Cardiovascular toxicity due to metoprolol poisoning in a patient with coronary artery disease

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What is already known about this subject

- Poisoning with β -blockers can result in cardiovascular and central nervous system effects.
- Although much has been reported about metoprolol poisoning's cardiovascular complications, little attention has been paid to acute myocardial infarction (AMI) accompanied by elevated cardiac markers.

What this study adds

- This case report demonstrates for the first time an association of metoprolol poisoning with acute myocardial infarction in a patient with a previous history of coronary artery disease.
- Metoprolol poisoning can induce acute myocardial reinfarction in patients with prior AMI or known coronary artery disease.
- In other words, metoprolol overdose can trigger myocardial ischaemia and dysrhythmia in patients with coronary artery disease.

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Aim

To demonstrate that β -blocker poisoning results in cardiovascular and central nervous system findings.

Methods

A 56-year-old woman was brought to the emergency department, having been admitted to hospital with 1500 mg of metoprolol ingestion 2 h previously. She had undergone percutaneous transluminal coronary angioplasty and stenting because of acute myocardial infarction (AMI). Her ECG revealed ST segment elevation in inferior leads and junctional dysrhythmia. Her clinical symptoms relieved after pacing and hospitalization and she was discharged.

Results

Our patient demonstrated findings of AMI with hypotension and bradycardia that appeared to result from metoprolol poisoning. Although one patient has been reported to have AMI associated with metoprolol poisoning, our patient is unique with her ECG changes and elevated cardiac markers: this is the first time that AMI characterized by elevated cardiac markers associated with metoprolol toxicity has been reported.

Conclusions

Emergency physicians should bear in mind that AMI can accompany the presentation of metoprolol overdose in those with coronary artery disease. In other words, metoprolol poisoning can trigger myocardial ischaemia and dysrhythmia in those with coronary artery disease.

Introduction

β -Blocker agents are commonly used in the management of hypertension, tachydysrhythmias, acute coronary syndromes, diastolic dysfunction, hyperthyroidism, glaucoma, anxiety and other disorders. In 2004, the American Association of Poison Control Centers reported 2.4 million cases of toxic exposure and 1184 fatalities; 5.6% of all cases of adult poisoning were by cardiovascular medication [1]. Poisoning with β -blocker agents classically results in cardiovascular and central nervous system findings [2]. This case report represents an unprecedented association of β -blocker poisoning with acute myocardial infarction (AMI) in a patient with a previous history of coronary artery disease.

Case report

A 56-year-old woman was brought to the Emergency Department (ED) by her family. She had told relatives that she had ingested 15 tablets of 100-mg metoprolol pills 2 h before admission. She had already been on metoprolol and a combination of ramipril–hydrochlorothiazide for hypertension and tiotropium bromide for bronchial asthma. She had also undergone percutaneous transluminal coronary angioplasty (PTCA) and stenting of the right coronary artery because of AMI 2 years previously, but had had no recent stable or unstable angina. She had no endocrine disease, including diabetes mellitus, or any history of depression or other psychiatric illness.

This had been her first attempt at suicide involving any overdose of medication and she denied having ingested the pills to relieve symptoms, e.g. pain, anxiety, etc.

Her blood pressure was 66/44 mmHg, heart rate was 46 bpm, respiratory rate was 20 bpm and temperature was 36 °C on admission. Bradycardia, disorientation, uncooperativeness and confusion were noted on the initial physical examination. Bronchospasm, respiratory depression and hypoglycaemia were not found. She had no agitation.

Because of her confusion, we did not rely on her history of chest pain on presentation in the ED, but she also reported chest pain in the coronary intensive care unit after resolution of confusion. She described a 'squeezing-like' chest pain on the first day, which she had not declared in the ED. Glasgow coma scale score was noted as E3M6V4 on admission. Her ECG was taken in the ED and revealed ST segment elevation of 4 mm in DII, DIII, aVF and junctional dysrhythmia (Figure 1). In the right precordial leads (V4R), there was ST segment elevation of 2 mm associated with right

ventricular infarction. Atropine was given to the patient according to advanced cardiovascular life support guidelines in ED, as she had unstable bradycardia. Transcutaneous pacing was performed because of bradycardia and hypotension refractory to treatment with 1500 ml fluid replacement and 1 mg intravenous (i.v.) atropine. Gastric lavage and activated charcoal were not administered because >1 h had passed after metoprolol ingestion and haemodynamic instability. Glucagon was not available. She was admitted to the coronary intensive care unit with a diagnosis of inferior AMI and junctional dysrhythmia associated with possible β -blocker poisoning. She was paced in the right ventricle, accessed through an introducer in femoral vessels. Sinus rhythm was instituted with diminished ST segment elevation in the ECG. Hypotension and bradycardia also improved after transvenous pacing along with i.v. infusions of dopamine ($8 \mu\text{g kg}^{-1} \text{min}^{-1}$) and dobutamine ($8 \mu\text{g kg}^{-1} \text{min}^{-1}$) for nearly 6 h. However, persistent hypertension (190/140 mmHg) ensued just after institution of this treatment and the inotropic agents were stopped. Intravenous glycerol trinitrate ($10 \mu\text{g min}^{-1}$) was then given. Additionally, the elevated ST segment was normalized to baseline and eventually the whole ECG was normal immediately after transcutaneous pacing, except for a persistent negative T wave in DIII. PTCA was not administered because of resolution of the ST elevation. The transvenous pacing catheter was removed following an uneventful clinical course over the next day.

