Cardiovascular effects of epinephrine on hypertensive dental patients
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Authors' objectives
To assess the additional risks of adverse cardiovascular outcomes to hypertensive patients represented by the use of epinephrine-containing anaesthetic solutions and epinephrine-impregnated gingival retraction cords during dental treatment.

Searching
MEDLINE, EMBASE and the Cochrane Controlled Trials Register were searched from 1966 to March 2001 for English language publications; the search terms were reported. In addition, the references of identified studies were also checked. No attempts to locate unpublished studies were made.

Study selection
Study designs of evaluations included in the review
No inclusion criteria were stated in relation to the study design. Studies that included fewer than five hypertensive patients were excluded.

Specific interventions included in the review
Studies using known concentrations of epinephrine-containing local anaesthetic administered via either intra-oral submucosal block or infiltration injection, or the administration of epinephrine-impregnated gingival retraction cord, were eligible for inclusion. All of the included studies assessed epinephrine-containing local anaesthetic. The local anaesthetic involved 2% lidocaine, with epinephrine concentrations of either 1:100,000 or 1:80,000. The quantity of anaesthetic solution injected was reported in four of the 6 studies, with mean values ranging from 2 to 4.5 mL.

Participants included in the review
Studies of patients with controlled or uncontrolled hypertension who were undergoing dental surgery were eligible for inclusion. Studies in which the hypertensive status of patients was not confirmed were excluded. The dental procedure being undertaken was tooth extraction in five of the 6 studies; the remaining study included patients receiving minor oral surgery. The studies also included normotensive patients. Fourteen percent of the patients in the studies were taking medication for the control of hypertension.

Outcomes assessed in the review
Studies that reported at least one cardiovascular or haemodynamic outcome separately for hypertensive patients were eligible for inclusion. The outcomes of interest were blood-pressure (BP), heart rate, stroke volume, plasma epinephrine concentration, and electrocardiogram changes including transient arrhythmias. The adverse events considered were headache, syncope, angina, hypertensive crisis, longer term arrhythmias, cerebrovascular accident and myocardial infarction. The specific outcomes assessed were changes in systolic BP, diastolic BP and heart rate.

How were decisions on the relevance of primary studies made?
Two independent reviewers assessed studies for inclusion.

Assessment of study quality
The quality of the included studies was assessed according to the following: whether the study had a control group; sample size; the presence of a normotensive control group; determination of the status of hypertensive patients; description of the treatment; the reporting of the quantity of anaesthetic solution administered; the outcome measures assessed; the timing of the outcome assessments; measurement reliability; whether a statistical analysis was undertaken; the reporting of the results and measures of variance; and whether complications and adverse events were reported. The final rating of the thirteen items produced a score out of 20. Raw scores were then rescaled to a 0- to 100-scale. One reviewer performed the quality assessment.
Data extraction
One reviewer extracted the data, which were checked for accuracy by a second reviewer. Any discrepancies were resolved by consensus. Data were extracted on the systolic and diastolic BP and heart rate (both pre- and post-injection), adverse events, and reported changes in any other indicators.

Methods of synthesis
How were the studies combined?
The studies were grouped according to the intervention, and whether hypertensive and normotensive patients had received injections with and without epinephrine, then combined in a narrative. Two reviewers independently reviewed the strength of the evidence as good, fair or poor, based on the number of studies, sample size and consistency of the results.

How were differences between studies investigated?
Differences between the studies were discussed in relation to the timing of the outcomes assessments.

Results of the review
Six studies with a total of 325 patients (177 hypertensive, 148 normotensive) were included: 3 controlled studies (n=210), 2 pre-test post-test studies (n=101) and one uncontrolled study (n=14).

The strength of the evidence was graded as poor. The scores for study quality ranged from 35 to 70 out of 100 across the included studies. No studies of the effects of epinephrine-impregnated gingival retraction cord were included.

Three studies included both uncontrolled hypertensive and normotensive patients that received injections with or without epinephrine. The unweighted means from these studies showed that when dental extractions were performed using epinephrine, systolic BP was 4 mmHg higher for hypertensive patients receiving epinephrine compared with no epinephrine (absolute change was 15.3 versus 11.7 mmHg). In normotensive patients, there was no difference in systolic BP between those receiving epinephrine and those not receiving epinephrine (changes of 5 mmHg in both groups). Heart rate was slightly higher with epinephrine than without epinephrine for hypertensives and normotensives (6 beats per minute and 5.6 beats per minute, respectively). Diastolic BP was lower with epinephrine than without epinephrine for both hypertensives (1.0 mmHg) and normotensives (4.7 mmHg).

The increases in systolic BP and heart rate from baseline were higher for hypertensives than for normotensives (BP: 11.7 versus 5.0 mmHg; heart rate: 4.7 versus 0.7 beats per minute). The increases in diastolic BP from baseline were similar between hypertensive and normotensive patients (3.3 and 4.0 mmHg, respectively).

In studies where the timing of the maximum reading was reported, it tended to occur in conjunction with the surgical procedure rather than the injection in almost all cases. For both hypertensive and normotensive patients who received epinephrine, smaller increases in systolic BP and heart rate were associated with the injection. No increases in systolic BP were observed at the time of injection in patients who did not receive epinephrine.

Authors’ conclusions
Although the increased risk for adverse events among uncontrolled hypertensive patients was found to be low, and the occurrence of adverse events in hypertensive patients associated with the use of epinephrine in local anaesthetics during dental procedures was also low, the quantity and quality of the evidence base was problematic.

CRD commentary
The review question was clearly defined in relation to the interventions, participants and outcome measures that were to be included. The search was adequate, but no efforts were made to identify either foreign language or unpublished papers. This means that other relevant studies might have been missed. Efforts to minimise reviewer bias and errors were made in the study inclusion and data extraction processes. The quality of the primary studies was thoroughly
assessed but, as this process was conducted by only one reviewer, it is possible that bias might have been introduced into the review process. The use of a narrative synthesis was appropriate given the differences between the studies. The authors appropriately highlighted the short-comings in the primary studies. Overall, the authors’ conclusions were consistent with the results presented. However, owing to the paucity of the evidence base reviewed, they may not be particularly robust. The authors’ recommendations for prospective studies were therefore warranted.

**Implications of the review for practice and research**

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that a large-scale descriptive study of the effects of epinephrine-containing local anaesthetics in patients with hypertension who were receiving dental treatment was needed. They suggested that a prospective, long-term follow-up study in one or more high-volume clinics, involving electronic capture of pre-existing cardiovascular diagnoses and medication status of all patients, together with information describing all adverse events, was warranted. They also stated that studies were needed to assess the cardiovascular risk of the use of epinephrine-impregnated gingival retraction cord in hypertensive patients, in order to quantify the absorption of epinephrine from gingival tissues. Such studies should focus on the effects of time, tissue condition, cord construction and epinephrine concentration on the plasma concentration of epinephrine should be determined.

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