remained at 1.8 mmol/l until day 22. On day 15 the ECG revealed sinus rhythm with normal axis, P-R interval and QRS width but with a prolonged Q-Tc interval of 0.55 seconds. On day 22 the Q-Tc had shortened to 0.45 seconds.

Of the three biphosphonates licensed in Britain, pamidronate, etidronate and clodronate, pamidronate has the most profound and prolonged action.2 Patients may report short-lived symptoms of hypocalcaemia, such as paraesthesiae or demonstrate Chvostek's and Trouseau's signs as the serum calcium and in particular the ionized calcium falls. This may be related to the rate of fall rather than absolute calcium concentrations. Intravenous etidronate when given to dogs in high doses is known to predispose to lethal ventricular arrhythmias related to depression in serum ionized calcium concentrations and this is associated with prolongation of the Q-Tc interval.3 ECG changes have not been reported with pamidronate infusion in man. Significant hypocalcaemia due to pamidronate has been reported with concurrent administration of an aminoglycoside.4 Symptoms of hypocalcaemia have been reported to occur almost 2 weeks after infusion.3 Francis et al.,3 noted the ECG to be a sensitive indicator of ionized calcium concentration and suggested it could be used as a monitoring device. This may be useful in facilities where ionized calcium estimation may not be readily available. Of concern is that Q-Tc prolongation predisposes to malignant ventricular arrhythmias and in particular torsade de points. The incidence of ECG abnormalities and the need for rectification with, for example, intravenous calcium gluconate should be established and currently recommended infusion times altered if necessary, especially since recent data suggest that significant hypocalcaemia does occur (and may do so late and unpredictably) with intravenous biphosphonates.

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Sublingual captopril in hypertensive urgencies

Sir,

Treatment of hypertensive urgency requires gradual lowering of blood pressure over 24 hours. Several drugs (sublingual nifedipine, oral clonidine, labetalol and captopril) have been used with successful results. Recently, promising results have been shown with the use of sublingual captopril.1-5 All these reports on sublingual administration of captopril, except that conducted by Pujadas et al.,3 have been either non-randomized observations or have incorporated few patients. In a prospective randomized trial conducted by us, efficacy and toxicity profile of sublingual nifedipine and sublingual captopril were compared in 47 consecutive patients with hypertension with diastolic blood pressure (DBP) of more than 120 mmHg (Phase V) as shown in all three baseline readings taken 5 minutes apart in the emergency room. Patients were randomly given sublingual nifedipine capsule (10 mg capsule with multiple punctures) and evenly powdered captopril tablets (25 mg) in perforated capsules by the same route. Heart rate and blood pressure were measured at 5, 10, 15, 20, 30, 60, 120, 240 and 360 minute intervals by the same observer. The patients attaining DBP less than 100 mmHg, after institution of the appropriate treatment, were considered 'responders'. Statistical analysis was performed using t-test (for paired and unpaired data), Wilcoxon's test and Spearman's rank correlation coefficient test.

The nifedipine group (n = 25) and captopril group (n = 22) were similar in their clinical profiles. Onset and peak of action of nifedipine was earlier than captopril (Table I). Therapeutic efficacy of nifedipine declined after 2 hours with 44% patients sustaining DBP less than 110 mmHg at 4 hours and only 8% at 6 hours. In the captopril group, a larger number of patients maintained DBP less than 110 mmHg (90% at 4 hours; 50% at 6 hours). Mean DBP at 4 and 6 hours was significantly higher in the nifedipine group. With treatment, heart rate increased significantly more often in the nifedipine group.

Side effects were observed frequently in the nifedipine group: headache 11%, palpitations 16%, weakness and flushing 8%, precipitous fall of blood pressure 8% (maximum 90/65 mmHg) as compared to that seen in captopril group (burning mouth 9% and nausea 5%).

Earlier, several workers1,2 have observed efficacy and safety of sublingual captopril in hypertensive urgencies in fewer patients. Pujadas and coworkers3 observed that onset, duration and mean fall of blood pressure was similar in patients given sublingual nifedipine and captopril. However, a small study (n = 12) more closely follows our observations.6 A recent report,7 gives comparable blood pressure responses and side effect profile with sublingual captopril and nifedipine. Results of the present study indicate that sublingual captopril appears to offer various advantages over sublingual nifedipine in hypertensive urgencies, namely gradual reduction of blood pressure with persistence of action at 6 hours, minimal side effects, no risk of rapid hypotension and reflex tachycardia.

