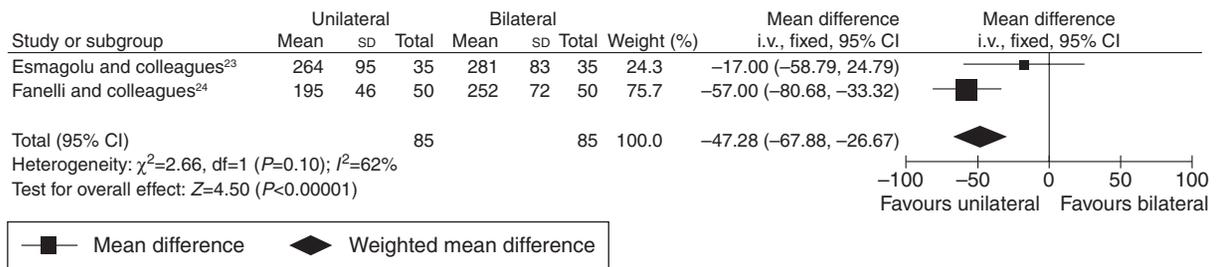
## Discussion

Our results suggest that low doses of hyperbaric bupivacaine 4–5 mg can effectively produce spinal anaesthesia

with unilateral positioning in knee arthroscopy. Higher doses or bilateral positioning may result in delayed recovery or high rate of failure, respectively. Ropivacaine or the addition of adjuvants did not improve the recovery time.

In terms of technique, almost all studies used unilateral patient position after the administration of spinal anaesthesia. This might explain the high rate of failure (25%) in the 5 mg group in one study.<sup>6</sup> In the supine position with a bilateral spinal, the medication is distributed over a larger area and less becomes available to produce sensory nerve block at the site of surgery. Using a unilateral position, doses of bupivacaine as low as 4–5 mg can be effective for knee arthroscopy.<sup>11 16 37</sup> The lower dose of 3 mg also showed no incidence of failure; however, it was used in only 20 patients in one study.<sup>37</sup> Increasing the dose to 6 or 7.5 mg did not make any significant change but delayed the recovery time. Among the unilateral spinal studies using a lower dose of 4 or 5 mg bupivacaine, there is varied time to recovery ranging from 170 to 240 min, translating to 1 h difference in time to home discharge. To draw a final conclusion on the optimal dose of bupivacaine, larger trials with head-to-head comparison between low doses of bupivacaine 4–5 mg given in the unilateral position are required.

In comparison with the other outpatient surgery, motor paralysis is not required and a lower level of spinal anaesthesia is sufficient in knee arthroscopy. This might explain the low rate of failure with 4–5 mg bupivacaine. However, similar failure rates of ~5%<sup>35</sup> and 6%<sup>24 38</sup> are seen in other observational studies of knee arthroscopy patients, irrespective of the dose of bupivacaine used.



**Fig 4** Meta-analysis of the discharge times comparing bupivacaine unilateral vs bilateral positioning for spinal anaesthesia using bupivacaine in knee arthroscopy. The horizontal line with box shows the respective odds ratio (95% CI) for individual studies and the dark diamond represents the pooled WMD.

Also, similar incidence of failure (5–10%) is seen in obstetric and general surgical patients<sup>29 47</sup> who received bupivacaine. Factors other than dose such as the technique of administration might be the cause of failure.

In this review, trials using intrathecal opioids in knee arthroscopy patients in day care anaesthesia showed a reduction in the postoperative pain score but caused higher side effects of opioids. The incidence of moderate-to-severe pain in postoperative day-case patients ranges from 30% to 40%<sup>50</sup> and hence any method that reduces pain is beneficial. However, the benefit of good postoperative analgesia obtained with opioids has to be balanced against their side effects. Among all the side effects of intrathecal opioids, pruritus (50–75%) was most common. This corroborates with a recent study<sup>46</sup> which reported a higher incidence of pruritus with knee arthroscopy than other surgical patients, and pruritus further increased with the use of bupivacaine rather than lignocaine. The increased pruritus can be a disadvantage in day care patients in whom anaesthetic management is tailored to reduce side effects. The incidence of other side effects such as nausea and vomiting, urinary retention,<sup>30</sup> and hypotension is low in the reviewed trials. Studies in mice,<sup>1</sup> and in obstetric<sup>7 10 21</sup> and orthopaedic<sup>5</sup> patients also showed that intrathecal opioids reduced the dose of local anaesthetic and improved the quality of anaesthesia. Other adjuvants that have been added to spinal anaesthesia such as clonidine<sup>48</sup> and neostigmine<sup>48</sup> prolonged recovery and may not be acceptable in day-case patients.

