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REVIEW ARTICLE

# Baricity of spinal bupivacaine and the incidence of hypotension in non-obstetric surgery

## *A systematic review*

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Bupivacaine is commonly used for spinal anaesthesia. The baricity of bupivacaine (isobaric *vs.* hyperbaric) may influence the spread, level of the block and the subsequent haemodynamic effects of the spinal anaesthesia. This review considers the available literature on the effect of baricity on the haemodynamic sequelae of spinal anaesthesia with bupivacaine. A literature search was conducted of the MEDLINE and EMBASE databases up to February 2024, following PRISMA guidelines. Randomised controlled trials (RCTs) comparing isobaric and hyperbaric bupivacaine in non-obstetric surgeries were included. Ten studies comprising 586 patients were included. While the literature suggests a trend towards greater incidence of hypotension with hyperbaric bupivacaine, no statistically significant difference was found. Variations in bupivacaine doses and volumes, spinal techniques and definitions of hypotension hindered definitive conclusions. Lower doses relevant to current practice also remain underexplored.

### KEY POINTS

- Baricity affects the spread of the local anaesthetic and could potentially elicit intra-operative hypotension.
- Multiple studies found a correlation between hyperbaric bupivacaine and hypotension, though not statistically significant.
- Nine out of 10 studies used volumes or doses of at least 3 ml or 15 mg bupivacaine.
- Future studies should consider doses below 15 mg and apply a standardised definition for hypotension.
- The patient's position may affect haemodynamic outcomes and should always be documented together with the sensory block achieved.

## Introduction

Spinal anaesthesia has become indispensable in the field of anaesthesiology, especially in obstetric, lower limb and lower abdominal procedures.[1,2] The technique involves the intrathecal administration of local anaesthetics, effectively inhibiting voltage-gated sodium channels within the spinal canal.[3] Clinically, this disruption of nerve impulse transmission results in both sensory and motor blockade. Bupivacaine was one of the first drugs to receive regulatory approval for intrathecal administration.[4] Due to its high potency and extended duration of action, it remains one of the most commonly used local anaesthetics for spinal anaesthesia in both obstetric and non-obstetric settings.[5,6] Bupivacaine is an amide and can be used in hyperbaric and isobaric forms. Multiple variables can influence the spread of the local anaesthetics,

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such as the level of the puncture, patient position, temperature, speed of injection, needle size and orientation of the bevel, but the baricity or density of the solution relative to the cerebrospinal fluid is the most important factor determining the spread within the spinal canal.[7] Plain bupivacaine is slightly hypobaric (baricity of 0.9990) but is commonly regarded and indeed used in clinical practice as if it were isobaric; hyperbaric bupivacaine is denser because of the addition of glucose.[8] In the supine position, hyperbaric bupivacaine tends to spread more cranially than its isobaric counterpart, potentially blocking higher sympathetic fibres of the autonomic nervous system and reducing systemic vascular resistance.[9] This can lead to decreased venous return and preload, which results in reduced cardiac output and concomitant hypotension.[10] Hence, hypotension is commonly reported as the most frequent side effect of spinal anaesthesia, with an incidence of 33%,[11,12] although no differences in the incidence of hypotension are reported between the use of isobaric and hyperbaric bupivacaine.[13] This finding was supported by a systematic review on caesarean sections, which showed that both forms of bupivacaine are safe and effective, exhibiting no major differences in haemodynamic effects.[14] In non-obstetric patients, when a block at a lower spinal level is desired, and thus a lower dose of bupivacaine is used, the impact of baricity on hypotension has not been directly studied. Therefore, this review investigates the effect of isobaric *vs.* hyperbaric bupivacaine on intra-operative hypotension following spinal anaesthesia in non-obstetric procedures.

## Methods

This review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[15] All relevant articles on isobaric and hyperbaric bupivacaine in non-obstetric surgery were identified by searching the MEDLINE and EMBASE databases until February 2024. A comprehensive search was performed with the following search strategy: ((‘glucose-free’ [Title/Abstract]) OR (‘plain’ [Title/Abstract]) OR (‘isobaric’ [Title/Abstract])) AND (‘hyperbaric’ [Title/Abstract])) OR (‘baricity’ [Title/Abstract]) AND (‘bupivacaine’ [Title/Abstract]). Filters for the language ‘English’ and the article type ‘Randomised Controlled Trial’ were applied.

