HEART RATE RESPONSE TO AN I.V. TEST DOSE OF ADRENALINE AND LIGNOCaine WITH AND WITHOUT ATROPINE PRETREATMENT

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SUMMARY

In order to evaluate the sensitivity of an adrenaline test dose for detecting intravascular injection and the effect of atropine pretreatment, 90 ASA physical status I and II patients were allocated randomly to two groups, to receive i.v. saline 1 ml (n = 46) or i.v. atropine 0.5 mg (n = 44). Five minutes later, all patients received an i.v. test dose of 2% lignocaine 3 ml with adrenaline 15 μg at a rate of 1 ml s⁻¹. The groups were similar with respect to basal heart rate (HR). HR remained unchanged after saline injection, but increased slightly 5 min after atropine injection (mean 78 (SD 15) beat min⁻¹ vs 87 (20) beat min⁻¹ (P < 0.05). After the test dose of lignocaine with adrenaline, HR increased significantly in both groups at 30 s, 1 and 2 min, and remained increased at 3 min in the atropine group. The maximum increase in HR was greater in the atropine group than in the saline group (31 (4) beat min⁻¹ vs 26 (11) beat min⁻¹ (P < 0.05). However, when individual maximum HR changes are considered, five patients in the saline group and four in the atropine group had an increase ≤ 10 beat min⁻¹, and three patients in the saline group had no change or a decrease in HR. Defining a positive result to a test dose as an increase in HR of > 10 beat min⁻¹, the sensitivity of the adrenaline test dose was 83 (5.5)% in the saline group and 91 (3.5)% in the atropine group (ns). Thus a test dose containing 2% lignocaine 3 ml and adrenaline 15 μg was not very sensitive for detecting intravascular injection, as moderate or false negative responses occurred frequently.

KEY WORDS

Regional blocks often require the use of large doses of local anaesthetics which, if accidentally injected i.v., may cause serious neurological and cardiovascular toxicity [1]. An i.v. test dose containing adrenaline 15 μg induced a consistent increase in heart rate in the 175 patients studied by Moore and Batra and therefore has been proposed as an effective means of detecting an i.v. injection [2]. However, subsequent publications have questioned the validity of an adrenaline test dose in parturients [3–5]. To be useful, a test dose must be both specific and sensitive. The lack of specificity has already been demonstrated in parturients who exhibited false positive responses to an adrenaline test dose (increases in HR after i.v. injection of bupivacaine without adrenaline) [6]. No data are available on the sensitivity of this test in non-pregnant adults, whereas the lack of sensitivity (false negative responses) has been reported in children anaesthetized with halothane [7]. Occasionally, atropine may be given before a regional block is performed, to prevent vagal attacks [8]; this may itself increase heart rate and modify the response to the test dose. The aim of this study, therefore, was to measure individual heart rate response to an i.v. adrenaline test dose with and without atropine pretreatment, in order to evaluate its sensitivity.

PATIENTS AND METHODS

The study was approved by the local Committee on Human Research, and informed consent was
obtained from 90 ASA physical status I or II patients. Patients receiving beta-blockers, calcium channel blockers or other anti-arrhythmic drugs were excluded from the study. Thirty-four patients received no premedication, and 66 received hydroxyzine 100 mg orally 2 h before surgery.

In the operating theatre, a cannula was inserted into a suitable vein and Ringer’s lactate solution was infused i.v. at a rate of 100 ml h⁻¹. Heart rate (HR) was measured continuously from the digital output of the ECG (lead 2). Systolic arterial pressure (SAP) was monitored using an automatic device (Dinamap). Five minutes later, patients received, in a random manner, either i.v. saline 1 ml (n = 46) or i.v. atropine 0.5 mg in 1 ml of saline (n = 44). Five minutes after this, patients in both groups received a test dose of 2 % lignocaine 3 ml with adrenaline 15 μg injected i.v. at a rate of 1 ml s⁻¹ as described previously [2]. HR was measured before and 5 min after injection of saline or atropine and 30 s, 1, 2 and 3 min after the test dose. In addition, the ECG was observed continuously and the maximum change in HR after test dose injection was recorded for each patient. SAP was measured before and 5 min after either saline or atropine and then 1, 2 and 3 min after the test dose injection. Any side effects were also noted.

Data were analysed using the chi-square test or Student’s t test to compare patients characteristics and basal HR. Changes in HR and SAP within and between groups were compared using one- or two-way repeated measures analysis of variance followed by a t test or Newman–Keuls test as appropriate. Results are expressed as the mean (SD). P < 0.05 was considered statistically significant.