Qualitative analysis of data from the five trials comparing bupivacaine and ropivacaine<sup>45</sup> in knee arthroscopy patients did not reveal any difference in terms of time to home discharge. However, comparisons of bupivacaine and ropivacaine in knee arthroscopy patients<sup>9 22</sup> suggest a delayed onset and early recovery with ropivacaine. The shorter duration of the action also corroborates with trials in Caesarean section.<sup>2 4 15 27 43</sup> The shorter duration of action of ropivacaine can be explained by the lower potency of ropivacaine as shown in human volunteer studies<sup>44</sup> and studies of ropivacaine in epidural anaesthesia.<sup>25 41</sup> However, the early recovery in these trials did not translate into early discharge, and this could be attributed

to other factors such as administrative factors that decided the time to home discharge.

Other local anaesthetics including mepivacaine,<sup>54 57</sup> chlorprocaine,<sup>17 20</sup> and prilocaine<sup>52 56</sup> have been used for spinal anaesthesia in ambulatory setting. These local anaesthetics are short-acting but have their own side effects.<sup>42 59</sup> The literature search for this review showed that there were no randomized controlled trials comparing bupivacaine with these short-acting agents for arthroscopic knee surgery.

This review shows that unilateral spinal anaesthesia is associated with a significantly early recovery and readiness for home discharge. Unilateral block allows a lower dose of local anaesthetic to be used by concentrating the drug on one side giving a denser block. The use of a smaller dose results in a reduced incidence of side effects such as bradycardia, hypotension, and urinary retention.<sup>18 19 55</sup> An important consideration while performing unilateral spinal anaesthesia is the extra time required for keeping the patient in the lateral position for the local anaesthetic to 'fix'. Overall, unilateral spinal anaesthesia offers early discharge with fewer side effects and can be utilized as a useful method in day-case knee arthroscopies.

The baricity of local anaesthetic agent is an important determinant of the outcome of spinal anaesthesia. In this review, the influence of different baricities on the results could not be evaluated because all used only hyperbaric bupivacaine.<sup>40</sup> It has been shown that both hyperbaric and plain bupivacaine can be suitable alternatives for adult outpatient knee arthroscopy but hyperbaric bupivacaine provides a more unilateral spinal block.<sup>40</sup> This is, however, one area for future research, as more studies comparing plain and hyperbaric bupivacaine in patients for outpatient knee arthroscopy are required to clarify which allows an early home discharge.

The results of this systematic review should be interpreted in the presence of the following limitations: the included RCTs are very diverse and heterogeneous with regard to the definition of the study outcomes, techniques, and their results. Each study used loss of sensation at different spinal levels to determine the onset of block. The method used to test for sensory loss also varied between

studies. The recovery endpoints also varied between studies. Recovery of sensation at S1 was considered in few studies, whereas some studies used time to voiding as time to recovery. There is also variation in the way the data were presented in the different studies. Some reported in mean and SD and others mentioned median and range. In terms of technique, all but one used a unilateral patient position after the administration of spinal anaesthesia.

Future studies require more consistent design and sample size. The dose of local anaesthetic needs to be standardized, patient positioning made more uniform, and concentration of the drug also made standard.

In conclusion, our review suggests that an appropriate low dose of bupivacaine for day-case knee arthroscopy is 4–5 mg given in the unilateral position. Higher doses resulted in delayed recovery, and bilateral positioning caused a higher rate of failure. The best recovery profile occurs with unilateral positioning. Ropivacaine or the addition of adjuvants did not improve the recovery time of patients. The level of evidence for all the conclusions described here is 1a and the grade of recommendation is A.<sup>3</sup> To draw a definite clinical conclusion about the optimum dose of bupivacaine, future quality RCTs with consistent design and more sample size are required.

## Acknowledgements

We would like to thank the authors of those original studies who responded to our requests for further data.