Titles and abstracts of the search were screened for their relevance by three independent authors. Only randomised controlled trials involving adults (>18 years of age) having non-obstetric surgery that directly compared different types of isobaric and hyperbaric bupivacaine in spinal anaesthesia were included. Abstracts were also excluded if they investigated neuraxial techniques other than single-shot spinal anaesthesia, used additives other than glucose, did not report haemodynamic data and if the content was not available. Next, full-text articles were evaluated based on similar exclusion criteria (Fig. 1).

Data collected from the included articles comprised the number of patients, type of surgery, spinal anaesthesia technique, dose and concentration of local anaesthetic, time to supine position, level of sensory block, noninvasive blood pressure (BP) or intra-arterial BP, definition of hypotension and any correlation between hyperbaric bupivacaine and hypotension.

## Results

Ten articles were selected for review (Fig. 1 and Table 1). In total, 586 patients were randomised in two groups with isobaric ($n = 282$) and hyperbaric bupivacaine ($n = 304$).

From the included studies, seven studies reported more hypotension when hyperbaric bupivacaine was used.[9,16–21] However, none of the studies showed an overall statistically significant result. Toptaş *et al.*[19] observed a significant difference in hypotension between 30 hyperbaric patients and 30 isobaric patients only during the first 5 min after spinal injection ($P < 0.05$), but there was no overall significant difference in the incidence of hypotension.

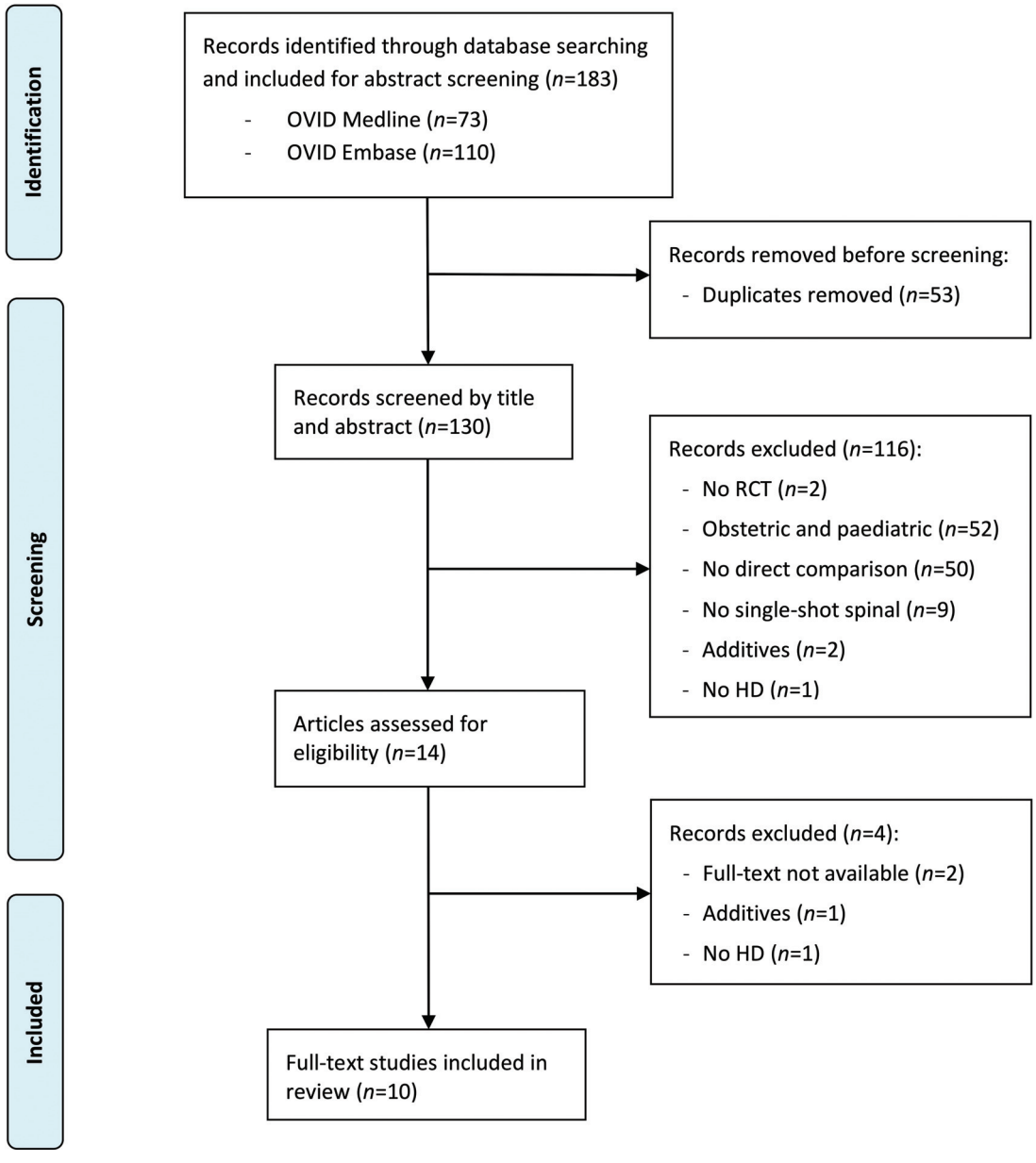
Five studies had a well described definition of hypotension,[16–20] although the definition of hypotension varied across the studies, ranging from a decrease in SBP greater than 20 to 30% from baseline, to a SBP lower than 80 or 90 mmHg.

