Prevention of spinal anaesthesia-induced hypotension in the elderly: i.m. methoxamine or combined hetastarch and crystalloid


Summary
We have compared two methods of reducing hypotension during spinal anaesthesia in elderly patients, 6% hetastarch and crystalloid or methoxamine 10 mg i.m., in terms of haemodynamic stability and requirements for additional vasopressors. Sixty-two patients (aged 60–97 yr) undergoing surgical fixation of fractured neck of femur were allocated randomly to receive 6% hetastarch (Hespan) 500 ml followed by Hartmann’s solution 500 ml (group HS, n = 32) or a bolus injection of methoxamine 10 mg i.m. (group MX, n = 30), 10 min before induction of spinal anaesthesia with 0.5% hyperbaric bupivacaine 2.25–3.0 ml. Arterial pressure was measured non-invasively by an oscillotonometer at 2-min intervals from 0 to 40 min and at 5-min intervals thereafter. Methoxamine 2 mg i.v. was given if systolic arterial pressure (SAP) decreased to <100 mm Hg. Hypotension was defined as a 25% decrease from baseline SAP or mean arterial pressure (MAP). Patient data, sensory level and blood loss were similar in the two groups. SAP and MAP increased initially from baseline until induction of spinal anaesthesia and then decreased for 30 min in both groups, but remained higher in group MX (P<0.05). Heart rate (HR) decreased from baseline in group MX (P<0.05) and was less than in group HS at all times from 2 to 60 min (P<0.01). The incidence of SAP hypotension (47% vs 75%; P = 0.03, odds ratio (OR) = 3.43) and MAP hypotension (47% vs 67%; P = 0.09, OR = 2.51) was less in group MX than in group HS. Requirements for rescue methoxamine i.v. (27% vs 53%; P = 0.04, OR = 3.11) was less in group MX than in group HS but the dose of rescue methoxamine given (mean 6.3 (95% confidence intervals 3.0–9.6) mg vs 8.9 (5.6–12.2) mg) and time to onset of hypotension (20.7 (14.5–26.7) vs 17.3 (11.4–23.1) min) were similar in groups MX and HS, respectively. We conclude that methoxamine 10 mg i.m., given 10 min before induction of spinal anaesthesia in normovolaemic elderly patients, reduced subsequent SAP and MAP hypotension, HR and requirements for rescue vasopressor therapy compared with a combination of 6% hetastarch 500 ml and crystalloid 500 ml. The previously reported benefit of such volume administration may not extend to the elderly. (Br. J. Anaesth. 1998; 80: 199–203)

Keywords: anaesthesia, subarachnoid; complications, hypotension; fluids, i.v.; fluid therapy; sympathetic nervous system, methoxamine.

Systemic hypotension is the most common complication of spinal anaesthesia, with an incidence of 25–82% in the elderly.1–3 Despite no prospective outcome data, it seems reasonable to be concerned that the elderly may be at increased risk of long-term complications from hypotension occurring during spinal anaesthesia, because of reduced physiological reserve and atherosclerosis, particularly coronary artery disease.3 A retrospective study suggested that patients who became hypotensive during anaesthesia had a five-fold increased risk of perioperative myocardial infarction compared with patients who did not develop hypotension.4

Strategies for treating spinal anaesthesia-induced hypotension include i.v. volume administration, which increases circulating volume and cardiac output in an effort to compensate for the expansion of the capacitance vessels, or pharmacological reversal of the reduction in systemic vascular resistance which inevitably accompanies spinal anaesthesia, using vasopressor agents.5

The practice of volume loading, that is rapid infusion of crystalloids before induction of spinal anaesthesia, dates from 30 yr ago, in which such infusions apparently reduced the high incidence of hypotension in obstetric patients.6 7 More recent work from this decade has cast doubt on the efficacy and benefit of this practice. Several studies in women undergoing spinal anaesthesia for Caesarean section or tubal ligation have found that volume administration produces marginal, if any, reduction in the incidence of hypotension8–10 while also causing significant increases in central venous pressure, pulmonary oedema and haemodilution, which may potentially have detrimental consequences.10–12 In a recent investigation comparing crystalloid, gelatin colloid and no volume administration for spinal anaesthesia in an elderly population, we found that withholding of fluids was not associated with any greater incidence of hypotension or ephedrine use than the use of either crystalloid or colloid volume administration.13

