Rapidly Reversible Cardiomyopathy Associated with Chronic Ipecac Ingestion

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Summary: Ipecac, an over-the-counter emetic agent, has been a drug of choice for abuse by patients with eating disorders. Its alkaloid emetine has been associated with serious cardiac toxicity; however, the dose effect has not been well established. We present a patient with anorexia and bulimia nervosa who ingested ipecac chronically and developed the characteristic manifestations of ipecac toxicity. Unexpectedly, her induced left ventricular dysfunction returned to normal after only 10 days of withholding the drug. This finding, in contrast with the findings of other reports, establishes that ipecac cardiomyopathy can be readily reversible. The cumulative experience thus far, nonetheless, provides no discernible pattern of the effect of ipecac on the myocardium. Thus, in the continuum of poisoning, the point at which the myocardium becomes irreversibly damaged is undetermined. With continued abuse, potentially lethal outcome, and limited experience with ipecac cardiotoxicity, further investigation and perhaps heightened restriction of the drug are warranted.

Key words: ipecac, emetine, cardiomyopathy, cardiotoxicity

Introduction

Ipecac, a derivative from dried roots and rhizomes of *Cephaelis acuminata* Karsten, was originally used as a diarrheal remedy by the natives of Brazil.¹ Cardiotoxicity from its alkaloid emetine was first described with its early use in the

treatment of amebiasis.^{1–4} Today, even though its approved use is as an emetic especially in the treatment of acute drug overdose or accidental poisoning,^{5,6} the associated cardiotoxicity is mostly observed in patients with anorexia and bulimia nervosa who abuse the drug as a form of diet control. In large doses, serious cardiotoxicity and even fatality have been reported often due to myocarditis / cardiomyopathy resulting in congestive heart failure and arrhythmia.^{3,5–7} Although certain toxic manifestations such as electrocardiographic (ECG) changes or skeletal myopathy have been well documented,^{5,6} observations on the time course and dose effect regarding the potentially lethal effect of ipecac on the myocardium are few. We report an unexpected case of a rapidly reversible ipecac-induced cardiomyopathy that was demonstrated by serial echocardiography. Data from our observation are compared with findings of other reported cases.

Case Report

A 26-year-old woman presented to an outpatient clinic with progressive generalized weakness, dyspnea on exertion, and an unexplained fall. She was admitted to the hospital for ECG monitoring because of concern for arrhythmia when QT-interval prolongation was noted on the ECG. The history revealed a pattern of extensive daily exercise and induced emesis with ipecac after eating. Approximately two tablespoonfuls (30 cc contains approximately 21 mg) of ipecac syrup were ingested two to three times every week for 5 months. She took no other medications and had no history of substance abuse. On physical examination, she weighed 45 kg and was 170 cm in height. Vital signs showed a blood pressure of 94/60 mmHg and a heart rate of 60 beats/min without orthostatic changes. Ecchymosis was noted below the right eye which was attributed to the fall. However, no loss of consciousness was reported. Mild basilar rales as well as occasional extrasystolic beats were present. Otherwise, her cardiovascular examination was unremarkable. Neurologic examination showed symmetrical motor weakness more pronounced in proximal muscles of all extremities. She exhibited mild difficulty in rising from a chair requiring arm support; however, elevation of each limb without active resistance was without difficulty. No muscle tenderness or wasting was

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FIG. 1 Presenting electrocardiogram showing some characteristic changes related to ipecac myocarditis: diffuse T-wave inversion and QT-interval prolongation.

found. Deep tendon reflexes, muscle tone and sensory examination were all normal. Her electrolytes, liver, renal, and thyroid function tests, serum creatine kinase, serum protein, and albumin were all normal. A serum emetine level was not obtained. The chest roentgenogram showed mild cephalization of the pulmonary vasculature. The ECG showed diffuse T-wave inversion and a corrected QT interval of 480 ms (Fig. 1). A transthoracic echocardiogram (Sonos 1000, 2.5/2.0 MHz probe, Hewlett Packard, Andover, Mass.) showed mild global left ventricular systolic dysfunction with an ejection fraction (EF) of 45% and a fractional shortening (FS) of 0.23. With supportive care and close observation, her basilar rales resolved and motor strength gradually improved. No arrhythmia was noted. Ten days later, her ECG abnormalities persisted, but a repeat echocardiogram showed normalized left ventricular function (EF 65%, FS 0.32) (Fig. 2).

Discussion

This case illustrates a patient with eating disorder suffering from the classic sequelae of chronic ipecac abuse: skeletal myopathy, ECG abnormalities, and cardiomyopathy. A comparative review with other reported cases is summarized in Table I. In the adult literature, there is only one other reported case showing serial echocardiographic improvement of left ventricular dysfunction associated with ipecac administration. In that report,⁵ ipecac cardiomyopathy was described in an anorexic patient who ingested a similar amount of ipecac as our patient; however, repeat echocardiogram was not performed until 15 months after discontinuation of ipecac. Con-

trary to our findings, mild systolic dysfunction persisted even after 15 months of withholding ipecac. In the pediatric population, reversible ipecac cardiomyopathy was demonstrated in two patients aged 2.5 and 5 years;^{8,9} however, the repeat echocardiograms were not performed until 4 and 8 months, respectively, after withholding the emetic. Unfortunately in these pediatric cases, the doses of ipecac ingested was undeterminable due to denial by the caregivers who allegedly administered the drug. A consistent pattern of ipecac cardiomyopathy has yet to emerge.