The bupivacaine dose used in the analysed studies ranged from 5 to 25 mg. One study used a low dose of 5 mg for perianal surgery and found a correlation between hyperbaric bupivacaine and hypotension.[16] However, the other studies ($n = 9$) used a higher dose ($\geq$15 mg), and six of these reported a higher incidence of hypotension in the hyperbaric group, although not statistically significant.[9,17–21]

All studies used concentrations of 0.5% bupivacaine with volumes ranging from 1 to 5 ml and employed glucose 8% to increase baricity. Four studies also compared glucose concentrations of 0.8, 4, and 5%.[9,17,22,23]

Three RCTs reported the mean sensory block levels for the hyperbaric and isobaric bupivacaine groups, ranging from to T4 to T5 and from T6 to T8, respectively, with higher levels observed in the hyperbaric groups.[9,21,24] Different positions were used for administering spinal anaesthesia: sitting ($n = 4$),[16,19,20,24] lateral decubitus ($n = 4$),[9,17,21,22] and two studies compared sitting and lateral decubitus within their study.[18,23] Six studies immediately changed to a supine position after the spinal procedure,[9,17,19,21–23] with two studies noting a higher sensory block in the hyperbaric group compared with the isobaric group.[9,21] Four RCTs administered spinal anaesthesia in the sitting position and kept the patient in this position for a short period of time before changing to a supine position.[16,18,20,24] Of these studies, three noted a higher incidence of hypotension in the hyperbaric group (Fig. 2).[16,18,20]

**Fig. 1** PRISMA flow diagram showing the article screening process.




HD, haemodynamics; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RCT, randomised controlled trial.

## Discussion

This review compared the use of spinal isobaric and hyperbaric bupivacaine and the incidence of hypotension. Our findings revealed that most studies reported a higher likelihood of hypotension in the hyperbaric bupivacaine group, but no overall statistically significant difference was found in any of the studies comparing both types of bupivacaine. Patients receiving hyperbaric bupivacaine were also observed to have a higher sensory block level, which results in a higher sympathetic block and can possibly explain the higher incidence of hypotension.