However, volume administration with a combination of 6% hetastarch as synthetic colloid and crystalloid, in equal proportions, has been shown to

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produce significantly less hypotension than an equal volume of crystalloid or colloid alone in parturients.11,12 Whether this regimen would be effective in the elderly is unknown. Hetastarch 6% in 0.9% saline is a synthetic colloid derived from amylpectin, with a molecular weight of 450 000. Its pH is 5.5, osmolarity 310 mosmol litre⁻¹ and its intravascular half-life is 25 h. Anaphylactoid reactions are less frequent than with other synthetic colloids, but it is expensive (approximately £30 per 500 ml compared with £0.65 for 1 litre of crystalloid) and may induce coagulopathy.14,15

The alternative strategy for management of spinal anaesthesia-induced hypotension is the use of vasopressor agents, of which the most popular is ephedrine, a combined alpha and beta adrenergic agonist. However, the unreliability of its vasoconstrictive efficacy and its tendency to cause a positive chronotrophic effect on the heart have raised doubts about its safety in elderly patients.16,17 It makes physiological sense to use an alpha adrenergic agonist, such as metaraminol, which would pharmacologically reverse undesirable peripheral vascular dilatation, maintaining systemic arterial pressure, which avoiding unwanted cardiac effects. Metaraminol is the only commonly used pure alpha adrenergic agonist that has been investigated specifically during spinal anaesthesia in an elderly population.18 These agents may be given by continuous infusion, but this requires an infusion pump, which may be too cumbersome for routine use, and has the potential for hazardous errors in its administration.

In this study, we have evaluated the incidence and onset time of hypotension and need for further vasopressor therapy in an elderly population given one of two prophylactic measures designed to minimize spinal anaesthesia-induced hypotension: metaraminol 10 mg i.m. or a 1-litre volume administration regimen comprising 6% hetastarch 500 ml and Hartmann’s solution 500 ml.

**Patients and methods**

After obtaining Institutional Ethics Committee approval and informed consent, we studied 65 ASA I, II or III patients (aged 60–96 yr) undergoing emergency hip surgery (insertion of Austin–Moore prosthesis or dynamic hip screw). Exclusion criteria were ASA IV or V patients, uncontrolled hypertension (i.e. SAP >160 mm Hg) or congestive cardiac failure, clinical evidence of significant dehydration (reduced skin turgor, dry mucous membranes, systolic arterial pressure <100 mm Hg, Na⁺ >145 mmol litre⁻¹, urea >10 mmol litre⁻¹), those aged less than 60 yr and those for whom spinal anaesthesia was contra-indicated. Patients were not premedicated, but all received continuous infusion of crystalloid as maintenance fluids (1.5 ml kg⁻¹ h⁻¹).

On arrival in the induction room all patients were met by an anaesthetist other than the one who would be in charge of induction and monitoring of anaesthesia. Having confirmed their hydration status clinically, and noted the duration of fasting from oral fluids together with preoperative Na⁺ and urea values, a 16-French gauge peripheral cannula was inserted. Patients were allocated randomly, using a sealed, sequentially numbered, envelope technique, to one of two groups: group HS received 6% hetastarch 500 ml (Hespan) followed by crystalloid (Hartmann’s solution) 500 ml over 10–15 min while the patient was positioned and prepared for spinal anaesthesia; group MX received methoxamine 10 mg by deep gluteal i.m. injection after being positioned for spinal anaesthesia. Maintenance fluid (1.5 ml kg⁻¹ h⁻¹) using crystalloid (Hartmann’s solution) was infused continuously in all patients.

