Case Report

Unstable Angina: A Rare Presentation of Minoxidil Intoxication: A Case Report and Literature Review

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Abstract

Minoxidil is an antihypertensive direct vasodilator that can cause severe toxicity when sufficiently ingested. We report a case of accidental ingestion of 5 ml topical minoxidil solution 5% presented with chest pain and new-onset ST depressions. After giving IV saline and performing echocardiography/angiography, the patient fully recovered without any pharmacotherapy such as vasopressors and discharged 4 days after admission. The clinical toxicology, treatment, and previous case reports of minoxidil poisoning have been reviewed.

Keywords: *Chest pain, electrocardiogram, Minoxidil, poisoning, vasodilator*

Introduction

Oral minoxidil is a direct smooth muscle vasodilator (via potassium channel) and has been used clinically as an antihypertensive. A topical solution with 2% or 5%, minoxidil is used to treat androgenic alopecia. The main clinical effects often seen in overdose are hypotension with reflex tachycardia, electrocardiogram (ECG) changes, and depressed mental status.[1-3]

At supra-pharmacological doses, it elicits foci of necrosis/fibrosis in the left ventricle of the heart in dog and rats. Minoxidil also produces coronary arterial lesions, hemorrhages, and foci of granulation tissue in the right atrium of the dog. The pathogenesis of these changes is unclear but is generally considered to be also related to hemodynamic changes. A similar lesion was observed in the left atrium of pigs treated with minoxidil. Minoxidil also produces cardiac lesions in rats but only at much higher doses than those in dogs. Few reports on minoxidil intoxication in humans, including minoxidil and its metabolite poisoning, exist.[3-8]

Case Report

The 61-year-old patient referred to the medical toxicology department of Noor Hospital in Isfahan on December 23, 2017. The patient accidentally ingested about 5 ml of local 5% solution of minoxidil 5 h before admission. He presented to the emergency department with severe chest pain. He had a medical history of uncontrolled hypertension managed with 25 mg losartan daily, and medical history was negative for other drugs and diseases. Initial vital signs included a blood pressure of 80/55 mmHg and a pulse of 85/min. The patient was alert and to some extent, agitated. Head, neck, chest, abdomen, and extremities were normal without any pathologic finding. The patient was given a dose of 50 g activated charcoal with 30 ml magnesium hydroxide. The systolic blood pressure improved to about 110 mmHg, in response to parenteral fluid infusion with dextrose-saline solution.

A 12-lead ECG was recorded and showed new-onset ST depressions was seen in II, III, aVF, V5, V6, and ST elevation in aVR, V1, and V2 [Figure 1].

The patient was given isotonic IV fluid. Troponin-I on presentation was 0.15 ng/mL and 6 h later was 0.17 ng/mL (normal, 0.03 ng/mL). Since the echocardiogram showed preserved ventricular function with an ejection fraction of 60% structural heart disease was ruled out. He was placed under coronary angiography. The angiography report was as follow: left anterior descending: NO significant lesion-left circumflex: patent-right coronary artery: patent-minimal vessel disease-recommend: Medical follow-up. The patient fully recovered with stable blood pressure, normal (ECG), and mild residual tachycardia [Figure 2]. The patient discharged 4 days after admission.

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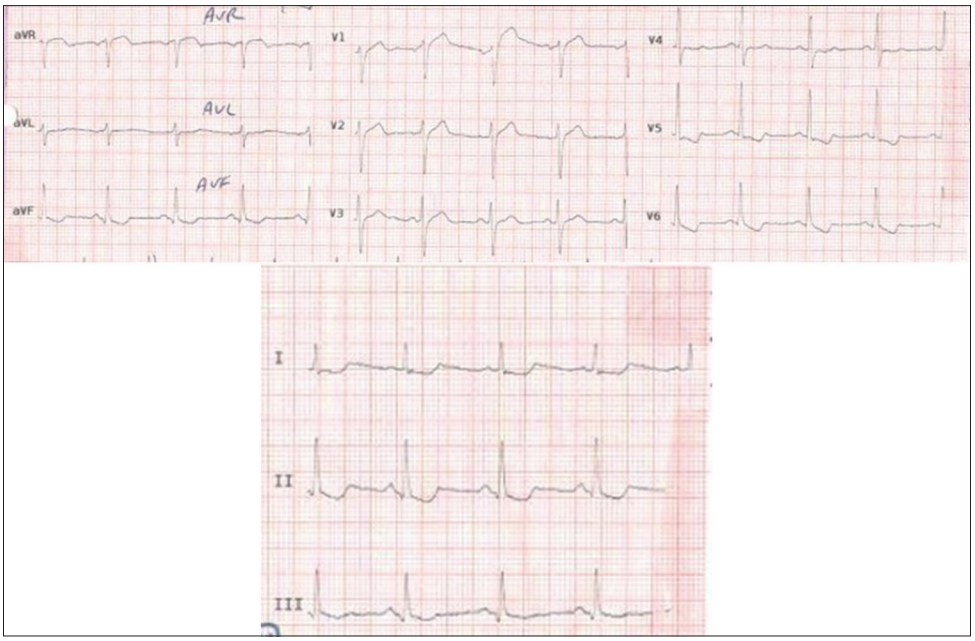

Figure 1: Electrocardiogram at the time of admission

Discussion

Only a few cases of minoxidil intoxication in humans have been described in the literature. This is the first case of topical minoxidil solution ingestion-induced EKG changes were resolving spontaneously without intervention in our center. Minoxidil is well absorbed from the gastrointestinal tract, and peak serum concentrations are seen within 1 h of administration. Minoxidil must be metabolized by hepatic sulfotransferase to the active molecule, minoxidil NO sulfate. Minoxidil sulfate activates the ATP-modulated K^+ channel. By opening K^+ channels in smooth muscle and thereby permitting K^+ efflux, it causes hyperpolarization and relaxation of smooth muscle.[9] Like hydralazine, minoxidil dilates arterioles but not veins.[5]