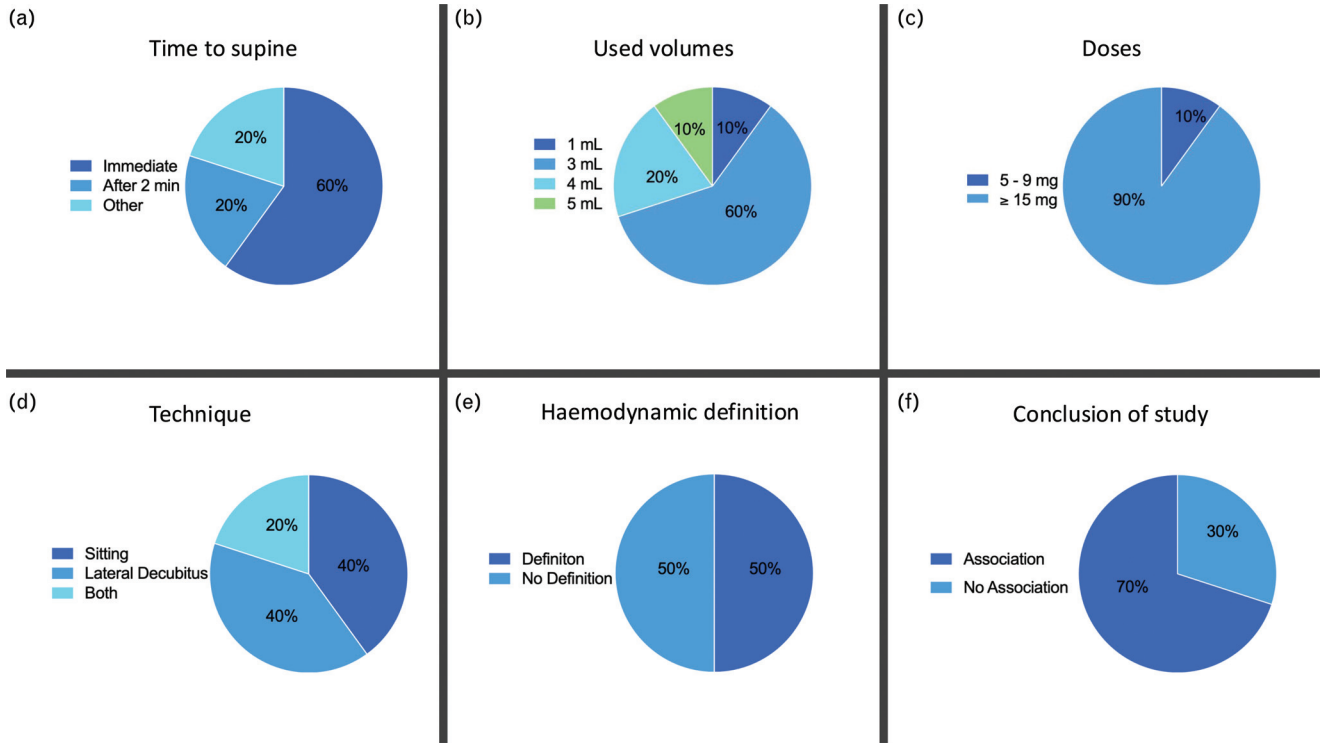
When interpreting these results, it is important to recognise that most studies investigated higher doses and volumes of bupivacaine. We found no studies that explored intermediate doses of between 10 and 14 mg, and only one study used a dose of 5 mg.[16] Lower doses and volumes could lead to greater variations in the level of sympathetic block, potentially causing more frequent hypotension than higher doses or volumes. Moreover, the reliance on studies investigating higher doses of bupivacaine fails to accurately represent the lower dosing regimens typically employed in contemporary clinical practice to achieve faster recovery room discharge and