Spinal anaesthesia was induced in all cases in the lateral position, the operative side inferior, at L2–3 or L3–4, using 0.5% hyperbaric bupivacaine 2.25–3.0 ml (Marcain; Astra Pharmaceuticals), with a 22-gauge spinal needle, injected over 15–20 s under aseptic conditions by an anaesthetist other than the one who had administered the preventative strategies described above and who was therefore unaware of the study groups. This physician also managed the patient during anaesthesia and noted the haemodynamic data. The volume of bupivacaine used was left to this anaesthetist, depending on the patient’s weight, height, sex and physical condition. Patients were kept in the lateral position for another 5 min to ensure they were pain free before transfer to the position for surgery. Sensory level was determined bilaterally at 15 min using pinprick.

Systolic (SAP), mean (MAP) and diastolic (DAP) arterial pressures were measured by automated, non-invasive oscillometrometry (Dinamap, Datex Cardio-cap II, Helsinki, Finland) on three successive occasions on arrival in the induction room to establish baseline levels, at 2-min intervals until 30 min after induction of spinal anaesthesia and at 5-min intervals thereafter. Heart rate (HR) was noted from continuous electrocardiography, and pulse oximetry was also monitored throughout spinal anaesthesia and surgery. Hypotension was defined as a 25% decrease from baseline for both SAP and MAP, or an absolute systolic value <100 mm Hg. Rescue therapy for hypotension comprised methoxamine 2–4 mg i.v., repeated at 2-min intervals as necessary. This was given if SAP was <100 mm Hg on two consecutive readings or if indicated on clinical grounds, that is if new pallor was noted or if the patient reported nausea, vomiting or unusual lightheadedness. Blood loss was estimated in the perioperative period by the sum of collected spilt blood and swab weighing. Observations were discontinued after 70 min or immediately after arrival in the recovery room, whichever occurred sooner.

Data were analysed using Statsview II. Mean (95% confidence intervals) values were obtained for normally distributed data and compared using the Student’s unpaired t test. Repeated measures analysis of variance was used for serial measures of SAP, MAP and HR. Paired Student’s t test and post hoc Bonferroni correction for multiple comparisons were used for comparison of these variables between baseline and sequential times. The Mann–Whitney U test was used to compare skewed data. Categorical data were compared with chi-square analysis of contingency tables with Yates’ correction or Fisher’s exact test where cell values were <5. The power of this study was calculated prospectively as follows: in a previous investigation, we found an incidence of spinal-induced hypotension in the elderly of 50%,11 consistent with other studies. The minimum clinically
Table 1 Patient and spinal block characteristics (mean (95% confidence interval) or number). No significant differences

<table>
<thead>
<tr>
<th></th>
<th>Group HS (n = 32)</th>
<th>Group MX (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>78.1 (60–93)</td>
<td>78.0 (60–96)</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>9/23</td>
<td>11/19</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>162 (156–165)</td>
<td>163 (160–170)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>64.4 (59.2–69.7)</td>
<td>64.1 (58.8–69.4)</td>
</tr>
<tr>
<td>Fasting time (h)</td>
<td>12.4 (11.3–13.6)</td>
<td>11.9 (10.9–12.8)</td>
</tr>
<tr>
<td>Na⁺ (mmol litre⁻¹)</td>
<td>134.5 (131–138)</td>
<td>136.1 (134–138)</td>
</tr>
<tr>
<td>Urea (mmol litre⁻¹)</td>
<td>7.1 (6.2–8.0)</td>
<td>6.6 (5.8–7.3)</td>
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<tr>
<td>ASA (I/II/III)</td>
<td>6/14/12</td>
<td>8/15/7</td>
</tr>
<tr>
<td>Block level</td>
<td>T7 (T2–12)</td>
<td>6 (T2–12)</td>
</tr>
<tr>
<td>High block (n)</td>
<td>16</td>
<td>17</td>
</tr>
<tr>
<td>Blood loss (ml)</td>
<td>217 (220–413)</td>
<td>196 (134–258)</td>
</tr>
<tr>
<td>Time to hypotension</td>
<td>17.2 (11.4–23.1)</td>
<td>20.7 (14.5–26.7)</td>
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</table>

Results

Although 65 patients were enrolled in the study, two (one in each group) were subsequently lost because of failure to establish spinal anaesthesia, and another (group MX) had inadequate subarachnoid block, all three requiring general anaesthesia. Thus, data from 62 patients were analysed; n = 32 in group HS and n = 30 in group MX.