## References

- Akerman B, Arwstrom E, Post C. Local anesthetics potentiate spinal morphine antinociception. *Anesth Analg* 1988; **67**: 943–8
- Al-Abdulhadi O, Biehl D, Ong B, Boker A. Hyperbaric spinal for elective Cesarean section—ropivacaine vs bupivacaine. *Middle East J Anaesthesiol* 2007; **19**: 385–96
- Atkins D, Best D, Briss PA, et al. Grading quality of evidence and strength of recommendations. *Br Med J* 2004; **328**: 1490
- Aveling W, Klineberg PL. Hyperbaric ropivacaine and bupivacaine. *Br J Anaesth* 2003; **91**: 301–2
- Ben-David B, Frankel R, Arzumov T, Marchevsky Y, Volpin G. Minidose bupivacaine–fentanyl spinal anesthesia for surgical repair of hip fracture in the aged. *Anesthesiology* 2000; **92**: 6–10
- Ben-David B, Levin H, Solomon E, Admoni H, Vaida S. Spinal bupivacaine in ambulatory surgery: the effect of saline dilution. *Anesth Analg* 1996; **83**: 716–20
- Ben-David B, Miller G, Gavriel R, Gurevitch A. Low-dose bupivacaine–fentanyl spinal anesthesia for cesarean delivery. *Reg Anesth Pain Med* 2000; **25**: 235–9
- Ben-David B, Solomon E, Levin H, Admoni H, Goldik Z. Intrathecal fentanyl with small-dose dilute bupivacaine: better anesthesia without prolonging recovery. *Anesth Analg* 1997; **85**: 560–5
- Bigat Z, Boztug N, Karsli B, Cete N, Ertok E. Comparison of hyperbaric ropivacaine and hyperbaric bupivacaine in unilateral spinal anaesthesia. *Clin Drug Invest* 2006; **26**: 35–41
- Bogra J, Arora N, Srivastava P. Synergistic effect of intrathecal fentanyl and bupivacaine in spinal anesthesia for cesarean section. *BMC Anesthesiol* 2005; **5**: 5
- Borghi B, Stagni F, Bugamelli S, et al. Unilateral spinal block for outpatient knee arthroscopy: a dose-finding study. *J Clin Anesth* 2003; **15**: 351–6
- Boztug N, Bigat Z, Karsli B, Saykal N, Ertok E. Comparison of ropivacaine and bupivacaine for intrathecal anesthesia during outpatient arthroscopic surgery 2. *J Clin Anesth* 2006; **18**: 521–5
- Breebaart MB, Vercauteren MP, Hoffmann VL, Adriaensen HA. Urinary bladder scanning after day-case arthroscopy under spinal anaesthesia: comparison between lidocaine, ropivacaine, and levobupivacaine. *Br J Anaesth* 2003; **90**: 309–13
- Bromage PR, Burfoot MF. Quality of epidural blockade. II. Influence of physico-chemical factors; hyaluronidase and potassium. *Br J Anaesth* 1966; **38**: 857–65
- Camorcia M, Capogna G, Berritta C, Columb MO. The relative potencies for motor block after intrathecal ropivacaine, levobupivacaine, and bupivacaine. *Anesth Analg* 2007; **104**: 904–7
- Cappelleri G, Aldegheri G, Danelli G, et al. Spinal anesthesia with hyperbaric levobupivacaine and ropivacaine for outpatient knee arthroscopy: a prospective, randomized, double-blind study. *Anesth Analg* 2005; **101**: 77–82
- Casati A, Danelli G, Berti M, et al. Intrathecal 2-chloroprocaine for lower limb outpatient surgery: a prospective, randomized, double-blind, clinical evaluation. *Anesth Analg* 2006; **103**: 234–8
- Casati A, Fanelli G, Aldegheri G, et al. Frequency of hypotension during conventional or asymmetric hyperbaric spinal block. *Reg Anesth Pain Med* 1999; **24**: 214–9
- Casati A, Fanelli G, Cappelleri G, et al. A clinical comparison of ropivacaine 0.75%, ropivacaine 1% or bupivacaine 0.5% for interscalene brachial plexus anaesthesia. *Eur J Anaesthesiol* 1999; **16**: 784–9
- Casati A, Fanelli G, Danelli G, et al. Spinal anesthesia with lidocaine or preservative-free 2-chloroprocaine for outpatient knee arthroscopy: a prospective, randomized, double-blind comparison. *Anesth Analg* 2007; **104**: 959–64
- Choi DH, Ahn HJ, Kim MH. Bupivacaine-sparing effect of fentanyl in spinal anesthesia for cesarean delivery. *Reg Anesth Pain Med* 2000; **25**: 240–5
- El-Halafawy YM. Hyperbaric spinal levobupivacaine for outpatient knee arthroscopy: a comparison to bupivacaine and ropivacaine. *Egypt J Anaesth* 2008; **20**: 83–9
- Esmooglu A, Karaoglu S, Mizrak A, Boyaci A. Bilateral vs. unilateral spinal anesthesia for outpatient knee arthroscopies. *Knee Surg Sports Traumatol Arthrosc* 2004; **12**: 155–8
- Fanelli G, Borghi B, Casati A, Bertini L, Montebugnolo M, Torri G. Unilateral bupivacaine spinal anesthesia for outpatient knee arthroscopy. Italian Study Group on Unilateral Spinal Anesthesia. *Can J Anaesth* 2000; **47**: 746–51
- Feldman HS, Covino BG. Comparative motor-blocking effects of bupivacaine and ropivacaine, a new amino amide local anesthetic, in the rat and dog. *Anesth Analg* 1988; **67**: 1047–52
- Freedman JM, Li DK, Drasner K, Jaskela MC, Larsen B, Wi S. Transient neurologic symptoms after spinal anesthesia: an epidemiologic study of 1,863 patients. *Anesthesiology* 1998; **89**: 633–41
- Gautier P, De KM, Huberty L, Demir T, Izydorczak M, Vanderick B. Comparison of the effects of intrathecal ropivacaine, levobupivacaine, and bupivacaine for Cesarean section. *Br J Anaesth* 2003; **91**: 684–9
- Gautier PE, De KM, Van SA, et al. Intrathecal ropivacaine for ambulatory surgery. *Anesthesiology* 1999; **91**: 1239–45
- Guasch E, Suarez A, Bermejo JM, Gilsanz F. Randomized controlled trial comparing a low dose to a conventional dose of hyperbaric bupivacaine for scheduled cesarean section. *Rev Esp Anesthesiol Reanim* 2005; **52**: 75–80

