Hyperosmolar non-ketotic diabetic coma induced by furosemide in modest dosage

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Summary
A case of hyperosmolar non-ketotic diabetic coma in a patient treated with a modest degree of furosemide is reported.

Introduction
Thiazides are known to diminish glucose tolerance and precipitate or aggravate diabetes, but that furosemide may do so is not so well appreciated (Walsh and O'Sullivan, 1974; Salvsteen, Olsen and Hansen, 1968; Toivonen and Mustala, 1966; Heimsoth and Bock, 1970). Large doses of furosemide may be a factor responsible in causing hyperosmolar non-ketotic diabetic coma (Tasker and Mitchell-Heggs, 1976). but quite modest or small doses such as are widely prescribed, may also be implicated (Lavender and McGill, 1974). This form of coma may also be brought on in certain circumstances by the consumption of large quantities of sweet drinks (Macaulay, 1971). The case described below shows a combination of these two factors.

Case report
A 62-year-old man whose father was diabetic gave a history of sudden collapse, with weakness of the legs. No neurological abnormality was found, but he was febrile with an inflamed throat. The pulse was regular 112/min, blood pressure 170/120 mmHg. He had a gallop rhythm, basal rales and hepatisation. Bronchopneumonia and heart failure secondary to hypertension was diagnosed. Chest X-ray showed a large heart, fluid in the right horizontal fissure and bilateral pulmonary basal shadowing. Electrocardiogram showed sinus tachycardia, left axis deviation and S-T-segment depression in the anterolateral leads. A throat swab grew β-haemolytic streptococci. There was no glycosuria and a post-prandial blood glucose was 6-6 mmol/l. Furosemide 40 mg twice daily, ampicillin and potassium supplements were prescribed and this resulted in clinical and radiological improvement one week later.

Hypertension was persistent and as urinary vanilmandelic acid estimations and midstream cultures were normal, the patient was given methyl-dopa (Aldomet) 250 mg twice daily. A repeat post-prandial glucose was now 12-8 mmol/l.

Three months after presentation the patient became more breathless and as he was in heart failure, the furosemide was increased to 80 mg twice daily. The breathing improved, but 6 days before admission he developed a dry mouth, thirst, polyuria, progressive drowsiness, vomiting and eventually became comatose. A notable feature was a craving for sweet fruit juices (orange, pineapple and lemon fizzy drinks). He consumed a dozen cups of sweet tea daily. On examination he was unconscious, dehydrated and dyspnoeic but there was no acetone in the breath. Blood pressure was 160/110 mmHg, pulse 110/min; and there were no focal neurological signs.

Urine showed 2% glycosuria without ketones. Blood glucose was 70 mmol/l, sodium 144 mmol/l, pH 7-23, Pco₂ was 42, bicarbonate 17 and base excess –9. Plasma osmolarity was 395 mosmol/l (normal, 283 ± 17). Two litres of isotonic saline were rapidly infused, changing to hypotonic (N/2) saline when the biochemistry was known. Insulin 10 u./hr i.m., together with intravenous potassium supplements and small doses of heparin were given, the latter to avert thrombotic complications. Nine litres of fluid in 24 hr and 13-5 l in 48 hr were infused and there was a diuresis of 2-5 l daily, indicating a net deficit of 8 l of fluid on admission. Soluble insulin 100 u. in 24 hr were needed. The patient regained consciousness in 12 hr, but remained confused for a further day. Five days after admission his blood pressure was in the normal range and heart failure and hypertension posed no further problems, even though drugs were discontinued. The insulin requirements fell rapidly and soon he was managed on tolbutamide alone. The biochemical improvement is shown on the graph (Fig. 1). The calculated osmolarity was derived from the equation:

\[
\text{osmolarity} = 2 (\text{Na} + \text{K}) + \text{urea} + \text{glucose (mosmol/l)}.
\]
The electrocardiogram showed slight S-T depression extending to the septal as well as the anterolateral leads. The serum enzymes are shown in Table 1.

<table>
<thead>
<tr>
<th>Enzyme</th>
<th>Day 2</th>
<th>Day 5</th>
<th>Day 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatine phosphokinase</td>
<td>29</td>
<td>—</td>
<td>470</td>
</tr>
<tr>
<td>Aspartate transferase</td>
<td>40</td>
<td>—</td>
<td>54</td>
</tr>
<tr>
<td>Alanine transferase</td>
<td>36</td>
<td>27</td>
<td>28</td>
</tr>
</tbody>
</table>

The fall in blood pressure, minor cardiographic changes and late rise in enzymes may indicate a late myocardial infarct occurring as a secondary phenomenon. Alternatively, frequent intramuscular injections might have been responsible for the high CPK levels.

**Discussion**

Furosemide probably precipitated both the diabetes at a dosage of 40 mg twice daily and later the hyperosmolar coma when the dose was doubled, in a patient with a family history of diabetes. The high carbohydrate intake no doubt accelerated the hyperosmolar state, as is common. The occurrence of a myocardial infarct may have been precipitated by the hyperosmolar state (despite heparin). The implications are that when an established diuresis has occurred with diuretics, care is needed to ensure diabetes is not missed. Furthermore, the modest dosage used in this case implies that other patients attending medical clinics may be at risk of developing these complications.

**Acknowledgments**

We would like to thank Dr S. Mhlongo for his help, Mrs S. Tachon for typing the manuscript, and the Medical Illustration Department who helped with the production of the figure.

**References**


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Postgrad Med J 1978 54: 43-44
doi: 10.1136/pgmj.54.627.43

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