**Table 1** The characteristics of the included studies

| First author, year (Ref) | Number of included patients | Type of surgery | Patient position in which the spinal anaesthesia was administered | Concentration, dose, and volume of spinal anaesthetic | Time to supine position | Sensory block level Median [range] | Cardiovascular variables | NIBP/ABP | Haemodynamic change definition[19] | Correlation between hyperbaricity and hypotension |
|---|---|---|---|---|---|---|---|---|---|---|
| Toptaş *et al.*, 2014[19] | 60 | Lower abdominal Urology Lower extremity | Sitting L3/4 | HB 0.5%: 15 mg (3 ml) IB 0.5%: 15 mg (3 ml) | Immediate 30° head up | HB: $T_7$ [$T_4$ to $T_{11}$] IB: $T_8$ [$T_4$ to $T_{12}$] | SBP + DBP + MAP + HR + Heart rate variability | NIBP | SBP decrease > 20% of baseline | Yes (overall not sign., after 5 min $P<0.05$) |
| Ariyama *et al.*, 2009 [16] | 180 | Perianal | Sitting L3/4 | HB 0.5%: 5 mg (1 ml) (8% glucose) IB 0.5%: 5 mg (1 ml) | After 2, 5, or 10 min | After 2 min.: $T_5$ After 5 min.: $T_9$ After 10 min.: $T_{11}$ | SBP + HR | NIBP | SBP <90 mmHg | Yes (not sign.) |
| Critchley *et al.*, 1999[17] | 36 | Urology (TURP or TURBT) | Lateral decubitus L2/3 or L3/4 | Heavy 0.5%: 15 mg (3 ml) (8% glucose) Mixed 0.5%: 15 mg (3 ml) (4% glucose) Plain 0.5%: 15 mg (3 ml) | Immediate | N/A | SBP + HR (CVP) | ABP/CVP | SBP decrease >25% of baseline | Yes (not sign.) |
| Sanderson *et al.*, 1994[23] | 80 | Urology (TURP and TURBT) Knee/hip replacement | Uro: sitting L3/4 Ortho: left lateral L2/3 | UroHB 0.5%: 15 mg (3 ml) (8% glucose) UroMixed: 0.5% 15 mg (3 ml) (0.8% glucose) OrthoMixed: 0.5% 15 mg (3 ml) (0.8% glucose) OrthoIB 0.5%: 15 mg (3 ml) | Immediate | UroHB: $T_{5.5}$ [$T_2$ to $T_9$] UroMixed: $T_{7.5}$ [$T_5$ to $T_9$] OrthoMixed: $T_{3.5}$ [$C_7$ to $T_8$] OrthoIB: $T_3$ [$C_5$ to $T_7$] | MAP + HR | NIBP | Not defined | No |
| Alston *et al.*, 1988[24] | 20 | Urology (TURP) | Sitting L2/3 or L3/4 | HB 0.5%: 15 mg (3 ml) (8% glucose) IB 0.5%: 15 mg (3 ml) | After 2 min | HB: $T_5$ (mean) IB: $T_6$ (mean) | SBP + HR | N/A | Not defined | No |
| Mitchell *et al.*, 1988[18] | 40 | Gynaecological | Sitting or right lateral decubitus (depends on group) L3/4 | HB 0.5%: 25 mg (5 ml) (8% glucose) IB 0.5%: 25 mg (5 ml) | (1) IB sitting: after 2 min (2) IB lat dec: immediate (3) HB sitting: after 2 min (4) HB lat dec: immediate | Mean all groups: $T_4$ to $T_6$ | SBP + HR | NIBP | SBP <80 mmHg | Yes (not sign.) |
| Pitkänen *et al.*, 1987[21] | 90 | Lower extremity | Lateral decubitus L3/4 | HB 0.5%: 15 mg (3 ml) IB 0.5%: 15 mg (3 ml) | Immediate | HB: $T_4$ (mean) IB: $T_8$ (mean) | SBP + HR | NIBP | Not defined | Yes (not sign.) |
| Axelsson *et al.*, 1985[20] | 20 | Urology (TURBT) | Sitting L3/4 | HB 0.5%: 20 mg (4 ml) (8% glucose) IB 0.5%: 20 mg (4 ml) | After 2 min (in lithotomy pos) | HB: $T_6$ to $T_8$ IB: $T_6$ to $T_8$ | SBP + HR | N/A | SBP decrease > 30% of baseline | Yes (not sign.) |
| Møller *et al.*, 1984[9] | 30 | Laparotomy | Lateral decubitus L2/3 or L3/4 | Heavy 0.5%: 20 mg (4 ml) (8% glucose) Mixed 0.5%: 20 mg (4 ml) (5% glucose) Plain 0.5%: 20 mg (4 ml) | Immediate | HB: $T_4$ to $T_5$ (mean) IB: $T_7$ to $T_8$ (mean) | DBP + SBP + HR | N/A | Not defined | Yes (not sign.) |
| Chambers *et al.*, 1981[22] | 30 | Gynaecological | Lateral decubitus L3/4 | Heavy 0.5%: 15 mg (3 ml) (8% glucose) Mixed 0.5%: 15 mg (3 ml) (5% glucose) Plain 0.5%: 15 mg (3 ml) | Immediate | N/A | DBP + SBP + HR | NIBP | Not defined | No |