The groups were similar in age, sex, characteristics, preoperative Na⁺ and urea values, and preoperative fasting time. Blood loss was not significantly different between groups (table 1). Median time to induction of spinal anaesthesia after commencement of therapy (volume administration or methoxamine i.m.) was 10.2 (range 8–13) min. Sensory level at 15 min and proportion of patients with a high block (defined as T8 or higher) were also similar in each group, and the overall proportion of patients with a high block was 53%. Mean time to onset of hypotension was 17.2 min in group HS and 20.7 min in group MX (ns) (table 1).

The incidence of SAP hypotension was 75% in group HS compared with 47% in group MX (P = 0.03, odds ratio (OR) = 3.43; 95% confidence interval (CI) for this 28% difference in the proportion of patients developing SAP hypotension was 4.7–51.3%). Similarly, 67% of patients in group HS compared with 47% in group MX demonstrated MAP hypotension (P = 0.09, OR = 2.51). The incidence of rescue methoxamine therapy was 38.5% (53% for group HS vs 27% for group MX; P = 0.04, OR = 3.11). However, in those patients given methoxamine, the mean dose was not significantly different between groups (8.9 (95% CI 5.6–12.2) vs 6.3 (3.0–9.6) mg) (table 2).

Discussion

Spinal anaesthesia blocks efferent sympathetic fibres and reduces systemic vascular resistance by decreasing the sympathetic tone of the arterial circulation. There is also peripheral venous pooling of blood, which may reduce cardiac output. Such changes frequently cause systemic hypotension, which may be harmful in the elderly with incipient cardiac and renal failure. However, baroreceptor-mediated compensatory cardiovascular responses result which tend to maintain arterial pressure. Should the sensory level extend to T8, release of catecholamines by the
adrenal gland is compromised and if it reaches T1, all cardiac compensation potential is lost.\(^5\)

Our comparison of two measures intended to reduce hypotension in elderly patients showed greater haemodynamic stability with pre-emptive methoxamine 10 mg i.m. given 10 min before spinal anaesthesia compared with an infusion of 6% hetastarch and crystalloid, in contrast with recent studies in parturients\(^11\) and in non-pregnant young women, which found fluid administration of apparent benefit.\(^20\) This may reflect the fact that we used a total volume of 1 litre (6% hetastarch 500 ml and crystalloid 500 ml) compared with 1.5 litre\(^15\) and 2 litre.\(^12\) Elderly patients with hip fractures are particularly susceptible to hypotension during spinal anaesthesia because they may be hypovolaemic from blood loss into the fractured joint and have a high incidence of co-existing disease. However, we believe that rapid infusion of up to 2 litre of fluid would possibly result in haemodynamic embarrassment from circulatory overload.

We propose that colloid solution would be more effective in preventing spinal-induced hypotension, as its large molecular weight ensures it remains in the plasma body fluid compartment. None the less, a recent study with large numbers of patients (\(n=85\)) comparing crystalloid, gelatin colloid and no fluid treatment in patients aged more than 60 yr found no significant difference in the incidence of hypotension or requirements for rescue vasopressor therapy.\(^13\) Intravascular fluids \textit{per se} do not reverse decreases in systemic vascular resistance, rather they may increase cardiac output.\(^15\)\(^21\) A more plausible explanation for the failure of this combined fluid administration regimen in the elderly may be that the reduced physiological reserve of older patients may make them less able to respond to volume with a corresponding increase in cardiac output.\(^13\) Moreover, 75% of any crystalloid infused rapidly diffuses into the interstitium, where it cannot be as effective as a volume expander.\(^22\) Furthermore, infused fluid (with either crystalloid alone or in combination with hetastarch) stimulates atrial natriuretic peptide (ANP) secretion in women undergoing spinal anaesthesia for Caesarean section,\(^23\) tending to decrease systemic vascular resistance and initiate diuresis. If this were also true in elderly patients, it may explain the ineffectiveness of fluid administration in preventing hypotension.

