SHORT REPORT

Ipecac myopathy and cardiomyopathy

Lee P Dresser, E Wayne Massey, Eric E Johnson, Edward Bossen

Abstract
Two cases of ipecac myopathy, one with associated cardiomyopathy are reported. Both patients were young women with eating disorders who came to medical attention because of diffuse muscle weakness. Clinical and electromyographic data suggested ipecac myopathy and muscle biopsies confirmed this diagnosis. One patient had associated clinical and echocardiographic evidence of significant cardiomyopathy. The myopathy resolved and the echocardiogram returned to normal after discontinuing the use of ipecac.

Table I  Echocardiogram results (patient 1)

<table>
<thead>
<tr>
<th></th>
<th>Study 1</th>
<th>Study 2 (15 months after discontinuing ipecac)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVIDd</td>
<td>5-1 cm</td>
<td>4-6 cm</td>
</tr>
<tr>
<td>LVIDs</td>
<td>4-2 cm</td>
<td>3-4 cm</td>
</tr>
<tr>
<td>EDV</td>
<td>109-4 ml</td>
<td>120-5 ml</td>
</tr>
<tr>
<td>ESV</td>
<td>69-5 ml</td>
<td>65-1 ml</td>
</tr>
<tr>
<td>EF</td>
<td>36-5%</td>
<td>46-0%</td>
</tr>
<tr>
<td>FS</td>
<td>17-6%</td>
<td>26-1%</td>
</tr>
</tbody>
</table>

Abbreviations: LVIDd (left ventricular internal dimension, diastole), LVIDs (left ventricular internal dimension, systole), EDV (end diastolic volume), ESV (end systolic volume), EF (ejection fraction), FS (fractional shortening).

The abuse of syrup of ipecac by patients with major eating disorders has been shown to have toxic effects on skeletal and cardiac muscle.1-7 These effects are most likely secondary to emetine, one of the major alkaloids in syrup of ipecac. Emetine is well known to produce myopathy in skeletal muscle,8 and is toxic to cardiac muscle,9 and may produce electrical disturbances and heart failure.4 Syrup of ipecac has been responsible for several deaths in patients with the binge-purge type eating pattern of bulimia.2 3 The use of syrup of ipecac by bulimic patients to stimulate emesis is now recognised to be widespread.6 It is important for physicians to be vigilant in seeking evidence of ipecac-induced myopathy and cardiomyopathy, especially in young women, because these disorders are potentially reversible. This report describes two patients with ipecac-induced myopathy and provides echocardiographic evidence of the reversibility of an associated cardiomyopathy.

Case reports
Patient 1
This was a 26 year old female admitted for evaluation of progressive muscle weakness. At the time of presentation, she had a two month history of progressive difficulty climbing stairs, carrying a laundry basket, and holding her head up while seated at work. She admitted to mild myalgia and had noted mild atrophy of her thigh and arm musculature. She had occasional palpitations, increased sweating, and mild pedal oedema. She denied chest pain or dyspnoea on exertion. She had a history of asthma, mild hypertension, depression and anorexia nervosa. At the time of her father’s death, four years before evaluation, she had lost 18 kilograms, dropping from 61 kilograms to 43 kilograms. Since then, her weight had increased to 57 kilograms and remained stable (height 165 cm). For the six month period before her evaluation, she had ingested several 30 ml doses of syrup of ipecac (containing approximately 21 mgs of emetine) per week to induce emesis after eating. She claimed only occasional alcohol use.

Her general physical examination revealed a well nourished, young, white woman. Her resting heart rate was 104 with S3 and S4 heart sounds present. Lungs were clear. Icthyosis was present on the extensor surface of her arms and legs. Her neurological examination was remarkable for diffuse mild atrophy and moderate diffuse weakness, greater proximally. Her sensory examination was normal.