**RESULTS**

The groups were similar in age, gender distribution, premedication and basal HR (table I). Mean HR remained unchanged after saline injection, whereas it increased by 9 beat min⁻¹ (P < 0.05) in the atropine group (fig. 1). Following the test dose, HR increased significantly in both groups; this change lasted for 2 min in the saline group and 3 min in the atropine group (fig. 1). Maximum change in HR occurred in all patients, within 2 min of test dose injection (fig. 2). The mean maximum increase in HR was significantly greater in the atropine group than in the saline group: 31 (14) beat min⁻¹ vs 26 (15) beat min⁻¹ (P < 0.05). There was considerable variation in both groups. The increase in HR was moderate (≤ 10 beat min⁻¹) in five patients in the saline group and four patients in the atropine group. Furthermore, in the saline group, HR was unchanged in one patient and actually decreased in two patients. No correlation was found between the increase in HR and either basal HR or the increase in HR in

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<th>Table I. Patient characteristics (mean (range or SD)). No statistical difference between the groups</th>
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**FIG. 1.** Mean (SD) changes in heart rate (upper part) and systolic arterial pressure (lower part) 5 min after injection of saline (●) or atropine (■) (first arrow) and 30 s, 1, 2 and 3 min after injection of adrenaline test dose (second arrow). P < 0.05 compared with: * before saline or atropine; † before adrenaline test dose (calculated using the total population for arterial pressure, as ANOVA failed to find any difference between the two groups).
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Fig. 2. Individual and mean values of maximum change in heart rate (HR) following i.v. injection of test dose in the saline and atropine groups.

Fig. 3. Correlation between the observed maximum change in systolic arterial pressure and the observed maximum change in heart rate (HR). No statistical correlation in the saline group, but significant correlation in the atropine group ($r = 0.403$ for both regression lines).

This study was designed to evaluate the sensitivity of an adrenaline test dose for detecting intravascular injection, and to determine if prior administration of atropine affected its sensitivity.

After i.v. test dose injection, in the saline group we observed a significant increase in HR within 2 min. The mean maximum HR increase of 26 (15) beat min$^{-1}$ is close to the 32-beat min$^{-1}$ increase reported by Moore and Batra [2]. However, because a test is useful only if it is highly sensitive (has a low rate of false negative responses), individual rather than mean responses must be considered.

In our study there was considerable individual variation in the HR change. As spontaneous changes in HR may occur during a block because of emotion, we believe that an increase in HR must exceed 10 beat min$^{-1}$ in order to be clinically significant. Using this criterion, eight patients of 46 in the saline group had a false negative response to the adrenaline test dose, which represent a sensitivity of 83 (5.5)% compared with 91 (13.5)% in the atropine group (ns). Moore and Batra reported a consistent increase in HR in 175 patients who received an adrenaline test dose; only three patients who were taking beta-adrenergic blockers had negative responses [2]. Because individual values were not reported in their study, the frequency of no change or only a
moderate increase in heart rate is unknown. Using a study design similar to ours, Desparmet and colleagues [7] found that an adrenaline test dose did not induce a reliable increase in heart rate in children anaesthetized with halothane and nitrous oxide. They reported an increase in heart rate of less than 10 beat min\(^{-1}\) in six of 21 children after a test dose (sensitivity 72 (10)\%).

This inconsistent increase in HR after i.v. injection of a test dose may be explained by the fact that adrenaline affects HR by two opposing mechanisms: stimulation of beta-adrenoreceptors leading to an increase in HR and stimulation of alpha-adrenoreceptors leading to an increase in arterial pressure; this stimulates baroreceptor reflexes, leading to a decrease in HR [9]. This indirectly mediated bradycardia may attenuate the direct chronotropic effect of adrenaline. Atropine may partially counteract bradycardia induced by adrenaline and this might explain the greater degree of tachycardia and the significant correlation between HR and SAP increases observed after test dose injection in the atropine group, compared with the saline group. However, despite an increase in HR in every patient in the atropine group, this was less than or equal to 10 beat min\(^{-1}\) in four patients—almost 10% of patients. Desparmet also found that pretreatment with atropine improved the reliability of an adrenaline test dose in anaesthetized children, but did not ensure total reliability [7]. A false negative response occurred in one of 20 children studied.

We designed our study to represent our usual clinical practice as closely as possible. Atropine 0.5 mg is used routinely in our institution before an extradural block is performed, in order to prevent vagal bradycardia. The tachycardia observed following this dose has been observed elsewhere in similar conditions, and is usually sustained for at least 10–15 min [10, 11].

The occurrence of ECG abnormalities in only 12% of the patients studied is considerably less than the 50% incidence reported previously in a similar study [2]. The other side effects observed were minor and infrequent, perhaps because of the relative youth and physical condition of the patients.

REFERENCES