The patient's laboratory findings (complete blood count, electrolytes, renal and liver function tests and glucose levels) were normal except for the cardiac markers, which were substantially elevated (troponin-I 1.2 ng mL^{-1} (range 0–1), CK 411 U L^{-1} (range 26–167), CK-MB 21.9 ng mL^{-1} (range 0–3.9) and myoglobin 299 ng mL^{-1} (range 0–70). Serum metoprolol concentration or toxicology screen could not be taken to confirm metoprolol ingestion, because of unavailability.

On the following day, cardiac markers remained supranormal, except for myoglobin (troponin-I 11.1 ng mL^{-1} , CK 384 U L^{-1} , CK-MB 28 ng mL^{-1} , myoglobin 30 ng mL^{-1}). An echocardiogram following day disclosed minimal mitral insufficiency, inferior and posterior wall hypokinesia and a global ejection fraction of 45%. A coronary angiography was performed on day 4, revealing 90% occlusion in the right coronary artery, and lack of any degree of restenosis on the stent. It was also found to have 80% occlusion in left coronary artery and 40% occlusion in the circumferential artery. Her symptoms improved and she was discharged 7 days after admission.

Figure 1

The patient's ECG

Discussion

Most patients with β -blocker overdose commonly have underlying cardiovascular disease [2]. The most common manifestations of β -blocker poisoning are hypotension, sinus bradycardia, high-grade atrioventricular block, ventricular dysrhythmias, prolonged PR, QRS and QT intervals, cardiogenic shock and collapse, hypoglycaemia, hyperkalaemia, seizures, psychosis, coma, respiratory arrest and asystole [2–7]. Also, in a study by Love *et al.* most clinically significant β -blocker intoxication demonstrated negative dromotropic effects on ECG, and first-degree heart block was the most common ECG finding [8]. Shore *et al.* have emphasized that metoprolol overdose often produces sudden and rapid clinical deterioration [9]. Satar *et al.* have reported unusual ECG changes, including diffuse negative T waves in a patient with β -blocker overdose [10]. A case with AMI due to a metoprolol overdose has been reported [11]. Autopsy findings revealed acute thrombosis of the left anterior descending coronary artery, whereas we found ECG findings and elevated cardiac

markers in our patient. Although one patient has been reported to have AMI associated with metoprolol poisoning [11], our patient is unique with her ECG changes related to acute coronary syndrome and elevated cardiac markers.

Blockade of β -receptors results in decreased production of intracellular cyclic adenosine monophosphate (cAMP), with a resultant blunting of multiple metabolic and cardiovascular effects of circulating catecholamines [3]. The most important predictive factor in β -blocker toxicity is whether the β -blocker possesses membrane-stabilizing activity [4]. It is known that metoprolol has low membrane-stabilizing activity and membrane-stabilizing effects only at high doses [4]. β -Adrenergic antagonists may also cause toxic effects independent of their action on catecholamine receptors [12]. Seizures are also more commonly observed in toxicity related to drugs with membrane-stabilizing activity. However, our patient's disturbance of consciousness was not a direct sign indicating membrane-stabilizing activity of the medication, as this particularly originates from block

of sodium channels in cardiomyocyte membranes. β -Blockers such as propranolol, labetalol and pindolol can more commonly have membrane-stabilizing activity, a property which is usually not evident with therapeutic doses but which may contribute to toxicity significantly by prolonging QRS duration and impairing cardiac conduction. Cardiovascular effects arising due to membrane-stabilizing activity may include severe bradycardia, atrioventricular block, ventricular dysrhythmias and intraventricular conduction delays. In our case, this was interpreted as a probable bradycardiac effect of metoprolol toxins that may cause membrane-stabilizing effects. A membrane-depressant effect may not explain the cardiac-depressant effects such as acute coronary syndrome of metoprolol in our case, but the existence of junctional dysrhythmia may explain why arrhythmia is the reason for AMI.

We conclude that acute coronary syndrome in our case resulted from severe intoxication with metoprolol, manifesting as hypotension and bradycardia, rather than from other causes.

Conclusion

Emergency physicians should bear in mind that presentation of AMI can accompany metoprolol overdose in those with coronary artery disease. Metoprolol poisoning can induce acute myocardial reinfarction in patients with prior AMI or known coronary artery disease. Metoprolol overdose can trigger myocardial ischaemia and dysrhythmia in such patients. Patients presenting with β -blocker ingestion should be followed in a healthcare facility with an intensive care unit.

Competing interests: None declared.

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