- 30 Gupta A, Axelsson K, Thorn SE, et al. Low-dose bupivacaine plus fentanyl for spinal anesthesia during ambulatory inguinal herniorrhaphy: a comparison between 6 mg and 7.5 mg of bupivacaine. *Acta Anaesthesiol Scand* 2003; **47**: 13–9
- 31 Gurkan Y, Canatay H, Ozdamar D, Solak M, Toker K. Spinal anesthesia for arthroscopic knee surgery. *Acta Anaesthesiol Scand* 2004; **48**: 513–7
- 32 Hampl KF, Heinzmann-Wiedmer S, Lugnbuehl I, et al. Transient neurologic symptoms after spinal anesthesia: a lower incidence with prilocaine and bupivacaine than with lidocaine. *Anesthesiology* 1998; **88**: 629–33
- 33 Hampl KF, Schneider MC, Drasner K. Toxicity of spinal local anaesthetics. *Curr Opin Anaesthesiol* 1999; **12**: 559–64
- 34 Higgins JPT, Green S. *Cochrane Handbook for Systematic Reviews of Interventions* 4.2.5 [Updated May 2005]. Chichester, UK: John Wiley & Sons, Ltd, 2005
- 35 Jankowski CJ, Hebl JR, Stuart MJ, et al. A comparison of psoas compartment block and spinal and general anesthesia for outpatient knee arthroscopy. *Anesth Analg* 2003; **97**: 1003–9
- 36 Keld DB, Hein L, Dalgaard M, Krogh L, Rodt SA. The incidence of transient neurologic symptoms (TNS) after spinal anaesthesia in patients undergoing surgery in the supine position. Hyperbaric lidocaine 5% versus hyperbaric bupivacaine 0.5%. *Acta Anaesthesiol Scand* 2000; **44**: 285–90
- 37 Kiran S, Upma B. Use of small-dose bupivacaine (3 mg vs 4 mg) for unilateral spinal anesthesia in the outpatient setting. *Anesth Analg* 2004; **99**: 302–3
- 38 Korhonen AM. Use of spinal anaesthesia in day surgery. *Curr Opin Anaesthesiol* 2006; **19**: 612–6
- 39 Korhonen AM, Valanne JV, Jokela RM, Ravaska P, Korttila K. Intrathecal hyperbaric bupivacaine 3 mg+fentanyl 10 microg for outpatient knee arthroscopy with tourniquet. *Acta Anaesthesiol Scand* 2003; **47**: 342–6
- 40 Kuusniemi KS, Pihlajamaki KK, Pitkanen MT. A low dose of plain or hyperbaric bupivacaine for unilateral spinal anesthesia. *Reg Anesth Pain Med* 2000; **25**: 605–10
- 41 Levin A, Datta S, Camann WR. Intrathecal ropivacaine for labor analgesia: a comparison with bupivacaine. *Anesth Analg* 1998; **87**: 624–7
- 42 Liguori GA, Zayas VM. Repeated episodes of transient radiating back and leg pain following spinal anesthesia with 1.5% mepivacaine and 2% lidocaine. *Reg Anesth Pain Med* 1998; **23**: 511–5
- 43 Lim Y, Ocampo CE, Sia AT. A comparison of duration of analgesia of intrathecal 2.5 mg of bupivacaine, ropivacaine, and levobupivacaine in combined spinal epidural analgesia for patients in labor. *Anesth Analg* 2004; **98**: 235–9
- 44 Liu SS, Ware PD, Allen HW, Neal JM, Pollock JE. Dose–response characteristics of spinal bupivacaine in volunteers. Clinical implications for ambulatory anesthesia. *Anesthesiology* 1996; **85**: 729–36
