



Case Study

Inadvertent Massive overdose of Isoproterenol During Electrophysiology Study Treated Successfully with Intravenous Metoprolol: Two Case Reports

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Abstract

Isoproterenol is a beta-adrenergic agonist used during electrophysiological studies (EPS) to enhance their sensitivity. Even though it is uncommon, medication overdose errors can occur due to different causes and may lead to life-threatening situations. In this article, we report two cases of inadvertent massive overdoses of isoproterenol during EPS. Both incidents resulted in characteristic symptoms like anxiety and palpitations, however, were successfully reversed with metoprolol administration. The aim is to emphasize the need for robust safety measures and clear communication within the healthcare team. Although both patients tolerated the overdose well, the outcome for severe complications, particularly in patients with underlying heart conditions, might not be favourable.

Keywords: Isoproterenol, Electrophysiologic Study, Beta-adrenergic receptor, overdose.

Abbreviations: Dextrose 5% (D5W), Intravenous (IV), Atrioventricular Re-entrant Tachycardia (AVNRT), Supraventricular Tachycardia (SVT), Electrophysiology (EP), Electrophysiologic Study (EPS).

Introduction

Isoproterenol is a beta-adrenergic receptor agonist that is routinely used in Electrophysiology during electrophysiologic studies for aiding in the induction of arrhythmia and for provocation of vasovagal syncope during tilt table testing which leads to an increase of these tests' sensitivity. Isoproterenol is available commercially as a solution in vials that contain 0.2 mg. usually, one vial is mixed in dextrose 5% (D5W) of a 50-cc bag. The solution

is administered intravenously by controlled continuous infusion using an infusion pump with a rate starting at 0.5-1 microgram (mcg)/min. Since its use is very common, cases of isoproterenol toxidromes are likely to occur. Based on a medical database search, there are no reported cases of isoproterenol overdose. We report two cases of inadvertent massive isoproterenol overdose in the electrophysiology laboratory, occurring in 75 and 78-year-old females that happened 25 years apart. Both patients were treated successfully with intravenous metoprolol.

Cases presentation

Case 1

The patient is a 75-year-old female with a history of angina and documented supraventricular tachycardia (SVT) on a 12-lead EKG. She was admitted for elective cardiac catheterization and coronary intervention. A coronary angiogram revealed one vessel

coronary artery disease with 90% stenosis in the mid-left anterior descending artery for which she had a stent. One day later, the patient was referred for catheter ablation of SVT. She underwent an electrophysiology procedure with the insertion of four catheters in the right femoral vein and positioned in the high right atrium, His region, right ventricular apex, and coronary sinus. Using the usual stimulation protocol in both the right atrium and right ventricle revealed the presence of dual atrioventricular nodal pathways but failed to induce SVT. On that day, the EP nurse was off duty, so a nurse from the catheterization laboratory was pulled to the EP laboratory to cover for the case. After finishing the baseline study, the covering nurse was ordered to start an infusion of isoproterenol at 1 mcg/min. While waiting for isoproterenol a few minutes later, the patient's sinus rhythm accelerated abruptly and rapidly to reach a heart rate of 170-180, from a baseline in the 70s. When she was asked about the isoproterenol dose that she was giving, the nurse replied that she gave a 1 mg IV push. The patient was noted to become very anxious and apprehensive. She complained of dyspnea, chest tightness, palpitations, tremors, and impending doom. Immediately, the patient was given repeated doses of intravenous metoprolol of 5 mg IV push-up to a total dose of 15 mg. Her symptoms improved quickly and over a few minutes resolved nearly completely. Her heart rate dropped progressively as metoprolol was being given and returned to baseline. No significant change in her blood pressure was observed. A review of the care surrounding this event revealed that the nurse was not familiar with isoproterenol at all. She reported that she used 5 vials each of which contained 0.2 mg in 1 mL of a syringe and delivered a total dose of 1 mg by IV push. After the patient returned to her normal state, the EP study was resumed, and electrical stimulation induced SVT which turned out to be atrioventricular nodal reentrant tachycardia (AVNRT). Using radio frequency energy, the slow pathway was ablated and eliminated successfully. The patient was discharged home the next day. On her three-month follow-up, the patient remains asymptomatic and free of palpitations or chest Pain.

Case 2

A 78-year-old female with recurrent palpitations was referred for EP evaluation. The patient underwent an EP study to assess the mechanism of her episodic palpitations and for possible ablation. Following the insertion of the usual four catheters in the right heart via the right femoral vein, programmed stimulation was performed in the right atrium and right ventricle. Stimulation at baseline failed to demonstrate evidence of dual AV nodal pathways or bypass tract. There was no inducible atrial or ventricular arrhythmia. Therefore, administration of isoproterenol was ordered and was communicated to the EP nurse to start infusion at 1 mcg/min. Isoproterenol solution was prepared by mixing the content of a 0.2 mg vial into a 50 ml bag of dextrose 5% solution. A few

minutes later while analyzing the baseline study and waiting to see the effects of isoproterenol, the heart rate on the monitor was noticed suddenly to be high and the rhythm was sinus tachycardia at a rate of 150-160 bpm. The patient started to complain of nervousness, tremors, palpitation, shortness of breath, and anxiety. There was no significant change in her blood pressure which remained around 110/60 mmHg. The nurse was questioned about the rate of infusion of isoproterenol that she set on the IV pump. When checking on the medications, she suddenly realized that the whole 50 CC bag was already infused. It was clear that the patient was experiencing symptoms and signs of isoproterenol overdose. Therefore, metoprolol 2.5 mg was immediately administered by intravenous push, followed by another similar dose 30 seconds later. The patient's heart rate slowly settled down and returned to baseline, and her symptoms resolved as well. EP study was resumed and demonstrated no inducible arrhythmias.