ABP, intra-arterial blood pressure; CVP, central venous pressure; HB, hyperbaric bupivacaine; HR, heart rate; IB, isobaric bupivacaine; MAP, mean arterial pressure; N/A, not applicable; NIBP, noninvasive intra-operative blood pressure; TURBT, transurethral resection of bladder tumour; TURP, transurethral resection of prostate.

**Fig. 2** Pie charts showing (a) the time to supine position, (b) the used volumes and (c) doses, (d) in which patient position spinal anaesthesia was administered, (e) whether hypotension was defined, and (f) if the studies found an association between hypotension and the baricity of bupivacaine.




ambulation.[25] Ariyama *et al.* [16] is the only study researching lower doses and provides valuable insights into the haemodynamic properties of bupivacaine at lower doses. However, it does not directly address the intermediate dose range of interest needed for orthopaedic or lower abdominal surgery. Nevertheless, their findings emphasise the importance of investigating the effects of bupivacaine across a spectrum of doses.

Several limitations need to be considered when interpreting the results of the studies included for review. Firstly, there is a lack of standardisation in the doses and thus volumes used, as well as the technique of spinal anaesthesia and the time to supine position. Tuffier's line, which corresponds to the L3–L4 intervertebral space, is often used to determine the level for puncture, as noted in Table 1. However, manual identification of this landmark has been shown to have an error rate as high as 70%. This will affect the distribution of anaesthesia and can lead to hypotension. Interestingly, there has not been a single study that has employed ultrasound to accurately identify the precise puncture level. This variability in methodology can introduce heterogeneity into the results and make it challenging to draw conclusions. Secondly, doses of 15 mg are used or higher ($n = 9$), which do not reflect the lower doses often used in current non-obstetric practice. Thirdly, the studies reflect considerable variety in the way hypotension is defined, making comparisons and conclusions difficult. Fourthly, some studies also had relatively small sample sizes, which may limit the generalisability of their findings. Finally, most of the studies reviewed in this article were conducted at least two decades ago or earlier, and may be considered outdated.[26]

Future randomised controlled trials should aim to compare isobaric and hyperbaric bupivacaine but with lower doses (<15 mg) and volumes (<3 ml). Additionally, it is imperative to establish a well defined and generalisable definition for hypotension to ensure consistency across studies and facilitate meaningful comparisons. As authors, we suggest defining hypotension as a decrease in absolute MAP below 65 mmHg or a relative decrease of more than 20% from the baseline MAP, described by Salmasi *et al.*[27] and commonly used. Future studies should also incorporate ultrasound guidance to ensure accurate identification of the spinal puncture level.

An older study by Chambers *et al.*[22] suggested that isobaric bupivacaine should be used for lower abdominal surgery while hyperbaric solutions tend to produce a better cephalad spread and are more appropriate for procedures involving the thoracic levels. Interestingly,

the literature does not link surgical indication with the spread of the local anaesthetic based on baricity of the local anaesthetic.

## Conclusion

This review studied the literature comparing the spinal use of isobaric and hyperbaric bupivacaine for non-obstetric surgery. Most studies showed a trend towards an increased incidence of hypotension in the hyperbaric bupivacaine group. However, none of the studies showed a clear statistical significance between hyperbaric bupivacaine and hypotension incidence. Moreover, this review also found varying methodologies, bupivacaine doses and the lack of a generalised definition of hypotension among the existing clinical trials, all contributing to the heterogeneity of the results. Further research on this topic is warranted.

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