- 45 McClure JH. Ropivacaine. *Br J Anaesth* 1996; **76**: 300–7
- 46 Mulroy MF, Larkin KL, Siddiqui A. Intrathecal fentanyl-induced pruritus is more severe in combination with procaine than with lidocaine or bupivacaine. *Reg Anesth Pain Med* 2001; **26**: 252–6
- 47 Nolte H, Schikor K, Gergs P, Meyer J, Stark P. On spinal anaesthesia with isobaric bupivacaine 0.5%. (Author's transl). *Anaesthesist* 1977; **26**: 33–7
- 48 Owen MD, Ozsarac O, Sahin S, Uckunkaya N, Kaplan N, Magunaci I. Low-dose clonidine and neostigmine prolong the duration of intrathecal bupivacaine–fentanyl for labor analgesia. *Anesthesiology* 2000; **92**: 361–6
- 49 Pollock JE, Neal JM, Stephenson CA, Wiley CE. Prospective study of the incidence of transient radicular irritation in patients undergoing spinal anesthesia. *Anesthesiology* 1996; **84**: 1361–7
- 50 Robaux S, Bouaziz H, Cornet C, Boivin JM, Lefevre N, Laxenaire MC. Acute postoperative pain management at home after ambulatory surgery: a French pilot survey of general practitioners' views. *Anesth Analg* 2002; **95**: 1258–62
- 51 Roussel JR, Heindel L. Effects of intrathecal fentanyl on duration of bupivacaine spinal blockade for outpatient knee arthroscopy. *AANA J* 1999; **67**: 337–43
- 52 Santiveri X, Arxer A, Plaja I, et al. Anaesthetic and postoperative analgesic effects of spinal clonidine as an additive to prilocaine in the transurethral resection of urinary bladder tumours. *Eur J Anaesthesiol* 2002; **19**: 589–93
- 53 Schneider M, Ettlin T, Kaufmann M, et al. Transient neurologic toxicity after hyperbaric subarachnoid anesthesia with 5% lidocaine. *Anesth Analg* 1993; **76**: 1154–7
- 54 Takenami T, Yagishita S, Nara Y, Hoka S. Intrathecal mepivacaine and prilocaine are less neurotoxic than lidocaine in a rat intrathecal model. *Reg Anesth Pain Med* 2004; **29**: 446–53
- 55 Tanasichuk MA, Schultz EA, Matthews JH, Van Bergen FH. Spinal hemianalgesia: an evaluation of a method, its applicability, and influence on the incidence of hypotension. *Anesthesiology* 1961; **22**: 74–85
- 56 Tauzin-Fin P, Maurette P, Vincon G, Hecquet D, Houdek MC, Bonnet F. Clinical and pharmacokinetic aspects of the combination of meperidine and prilocaine for spinal anaesthesia. *Can J Anaesth* 1992; **39**: 655–60
- 57 Urmey WF. Spinal anaesthesia for outpatient surgery. *Best Pract Res Clin Anaesthesiol* 2003; **17**: 335–46
- 58 Valanne JV, Korhonen AM, Jokela RM, Ravaska P, Korttila KK. Selective spinal anesthesia: a comparison of hyperbaric bupivacaine 4 mg versus 6 mg for outpatient knee arthroscopy. *Anesth Analg* 2001; **93**: 1377–9
- 59 Zaric D, Christiansen C, Pace NL, Punjasawadwong Y. Transient neurologic symptoms after spinal anesthesia with lidocaine versus other local anesthetics: a systematic review of randomized, controlled trials. *Anesth Analg* 2005; **100**: 1811–6