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References

Table I  Effect of sublingual nifedipine and sublingual captopril in patients with hypertensive urgencies

<table>
<thead>
<tr>
<th>Time (minutes)</th>
<th>Nifedipine group (n = 25)</th>
<th>Captopril group (n = 22)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SBP (mmHg)</td>
<td>Heart rate (beats/minute)</td>
</tr>
<tr>
<td>0</td>
<td></td>
<td>88 ± 10</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>90 ± 8</td>
</tr>
<tr>
<td>15</td>
<td></td>
<td>96 ± 6*</td>
</tr>
<tr>
<td>30</td>
<td></td>
<td>100 ± 8*</td>
</tr>
<tr>
<td>60</td>
<td></td>
<td>98 ± 5*</td>
</tr>
<tr>
<td>120</td>
<td></td>
<td>96 ± 7*</td>
</tr>
<tr>
<td>240</td>
<td></td>
<td>92 ± 8</td>
</tr>
<tr>
<td>360</td>
<td></td>
<td>90 ± 6</td>
</tr>
</tbody>
</table>

*P < 0.001 (comparing nifedipine and captopril groups); SBP = systolic blood pressure; DBP = diastolic blood pressure.

References


Primary anaerobic bacterial meningitis caused by Propionibacterium acnes

Sir,

The association of acute bacterial meningitis and Propionibacterium acnes is a rare event. We would like to report a case with complete recovery on chloramphenicol therapy.

A 4 year old female child presented with high grade fever associated with vomiting of 24 hours duration before admission to the hospital. Her past medical history included tuberculosis of bone (right foot) for which she had received anti-tubercular therapy for one and half years, stopped one year before the current illness. The child was fully immunized. On examination, her temperature was 102°F. She was drowsy, responding only to painful stimuli but not to verbal commands. Neck stiffness and Kernig's signs were positive. There was no neurological deficit. Total leucocyte count was 16.8 × 10^9/l with 90% polymorphs. Lumbar puncture yielded opalescent cerebrospinal fluid (CSF) under normal pressure with 750 cells/mm^3 95% polymorphs. The glucose was 1.6 mmHg against blood glucose 5.04 mmHg and CSF protein was 108 mg/dl. No organisms were seen on Gram staining, simple methylene blue and Ziehl–Neelsen staining of the centrifuged deposit of CSF. Latex agglutination test for N. meningitidis Gr A and C. H. influenzae type b and St. pneumoniae by using 'slide meningite kit' (Biomerieux, France) was negative. Aerobic culture was done on chocolate and blood agar plates and incubated at 37°C for 48 hours. Supplemented brain heart infusion Agar (SBHIA) and Robertson's cooked meat (RCM) broth were used for isolation of anaerobic bacteria. These cultures were incubated at 37°C under appropriate gaseous atmosphere for 48 hours to 7 days.

Treatment was instituted by chloramphenicol in the dose of 100 mg/kg/day in four divided doses intravenously. No bacterial growth was observed in any agar plates after 48 hours except RCM which was incubated further. On Gram staining and wet mount preparation, it revealed numerous slender non-motile, non-sporing pleomorphic (diphtheroid like) Gram-positive bacilli. Anaerobic subculture of the isolate showed initially a small white-coloured colony which became larger with more or less yellow. Aerobic subculture was negative. Biochemically the isolate was consistent with P. acnes. However, gas-liquid chromatography was negative. Chloramphenicol was given orally after 5 days and administered for a duration of 14 days. Repeat CSF culture was sterile and the patient had complete clinical recovery.

P. acnes is considered to be a commensal of the normal skin, upper respiratory tract and intestinal tract. It is also a common contaminant of CSF specimens. However, when isolated from patients with signs and symptoms of central nervous system infection, the organism should not be automatically disregarded as a contaminant. It is recognized that anaerobic infections of the central nervous system including meningitis are most likely to occur in the setting of preceding chronic infections of head and neck and often part of a more extensive intracranial infection. There have also been reports of clinically significant infections related to prosthetic devices such as indwelling intravascular catheters and prosthetic heart valves. In the present case the significant past medical history was tuberculosis of bone, fully treated and asymptomatic. However, this is very unlikely to bear any correlation with the current illness. Anaerobic meningitis...
Sublingual captopril in hypertensive urgencies.

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