Maximal hypotensive effects may be delayed due to the delayed in the formation of the active metabolite. Minoxidil has a plasma $t_{1/2}$ of 3–4 h, but its duration of action is 24 h or occasionally even longer. It has been proposed that the persistence of minoxidil in vascular smooth muscle is responsible for this discrepancy.[9] The cardiac consequences of the baroreceptor-mediated activation of the sympathetic nervous system during minoxidil therapy are an increase in heart rate, myocardial contractility, and myocardial O_2 consumption. Thus, myocardial ischemia can be induced by minoxidil in patients with coronary artery disease.[9]

In our case, the patient ingested 5 mL of the 5% solution, equaling 250 mg minoxidil, which is approximately 6–25 times greater than the recommended therapeutic oral dose for controlling hypertension (10–40 mg daily dose for adults). The initial daily dose of minoxidil may be as little as 1.25 mg, which can be increased gradually to 40 mg in one or two daily doses.[4]

Poff and Rose reported a 20-year-old female that ingested an unknown quantity of minoxidil tablets and presented with tachycardia, diffuse T-wave inversion and S-T segment depression on the ECG and labile hypotension. The ECG symptoms of this patient were similar to our case.[10] In our patient, ECG changes were seen in the form of ST Depression, and T-wave inversion in inferolateral leads and ST elevation in anterior leads. Flattened and inverted T waves frequently are observed in the ECG following the initiation of minoxidil treatment. These are not ischemic in origin and are seen with other drugs that activate K^+ channels.[9]

Unlike our patient, most patients need a bolus of normal saline fluid, and some with hemodynamic problems need vasoactive drugs such as dopamine and/or phenylephrine.[11] Garrard *et al*. reported a 48-year-old male who ingested an eight-ounce bottle of Rogaine presented with a blood pressure of 57/45 mmHg and a pulse of 84 beats/min. The patient because of his refractory hypotension received IV fluids and multiple vasopressors to maintain an adequate mean arterial pressure. Our patient's pulse rate was normal as this report, but our patient's blood pressure unlike this and McCormick *et al*. report responded to supportive treatment.[12,13]

Isles *et al*. reported a 2-year-old boy allegedly ingested 100 mg minoxidil tablets 1 h before presentation at an emergency department. Emesis and lavage were the only treatments provided. He was observed until 13 h after

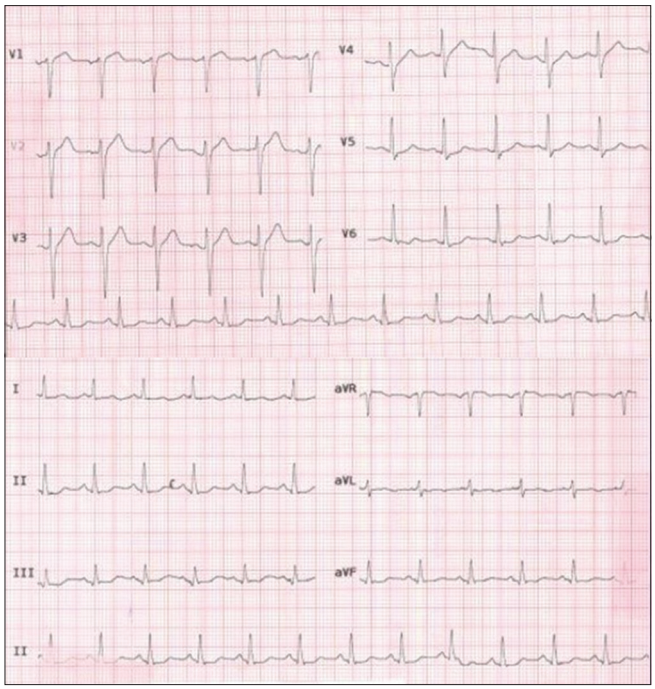

Figure 2: ECG at the time of discharge

the ingestion; the only symptom he developed was a tachycardia of 160 beats/min.[14]

The plasma half-life of minoxidil is about 4.2 h although the hemodynamic effect may persist for up to 75 h, presumably due to accumulation at its site of action.[15] Considering that minoxidil has a large volume of distribution (mean of 197 L in healthy controls), persistent effects at the site of action, such as in the smooth muscles, may lead to the effects.[4] In our case, symptoms prolonged for 4 days. In other studies, the symptoms of patients lasted several days.[12,13,16,17] As seen in our case, minoxidil may aggravate or uncover angina pectoris.[15]

The measurement of serum levels of minoxidil would strengthen our report, but minoxidil is not detectable in the routinely performed toxic screen analysis in our country.

Our case showed that ingestion of large amounts of a topical minoxidil solution can lead to prolonged cardiovascular symptoms and supportive treatment may be sufficient for treatment in some cases.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Authors' Contribution

Farzad Gheshlaghi, Shafeajafar Zoofaghari, and Gholamali Dorooshi contributed for the idea and design of the study. Shafeajafar Zoofaghari, and Gholamali Dorooshi gathered the data. Farzad Gheshlaghi, Shafeajafar Zoofaghari, and Gholamali Dorooshi made data interpretation. Gholamali Dorooshi drafted the manuscript and all authors critically revised it for important intellectual content and approved the final version.

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Conflicts of interest

There are no conflicts of interest.

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