Ephedrine, a combined alpha and beta agonist, is the most commonly used vasopressor in the elderly.\(^3\) It may be ineffective in reversing the spinal-induced decrease in SVR, possibly because of its beta effect, causing arteriolar vasodilatation in opposition to its alpha vasoconstrictive effect.\(^16\)\(^17\) Moreover, its beta-mediated increase in heart rate exposes elderly patients with latent coronary artery disease to myocardial ischaemia. However, in ASA III patients, many of whom would be in the elderly age range, a combination of prophylactic i.m. and i.v. ephedrine improved haemodynamic stability, albeit with tachycardia.\(^24\)\(^25\) In contrast, a pure alpha adrenergic agonist (metaraminol), given as a continuous infusion (0.5–5.0 mg h\(^{-1}\)), maintained SAP by increasing SVR and central venous pressure, compared with a similar group of elderly patients receiving synthetic colloid alone. However, one-third of patients receiving the metaraminol infusion developed inadvertent hypertension.\(^18\) The increased SVR was associated with a decrease in heart rate both in this and our present study, presumably because of a baroreceptor-mediated reflex bradycardia. Despite the fact that we did not find inadvertent hypertension after methoxamine, it could be that a prolonged delay or failure to establish spinal anaesthesia would cause inadvertent hypertension.

Our finding of improved haemodynamic stability with methoxamine is the first report of its efficacy in male and female elderly patients undergoing spinal anaesthesia for emergency orthopaedic surgery, and is consistent with the results of another small study (\(n=36\)) in which MAP was maintained and blood loss reduced in males undergoing transurethral resection of the prostate, given methoxamine 10 mg i.m., 15 min before induction of spinal anaesthesia.\(^26\) In our study, there was no significant difference in blood loss between those receiving methoxamine and those receiving fluid administration. We chose to study methoxamine i.m. believing this to be a more convenient form of administration and less expensive because an infusion pump is not required. Although we have shown that arterial pressures were better preserved using pre-emptive methoxamine, its effect on cerebral and coronary perfusion remains unknown. Such measurements are beyond the scope of this study and are not widely available in current clinical practice.

Our data may have been adversely affected by some of the design features of this study. Baseline arterial pressure was calculated from the mean of three readings, obtained in the semi-recumbent position immediately on arrival in the induction room when many patients would be quite anxious. Subsequently, readings were obtained in the supine or lateral position of surgery. Non-invasive (Dinamap) recording of arterial pressure is accurate only to within ±10%, but the same machine was used in all patients and invasive arterial pressure measurements are rarely used in our practice in this setting. The fasting time varied from 10 to 15 h but all patients were given i.v. fluids at maintenance rates during this time. It was not practical for one anaesthetist to perform all spinal blocks, thus some variation in technique may have occurred. Sensory level was assessed at 15 min, which may have been too early, even using a hyperbaric solution. It would have been interesting to re-assess sensory level and to continue our observations for another 30–60 min in the recovery room to confirm that haemodynamic values were beginning to stabilize.

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**Figure 2**  Mean (±SEM) mean arterial pressure (MAP) in groups HS and MX. Ind. = Induction of spinal anaesthesia; arrow indicates time of volume administration or administration of methoxamine i.m. *\(P<0.05\).
Methoxamine or volume administration for spinal anaesthesia

There is widespread consensus that normovolaemia must be maintained during spinal anaesthesia, and crystalloid 8 ml kg\(^{-1}\) has been suggested by Critchley as an appropriate infusion volume to be given as the block is evolving, that is over the initial 10–20 min. However, use of large pre-emptive infusions over a shorter time span are demonstrably ineffective in preventing spinal-induced hypotension and may be detrimental, especially in the elderly.\(^{3,5,11-13,16-19,27}\)

In summary, in this prospective, randomized, double-blind, clinical study, methoxamine 10 mg i.m., given 10 min before spinal anaesthesia, resulted in greater haemodynamic stability in normovolaemic elderly patients undergoing emergency hip surgery compared with i.v. administration of 6% hetastarch 500 ml and crystalloid solution 500 ml. The previously reported benefit of this fluid regimen may not extend to the elderly.

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References