EPINEPHRINE-CONTAINING TEST DOSE DURING BETA-BLOCKADE
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Mackie K, Lam A. Epinephrine-containing test dose during beta-blockade.
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ABSTRACT. Epinephrine is routinely used as a marker for intravascular injection during administration of regional anesthesia. The cardiovascular response of patients on beta-blockers to such a test dose has been reported to be unpredictable. We investigated this interaction by administering 15 μg of epinephrine intravenously to 6 healthy volunteers 39 to 48 years old before and after beta-blockade, accomplished by intravenous injection of propranolol, 0.04 mg/kg. Epinephrine administration caused a 20 ± 4% (mean ± SEM) increase in heart rate before beta-blockade but a 38 ± 3% reduction after beta-blockade. The lowest heart rate recorded was 28 beats/min. We conclude that, in middle-aged beta-blocked men, intravenous injection of a standard epinephrine-containing test dose will predictably cause significant hypertension followed by marked bradycardia.


The practice of including 15 μg of epinephrine in a test dose of local anesthetic as a marker for intravascular injection has gained wide acceptance since Moore and Batra [1] illustrated its efficacy. A recurring issue has been its appropriateness in patients taking beta-adrenergic blocking drugs. Anecdotal reports suggest that the pulse rise in such patients following inadvertent intravascular injection is unpredictable, being absent or negative [1-4]. A study involving young subjects 24 to 36 years old found that in the presence of moderate beta-blockade, 15 μg of epinephrine produced a 30% rise in mean blood pressure (BP) and a 36% decrease in heart rate (HR) [4]. However, surgical patients in the fourth and fifth decades are the ones most likely to receive beta-blockers. Therefore, we investigated the effects of beta-blockade on the response to 15 μg of epinephrine in an older group of volunteers 39 to 48 years old.

SUBJECTS AND METHODS

The experimental protocol was approved by our institutional Human Subjects Committee and informed consent was obtained. We studied 6 volunteer, nonpremedicated men 39 to 48 years old who were free from systemic illness. The subjects were studied while supine. BP was determined at 1-minute intervals by using an automated oscillometric cuff (Dinamap, Critikon, Tampa, FL), while electrocardiogram and HR were monitored and displayed continuously. After stable BP and HR were determined, 15 μg of epinephrine was administered intravenously and BP and HR recorded for 20 minutes, during which time BP and HR returned to control levels. Beta-blockade was accomplished by
the administration of propranolol, 0.04 mg/kg, intravenously [5]. After 5 minutes, during which time stabilization of BP and HR occurred, 15 μg of epinephrine was again administered and BP and HR recorded for 20 minutes. In 1 subject, direct intraarterial BP was monitored and recorded continuously during the study.

The maximum changes in HR and BP following epinephrine injection both before and after beta-blockade were recorded and analyzed by one-way analysis of variance for repeated measures. A P value of less than 0.05 was considered statistically significant and a multiple comparison procedure (Scheffe’s test) was used for subsequent analysis. Because there was considerable variation in baseline HR among the subjects, the percent change from control values following epinephrine injection both before and after beta-blockade was also used for statistical analysis using Student’s paired t test.

RESULTS

As expected, 15 μg of epinephrine, administered before beta-blockade, led to a significant increase in HR (P < 0.001) and a mild increase in BP (see the Table and Figs 1 and 2). Beta-blockade with 0.04 mg/kg of propranolol in these supine subjects resulted in a slight but consistent decrease in HR of 12 ± 2% (mean ± SEM; P < 0.05 compared with resting control values). In the presence of beta-blockade, 15 μg of epinephrine caused profound bradycardia, with HR decreasing an average of 37 ± 3% (P < 0.0001) from the post–beta-blockade HR; the greatest changes occurred within 3 minutes of epinephrine injection, both before and after beta-blockade (see Table). The lowest HR observed was 28 beats/min. Changes in individual HR with epinephrine injection following beta-blockade are shown in Figure 3. Arrhythmias were seen in 2 subjects, 1 having ventricular and the other junctional escape beats. In 2 instances, the rise in BP was missed because the cuff was unable to compute a reading, presumably because of the slow heart rate [6]. One subject experienced chest tightness but showed no other concomitant signs of myocardial ischemia and no electrocardiographic changes.

DISCUSSION

Our findings demonstrate that in a population likely to be taking beta-adrenergic blocking drugs (middle-aged men), intravenous administration of a test dose of epinephrine causes marked bradycardia. This is likely the consequence of several events: The nonselective beta-blockade allows unopposed vasoconstriction from the epinephrine, leading to systemic hypertension and subsequent activation of the carotid and aortic baroreceptors. Vagal tone then increases reflexively, resulting in bradycardia. The implications are twofold. Firstly, a rise in HR cannot be used as an indication of inadvertent intravenous injection of an epinephrine-containing test

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control</th>
<th>First Injection of Epinephrine</th>
<th>Second Injection of Epinephrine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (beats/min)</td>
<td>66 ± 9</td>
<td>82 ± 9</td>
<td>38 ± 8</td>
</tr>
<tr>
<td>Mean arterial pressure (mm Hg)</td>
<td>103 ± 8</td>
<td>108 ± 9</td>
<td>107 ± 8</td>
</tr>
</tbody>
</table>

*Values are means ± SD.

bP < 0.05 compared with control.

°P < 0.05 compared with beta-blockade before epinephrine.

Fig 1. Average heart rate changes in 6 volunteers during the entire study. Arrows indicate the time of epinephrine (EPI) injection and the asterisk denotes the time of propranolol administration. BPM = beats per minute.