A review of her care surrounding this event revealed the mechanism of the mistake of the inadvertent rapid administration of the whole isoproterenol bag. There were 2 intravenous tubes connected to the same femoral venous sheath, a main line of 0.9% NS and the isoproterenol line. Instead of inserting the isoproterenol tube through the IV pump, the NS tube was inadvertently inserted, and the pump was programmed at 1 mcg/min. Hence, isoproterenol was opened free, and the entire bag of 0.2 mg was delivered to the patient in approximately 30 seconds. The patient was stable after the EP study, and she was discharged home 3 hours later on metoprolol succinate 25 mg once daily.

Discussion and Conclusion

Isoproterenol is a synthetic sympathomimetic with nonselective β -adrenergic effects. It has Beta-1 and Beta-2 adrenergic agonist activities but no alpha-adrenergic activity. Isoproterenol was approved by the U.S. Food and Drug Administration (FDA) in 1947 and was used initially to treat asthma because of its Beta-2 bronchodilation effect. Isoproterenol is immediately active upon infusion, but it has a short half-life of 2.5 to 5 minutes, hence it is administered by continuous infusion. Conjugation in hepatic and pulmonary tissues is the major method of metabolism. Excretion occurs via urine in the form of sulphate conjugates [1]. Isoproterenol produces positive chronotropic and inotropic cardiac effects via β_1 adrenoceptor stimulation, and bronchodilation and vasodilation in vascular smooth muscle through β_2 activation.

Isoproterenol is widely used in the EP laboratory to aid in the induction of arrhythmia during electrophysiologic study (EPS). It is also used in the setting of a tilt table test to augment the sensitivity of the test [2]. In these patients, isoproterenol is used to enhance the level of sympathetic activity [3]. Isoproterenol can be used also for severe bradycardia such as in third-degree heart

block, hence it used to be called a chemical “pacer”.

Our 2 cases represent, to our knowledge, the first reported occurrences of isoproterenol overdose in the literature. In this report, we described 2 cases of patients who developed an iatrogenic overdose of isoproterenol with reversal of its manifestations with rapid administration of intravenous beta blocker. The first patient received a massive dose of 1 mg (1000 mcg) of isoproterenol, which is an amount when delivered at a rate of 1 mic/min, is sufficient for continuous infusion that lasts for 16.6 hours. This massive amount was delivered by IV push in a few seconds. Our second patient received 0.2 mg, a fifth of the first patient’s dose, which was also infused in 10-20 seconds. This amount of isoproterenol is sufficient for 3.3 hours when infusion is set at a rate of 1 mic/min.

The situation for the overdose is different in the 2 events. While the cause in the first case is related to the lack of familiarity with the drug by the covering nurse, the cause in the second case was related to the inadvertent switching between the intravenous tubes by a specialized EP nurse, who is very familiar with the administration of the drug.

Several studies indicated that intravenous medications are associated with the highest frequency of errors and serious consequences [4, 5]. A systematic review by Sini Kuitunen et al [6], revealed that insufficient actions to secure the safe use of high-alert medications and lack of knowledge of the drug, as per case 1, are the most common causes affecting the most process stages, followed by calculation tasks and confusion between similar drugs. The study also demonstrated other causes like failure of systemic defenses including double check during the preparation and administration process, as per case 2 [6,7].

Our case aims to emphasize the beneficence of safety actions to secure the safe use of high-alert medications and the importance of good communication between the entire team, as well as the responsibility of every individual to be familiar with all the principles of the procedure. There are so many quality improvement studies that demonstrated the beneficence of several strategies in reducing the incidence of some medical errors including closed-loop communication and look-alike drugs stocked in different locations.

The report adds to our knowledge in several ways specifically for healthcare workers in the EP laboratories who use isoproterenol regularly. This report should prompt one to consider iatrogenic isoproterenol toxicity when excessive sinus tachycardia is observed in the EP lab which can mistakenly be diagnosed as atrial tachycardia originating from the high right atrium.

We learned surprisingly that massive isoproterenol doses don’t seem to be life-threatening. However, the outcome of such magnitude toxicity when a comorbidity exists might not be favorable such as in the case of critical coronary artery stenosis.

In patients with coronary artery disease, the combination of increased heart rate, increased myocardial contractility, and decreased diastolic blood pressure by isoproterenol may decrease the already compromised coronary blood flow and can lead to acute coronary syndrome. It is acknowledged in the literature that there is no known reversal agent for humans. However, in our experience, intravenous beta blockers can rapidly correct the symptoms of isoproterenol massive overdose.

Conflict of Interests

The authors declare there no conflict of interest regarding this case report.

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work the authors did not use any generative AI or AI-assisted technologies in the writing process.

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