Laboratory evaluation revealed blood counts, serum electrolytes, LDH, SGOT, SGPT, and alkaline phosphatase to all be within normal limits. A rheumatoid factor and antinuclear antibody were negative. A serum creatinine kinase (CK) level was elevated, with a peak at 1027 units/1. An ECG showed sinus tachycardia with a prolonged QT interval and T-wave inversion in the lateral leads. An echocardiogram showed left ventricular dilatation and diffuse hypocontractility with an ejection fraction of 36-5% (see table). Electromyography showed low-amplitude, polyphasic units in proximal muscles, without increased spontaneous activity.

A left deltoid biopsy showed slight variation in fibre size without evidence of inflammation. ATPase and NADH stains showed targetoid changes in both type 1 and 2 fibres with...
Ipecac myopathy and cardiomyopathy

Patient 2

This was a 29 year old, white female who was evaluated for muscle weakness during a psychiatric admission for an eating disorder. She had a several month history of progressive generalised weakness, exercise intolerance and amenorrhoea. For the six months before evaluation, she drank approximately one bottle of wine per day. During this period, she had a pattern of minimal food intake alternating with binge eating, always followed by ipecac-induced emesis. General physical examination showed a thin white female with dry skin. Heart and lungs examination were normal. Diffuse moderate muscle atrophy and weakness were present, more prominent proximally. Sensory examination was normal.

Laboratory evaluation showed blood counts, serum chemistries, thyroid function test, and serum CK to be within normal limits. An ECG showed nonspecific T-wave abnormalities. Electromyography showed long, polyphasic motor units with no increased insertion or spontaneous activity.

A biopsy of the left vastus lateralis muscle showed foci of fibres with increased numbers of internal nuclei with minimal atrophy. Tri-chrome staining showed focal groups of fibres with blurring of the myofibrillar network and aggregations of dense staining material (fig 2). These aggregates were seen by electron microscopy to represent Z-band streaming. NADH staining also showed loss of the myofibrillar network in many fibres, resulting in a targetoid appearance similar to that seen in patient 1. There was no evidence of inflammation, and phosphorylase and myoadenylate deaminase staining showed normal activity.

Discussion

Ipecac is isolated from the root of Cephaelis ipecacuanha. It contains two major alkaloids, emetine and cephaeline. Cephaeline is primarily responsible for producing nausea and emesis, whereas emetine is more toxic to skeletal muscle and the heart. Ipecac has long been used by natives of Brazil to treat diarrhoea and has had widespread use in the treatment of amebiasis. It has also been used in aversive therapy for alcoholism and has been employed experimentally as an antineoplastic agent. In the USA, the only official use of ipecac is as an emetic to treat accidental poisoning. It is available without prescription only in syrup form. Through experiences with its use as a treatment for amebiasis, ipecac has been shown to cause a myopathy.

In one study, nearly 5% of high school age females admitted to bulimic activity. They may resort to ipecac abuse if they cannot effectively induce mechanical emesis. It is estimated that there are one million bulimic women in America and that 35 000 abuse ipecac.

Ipecac myopathy should be considered in all young women with progressive proximal muscle weakness, atrophy, or stiffness, especially when there is any suggestion of an eating disorder. Both of our patients had dry skin,

normal fibre distribution. Phosphorylase, myoadenylate deaminase, congo red, and lipid stains were normal. Electron microscopy showed extensive disorganisation of myofibrils with extreme smudging of Z-band material (fig 1). The patient stopped using ipecac and after three months her strength returned to near normal and she had no further complaints of palpitations or ankle oedema. A repeat echocardiogram performed 15 months after the first study demonstrated normal left ventricular function (see table).
and several other cases have been reported in which patients were noted to have dry or
erythematous skin. The serum CK level may be elevated, but it can also be within normal
limits in the presence of significant weakness. The electromyogram shows nonspecific myo-
pathic changes, but a muscle biopsy will help distinguish ipecac myopathy from inflamma-
tory or alcohol-induced myopathy. Nerve conduction velocity is normal.

