We investigated the efficacy of IV atropine for preventing spinal anesthesia-induced hypotension in elderly patients. Seventy-five patients undergoing transurethral prostate or bladder surgery were randomized to receive either placebo (n = 25), atropine 5 μg/kg (small-dose atropine, n = 25) or atropine 10 μg/kg (large-dose atropine, n = 25) after the induction of spinal anesthesia. All the patients received an IV infusion of 10 mL/kg 0.9% normal saline over 10 min before the induction of anesthesia. The systolic blood pressure decreased in all three groups after spinal anesthesia. There was a significant increase in the mean heart rate in both atropine groups as compared to the placebo group (placebo group: 78 bpm, 95% confidence interval [CI]: 76.6–78.5; small-dose atropine group: 86 bpm, 95% CI: 83.9–88.8; large-dose atropine group: 97 bpm, 95% CI: 94.5–100.3; P = 0.001). There was a significant decrease in the incidence of hypotension in patients who received atropine (placebo group: 76%, small-dose atropine group: 52%, large-dose atropine group: 40%, P = 0.03). The mean dose of ephedrine required was significantly decreased in the atropine groups (placebo group: 12.2 mg [sd = 10.5], small-dose atropine group: 7.4 mg [sd = 10.1], large-dose atropine group: 5.4 mg [sd = 8.7 mg], P = 0.048). The total amount of IV fluid and number of patients requiring metaraminol in addition to 30 mg of ephedrine were not significantly different among the three groups. Significant side effects, such as confusion, ST segment changes or angina were not detected in any of the patients. We conclude that IV atropine may be a useful supplement to the existing methods in preventing hypotension induced by spinal anesthesia.

Accepted for publication July 11, 2000
Address correspondence and reprint requests to H. H. Lim, MBBS, M Med, Department of Anaesthesiology, Queen Mary Hospital, Pokfulam Road, Hong Kong. Address e-mail to rmgwong@netvigator.com.
the use of IV atropine in elderly patients were also assessed.

**Methods**

Considering a power of 80% and the incidence of hypotension being 80% after SA, 24 patients would be needed in each group if we consider a 50% reduction in the incidence of hypotension being a clinically important end point for a new intervention (11). After obtaining hospital ethics committee approval and written informed patient consent, we randomized 75 patients of more than 60 yr of age, ASA physical status I to III, presenting for transurethral prostate or bladder surgery into three groups using the sealed envelope method. Patients with contraindications to SA, with cardiac arrhythmia such as atrial fibrillation, uncontrolled hypertension (defined as systolic blood pressure more than 180 mm Hg or diastolic blood pressure more than 110 mm Hg), and severe cardiac disease such as unstable angina, were excluded. Patients who were taking β-adrenergic blockers, or any drugs that may alter normal response to atropine, were also excluded.

No premedication was given to any of the patients. Baseline noninvasive blood pressure, electrocardiogram (ECG) lead II with ST segment analysis, and pulse oximetry were monitored using a Spacelabs monitor (Spacelabs Medical, Redmond, WA). A preload of 10 mL/kg of 0.9% normal saline was given over 10 min before SA. With the patient in the left lateral position, 2.8 mL 0.5% hyperbaric bupivacaine was injected intrathecally over 15 to 20 s by using a 25-gauge pencil point spinal needle (Pencan; B. Braun Melsungen AG, Melsungen, Germany) at the L3-4 or L2-3 spinal space. Each patient received 0.9% normal saline (placebo group), atropine 5 μg/kg (small-dose atropine group), or atropine 10 μg/kg (large-dose atropine group), all diluted to 2 mL with 0.9% normal saline and given IV 1 min after the administration of SA. Arterial blood pressure was monitored every minute for the first 5 min, every 3 min for the subsequent 30 min, and then every 5 min until 60 min after the SA. Another anesthesiologist, who was blinded to the treatment group, performed the anesthesia and collected data for the entire study period.

Patients were kept in the supine position for 5 min after SA before they were transferred to the lithotomy position for surgery. Sensory level, as defined by the loss of cold sensation to ice, was assessed at 15 min after SA. Ephedrine 5 mg IV was given every 3 min for the first 35 min and every 5 min for the subsequent 25 min if significant hypotension occurred. Significant hypotension was defined as 30% decrease from the baseline systolic blood pressure or an absolute systolic blood pressure of <100 mm Hg. Metaraminol 0.1 mg IV was given as a rescue drug if more than 30 mg of ephedrine was required. The amount of IV fluid given was left to the discretion of the individual anesthesiologist.