The temporal relationship of cardiomyopathy with other manifestations of ipecac poisoning also appears to have no consistent pattern. In a 21-year-old patient with an eating disorder⁶ who ingested a slightly larger amount of ipecac over a comparable period of time as our patient, no clinical heart failure was found; however, prominent skeletal myopathy was present. In our patient, skeletal myopathy was present along with findings of congestive heart failure. In a 5-year-old boy with ipecac poisoning,⁹ who manifested no left ventricular dysfunction by echocardiography, characteristic ECG changes were noted. Our patient demonstrated all of these findings; however, at hospital discharge the cardiomyopathy resolved, the skeletal myopathy improved, but the ECG alteration was unchanged and persisted. Nonetheless, in cases reported to date, all of the effects of ipecac poisoning appeared eventually to resolve completely if the drug was stopped before significant cardiac toxicity occurred.^{1,7,10} There is no known indicator as to when such devastating cardiac toxicity would occur.

The acute lethal dose has been determined to be as low as 600–1250 mg for adults.^{6,10} The total ingested dose estimated for our patient was 840–1380 mg over 5 months; even at high-

FIG. 2 Comparable short-axis views of the echocardiographic studies at presentation and at 10 days after the discontinuation of ipecac. The measured left ventricular dimensions are as follows:

	EDD (cm)	ESD (cm)	FS	EF (%)
At presentation	4.7 (Frame A)	3.6 (Frame B)	0.23	45
At 10 days	4.7 (Frame C)	3.2 (Frame D)	0.32	65

LV = left ventricle, RV = right ventricle, EDD = end-diastolic dimension, ESD = end-systolic dimension, FS = fractional shortening, EF = ejection fraction.

er doses,^{5,6} fatality was avoided in these cases, probably due to prolonged administration. The chronic nature of most ipecac abuse, on the other hand, is likely to potentiate its toxicity. This

relates to ipecac's slow elimination and inability to stimulate emesis continuously, leading to further intestinal absorption.⁶ Thus, accumulation of emetine can readily occur. The serum

TABLE I Summary of representative case reports

Reports Author (Ref. No.)	Patients ages (years)	Estimated total amount ingested (mg)	Duration of ingestion	Repeat echo performed	Fractional shortening (%)
Ho <i>et al.</i>	26	840–1380 mg	5 Months	at 10 days	23–32
Dresser <i>et al.</i> (5)	26	1360–3020 mg	6 Months	at 15 months	17.6–26.1
Palmer and Gray (6)	21	2240–6720 mg	4 Months	—	—
Goebel <i>et al.</i> (8)	2.5	N/R	N/R	at 4 months	14–36
Schneider <i>et al.</i> (9)	5	N/R	N/R	at 8 months	31 to normal

Comparative review of cases of ipecac cardiomyopathy in which serial echocardiography was used to assess changes in the left ventricular function.

Abbreviations: echo = echocardiography, N/R = not reported.

emetine level has no prognostic value and therefore was not obtained in our study.

Electrocardiographic manifestations demonstrated by our patient included T-wave inversion and QT-interval prolongation. Other findings may include premature atrial complexes, supraventricular and ventricular tachycardias, ventricular fibrillation, and PR-interval prolongation.²⁻⁴ These ECG changes have been widely observed to be a reversible process, usually resolving in weeks to months.²⁻⁴

The psychosocial profile of patients abusing ipecac should always be considered. In patients with bulimia, increasing ipecac abuse has been reported from approximately 3.5% in 1986 to 7.8% in 1993.^{11, 12} The choice of ipecac seems to relate to its over-the-counter availability, low cost, ease of use, and its initial emetic efficacy. With ipecac's continued accessibility and serious toxicity, heightened awareness is required when evaluating patients with eating disorders who present with muscle weakness, heart failure, and/or ECG abnormalities.

Treatment is supportive. In severe cases intensive management of heart failure and the use of a pacemaker may be necessary.¹⁰ There is no antidote; the dialyzability of ipecac is not known.

Conclusions

This case suggests that left ventricular dysfunction due to ipecac overdose can be mild and readily reversible over a short time. With high prevalence of abuse, ipecac cardiomyopathy may be subclinical in most cases. The degree of toxicity leading to irreversible myocardial damage and death is not known and warrants further investigation. Serial echocardiography, correlating with administered doses, may be helpful in this regard. As suggested,¹³ with continued abuse ipecac's over-the-counter status is questioned.

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