Idiopathic oedema and diuretics

M.G. Dunnigan¹, D.W. Denning¹, J.A. Henry² and F.A. de Wolff³

¹Department of Medicine, Stobhill Hospital, Glasgow G21 3UW, ²Poisons Unit, Guy's Hospital, London SE1 9RT, UK, and ³Department of Toxicology, Academisch Ziekenhuis, 2333AA Leiden, Holland

Summary: Diuretic abuse has been invoked as the cause of idiopathic oedema. In this study, eight patients with idiopathic oedema were studied. Symptoms and weight variation continued despite the proven absence of diuretics in seven of them as determined by urinary chromatograms. Idiopathic oedema cannot therefore be attributed to diuretic use alone.

Introduction

In 1979, based on observations in 10 patients, MacGregor et al.¹ proposed that 'intermittent oedema of unknown cause in most, if not all, otherwise healthy women is due to their use of diuretics'. While this hypothesis has been challenged,²,³ it remains possible that women with fluid-retaining symptoms who deny diuretic administration may be covertly abusing diuretics. We therefore designed a small study to examine this possibility.

Materials and methods

Routine urine samples brought to a medical clinic by 8 patients with symptoms of idiopathic oedema were collected. Patients were included in order of attendance at the clinic which has a special interest in this condition. Four patients who stated that they had been taking diuretics regularly or intermittently were asked to discontinue them. All 8 patients were asked to record their weights morning and evening and to collect a 24-hour sample of urine before returning in 4 weeks for a further clinic attendance, the reason for which was not specified. They were also instructed to continue their normal diet. Each patient was directly questioned about laxative abuse which was denied by all. In each patient the diagnosis of idiopathic oedema was established by a typical history, recorded diurnal weight variation of more than 1.4 kg and a weekly weight variation of more than 1.8 kg. Cardiac, renal, hypoproteinaemic and obstructive causes of oedema were excluded by appropriate investigations. The initial urine sample and two 20 ml aliquots from the 24-hour sample of urine were frozen at −20°C. Diuretics were identified by an as yet unpublished high-performance thin-layer chromatographic method which is based on a procedure for screening of laxative abuse.⁴ With this method, the following drugs can be detected in urine extracts after intake of therapeutic doses (1.5–10 μg/spot): amiloride, canrenoate, chlorothalidone, ethacrynic acid, frusemide, hydrochlorothiazide, hydroflumethiazide, mefurside and triamterene. Analysis was performed blind and positive controls were included which were correctly identified (see Table I).

Results

Diuretics were absent from the initial and 24-hour urine samples of the 4 patients who stated that they had never received diuretics (Table I). No diuretic was found in urine samples from 2 patients who stated that they had been taking diuretics intermittently. Diuretic was found in both initial urine samples and in one of the 24-hour urine samples from 2 patients who admitted to regular diuretic use. All 8 patients showed continuing evidence of idiopathic oedema over the whole of the 4-week period between clinic visits as judged by the persistence of symptoms and mild to severe diurnal and weekly weight variation (Table I).

Discussion

These results contradict the hypothesis of MacGregor et al.¹ that idiopathic oedema is an iatrogenic disease caused by diuretic administration. The 4 women who stated that they had never taken diuretics did not have diuretics in their urine and yet had clear evidence of fluid retention. Three of the 4 women who admitted
Table I  Diuretics detected in the urine of four controls and eight women with idiopathic oedema at an initial clinic visit and in 24-hour urine collections one month later.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Maximum weekly weight variation (kg)</th>
<th>Previously stated diuretic use</th>
<th>Diuretics detected</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Initial urine sample</td>
<td>24-hour urine sample</td>
</tr>
<tr>
<td>45</td>
<td>2.3</td>
<td>Moduretic*</td>
<td>+</td>
</tr>
<tr>
<td>38</td>
<td>3.2</td>
<td>Moduretic</td>
<td>+</td>
</tr>
<tr>
<td>40</td>
<td>5.6</td>
<td>Navidrex K†</td>
<td>−</td>
</tr>
<tr>
<td>46</td>
<td>2.3</td>
<td>Navidrex K</td>
<td>−</td>
</tr>
<tr>
<td>28</td>
<td>3.2</td>
<td>none</td>
<td>−</td>
</tr>
<tr>
<td>21</td>
<td>2.3</td>
<td>none</td>
<td>−</td>
</tr>
<tr>
<td>47</td>
<td>3.6</td>
<td>none</td>
<td>−</td>
</tr>
<tr>
<td>51</td>
<td>2.3</td>
<td>none</td>
<td>−</td>
</tr>
<tr>
<td>42</td>
<td>Control</td>
<td>Spironolactone</td>
<td>+</td>
</tr>
<tr>
<td>36</td>
<td>Control</td>
<td>Spironolactone</td>
<td>+</td>
</tr>
<tr>
<td>57</td>
<td>Control</td>
<td>Frusemide</td>
<td>+</td>
</tr>
<tr>
<td>23</td>
<td>Control</td>
<td>Frusemide</td>
<td>+</td>
</tr>
</tbody>
</table>

* Moduretic – amiloride and hydrochlorothiazide
† Navidrex K – cyclopenthiazide and potassium chloride

taking diuretics stopped them on request; this did not lead to cessation of their symptoms or of objective evidence of fluid retention or of worsening of their idiopathic oedema. The women did not know that the purpose of both urine collections was to identify diuretic use.

In our experience laxative abusers and patients with eating disorders characterized by bulimic and fasting episodes comprise a very small proportion of fluid-retaining women. Patients with idiopathic oedema may suffer a rebound in symptoms after stopping diuretics. In MacGregor's selected group of patients, 7 of 10 patients were asymptomatic less than 3 weeks after stopping diuretics; the remaining 3 patients had been taking large doses of diuretics for long periods. In these 3 patients juxtaglomerular hyperplasia may have been responsible for more prolonged rebound oedema following the cessation of diuretic administration. This does not explain the original pathophysiology of idiopathic oedema.

Over 300 patients with idiopathic oedema have attended an outpatient clinic at Stobhill Hospital in the last 11 years. Diuretics were prescribed for many of these patients by their general practitioners for previously established symptoms of fluid retention. The majority of our patients are concerned at their continuing use of diuretics and are anxious to discontinue them if possible. In many, but not all, cases this can be achieved by dietary means.

References

Idiopathic oedema and diuretics.

M. G. Dunnigan, D. W. Denning, J. A. Henry and F. A. de Wolff

doi: 10.1136/pgmj.63.735.25

Updated information and services can be found at:
http://pmj.bmj.com/content/63/735/25

These include:

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/