The hemodynamic changes for the first 60 min after SA, the amount of vasopressor required, the sensory level at 15 min after SA, the total amount of IV fluid given, the presence of angina and postoperative confusion, and the difference between preoperative and postoperative hemoglobin were recorded. Parametric data (except data for the dose of ephedrine) were analyzed by using the analysis of variance, and non-parametric data were analyzed by the χ² test. Data for dose of ephedrine was analyzed by using the Kruskal-Wallis test. P value < 0.05 was regarded as statistically significant.
Results

All three groups were comparable in sex, weight, and ASA physical status. However, the subjects in the placebo group were significantly older (Table 1). Although the systolic blood pressure profile was comparable among the three groups (Figure 1), there was a significant dose-dependent difference in the HR profile among the three groups (mean HR of the placebo group: 78 bpm, 95% confidence interval [CI]: 76.6–78.5; small-dose atropine group: 86 bpm, 95% CI: 83.9–88.8; large-dose atropine group: 97 bpm, 95% CI: 94.5–100.3; P = 0.001; Figure 2). There was also a significant difference among the three groups in the incidence of hypotension (Figure 3) and the mean dose of ephedrine required (Table 2). The sensory levels and fluid requirements were not significantly different, although there was a trend toward a decrease in IV fluid requirement in the atropine groups. The small-dose atropine group had a smaller reduction in postoperative hemoglobin level as compared to the other two groups (Table 2). This may be a result of less blood loss in the small-dose atropine group. Intraoperative angina, ST segment changes in ECG, and postoperative confusion were not detected.

Discussion

Hypotension is common in elderly patients after SA, and reached 76% in the placebo group in this study. Although the incidence of hypotension was different, the systolic blood pressure profile was comparable in all three groups. This was because of a strict treatment protocol to prevent excessive hypotension in any patient.

Systemic vasodilation induced by sympathetic blockade, resulting in venous pooling of blood and reduction in systemic vascular resistance, has been regarded as the predominant mechanism for hypotension induced by SA. However, the absence of significant reflex tachycardia has been observed by Dobson et al. (7) and us, despite the presence of hypotension and use of ephedrine. This phenomenon may result from blockade of cardioaccelerator sympathetic fibers at T1 to T4, and possibly the “reverse” of the Bainbridge reflex. We postulate that the absence of reflex tachycardia may be an important component in the pathogenesis of hypotension induced by SA in addition to effects of venous and arterial dilation. Similarly, Caplan et al. (12) postulated that reduced atrial filling and unopposed vagal tone after SA produced a sufficient degree of bradycardia and hypotension, resulting in cardiac arrest.

Atropine, a widely used antimuscarinic drug, accelerates the HR. The dose-response effect of atropine in patients undergoing SA has not been investigated. We demonstrated that IV atropine after a crystalloid infusion could increase HR very quickly in a dose-dependent manner and decrease the incidence of significant hypotension also in a dose-dependent manner. However when IM atropine was used, Hirabayashi et al. (13) did not demonstrate any beneficial effect in hemodynamic stability during SA. The sample size in that study was small, and the subjects were not randomized. In addition, the absorption of IM atropine may be unpredictable, and the onset may have been too slow in comparison to the onset of hypotension after SA. Recently, another anticholinergic agent, glycopyrrolate, when given IV increased HR after SA and reduced the severity
of hypotension (14). In our study, the number needed to treat to prevent one case of significant hypotension in the small-dose atropine group was four, and the number needed to treat in the large-dose atropine group was three. The efficacy is comparable to prophylactic IM ephedrine in preventing hypotension induced by SA (11). However, large-dose atropine will invariably increase the HR to more than 100 bpm. This may be potentially harmful in patients with significant ischemic heart disease. Moreover, increasing HR to more than 100 bpm, as in the large-dose atropine group, cannot completely prevent hypotension induced by SA. Hence, small-dose IV atropine may be preferred as a supplement, but not as a replacement, to the existing methods in preventing hypotension induced by SA.

There were a few limitations in this study. Patients with severe ischemic heart disease or those taking β-blockers were excluded. The ECG was also not monitored with the 5-lead system (II, V1, V5) (15). Therefore, the safety of IV atropine at these doses cannot be extrapolated to high-risk cardiac patients despite the absence of new arrhythmia or chest pain as in our study subjects. The patients in the placebo group were also slightly older than the patients in the atropine groups. This, coupled with less blood loss in the small-dose atropine group, may have accounted for an apparently increased incidence of hypotension in the placebo group. However, the incidence of hypotension in the placebo group was similar to the study by Sternlo et al. (11) despite the patients in our study being older. In addition, the amount of blood loss was comparable between the large-dose atropine group and the placebo group.

In summary, IV atropine given after an infusion of crystalloid increases HR in a dose-dependent manner and reduces the need to use vasopressors for significant SA-induced hypotension. The absence of normal reflex tachycardia may contribute to the pathogenesis of hypotension after SA. Although routine pretreatment with atropine in patients undergoing SA is not recommended, small-dose atropine may help patients with low baseline HR or patients who are hypotensive and relatively bradycardic after SA is induced.