If ipecac abuse is suspected, an evaluation for cardiomyopathy is warranted. Historical or
physical evidence of cardiac failure may be present. The electrocardiogram may show rest-
ting tachycardia, prolongation of the QT and PR intervals, inverted T-waves, and ST seg-
ment abnormalities. As in the case of patient 1, significant depression of left ventricular
function may be detected by echocardiogram or radionuclide tests. The serial echocardiog-
grams performed on our patient demonstrated that ipecac cardiomyopathy is largely reversi-
ble.

The lethal dose of emetine has been esti-
mated to be 10 to 25 mgs, or approximately
1.25 grams for an adult. Death is usually
caused by ventricular arrhythmias or heart
failure. Emetine is so slowly excreted from
the body that doses may accumulate over time to approxi-
mate the lethal dose, even when emesis
is stimulated. Syrup of ipecac is available in
30 ml doses, each dose containing approxi-
mately 21 mgs of emetine. It is therefore
possible to accumulate a lethal amount of
emetine within the body over several months
when ipecac is used daily. It has been proposed
that emetine inhibits protein synthesis and
mitochondrial oxidative phosphorylation in
skeletal muscle. These effects may cause
decreased ATP formation and a subsequent
increased release of calcium into the sarco-
plasm that, in turn, activates proteases which
cause Z-band lysis, granule formation, and
myofilament disorganisation. In the heart,
emetine is thought to depress glycolysis and
Kreb's cycle, as well as inhibit synthesis of
contractile proteins.

The microscopic pathological changes seen
in the muscle biopsies from our patients are
very similar to those reported in previous cases
of ipecac myopathy and experimental
emetine-induced myopathy in rats. Light
microscopy reveals variation in fibre size,
internal nuclei, granular breakdown of myofi-
laments, and central core changes or targetoid
changes in fibres with ATPase or NADH
stains. Electron microscopy shows Z-band
streaming and dense bodies. Inflammatory
infiltrates are not seen. These findings are
characteristic of ipecac myopathy, but are also
seen in a variety of other conditions. Although patient 2 was a heavy consumer of
alcohol, her muscle biopsy was quite similar
to that of patient 1 and demonstrated the charac-
teristic targetoid changes and Z-band stream-
ing of emetine myopathy. The characteristic
type II fibre atrophy of chronic alcoholic
myopathy was absent and therefore her
myopathy was likely predominately due to
emetine toxicity. The effects on cardiac muscle
are not as well documented, but interstitial
oedema, inflammation, and degenerative
change of myocardial fibres have been report-
ed.

Therapy consists of discontinuing ipecac use
and employing supportive measures. If cardio-
myopathy is significant, inotropic and afterload
reducing agents may be used. As shown in
patient 1, both the cardiomyopathy and myo-
pathy improved after discontinuing ipecac
abuse. Electrical and pathological evidence of
muscle recovery has also been demonstrated.

1. Mateer JE, Farrell BJ, Chou SM, Gutmann L. Reversible
2. Dawson JA, Yager J. A case of syrup of ipecac resulting in
3. Adler AG, Walinsky P, Krall RA, Cho SK. Death resulting
1977;10:221-42.
1986;313:1253-5.
6. Pope HS, Hudson JL, Nixon RA, Herridge PL. The
epidemiology of ipecac abuse. (Letter) New Eng J Med
7. Bennett HS, Spiro AJ, Pollock MA, Zueker P. Ipecac-
induced myopathy simulating dermatomyositis. Neurology
reports with pathobiocemical analysis. Muscle Nerve
10. Anderson HH, Reed AC. Untoward effects of anti-ambic
11. Halbig L, Gutmann L, Goebel HH, Beck JF, Schochert S.
12. Goebel HH. Neuropathological aspects of congenital myo-
13. Hanif A, Slavin G, Mair W et al. Fibre type changes in
striated muscles of alcoholics. J Clin Pathol 1981;34:
991-7.