



Case Report

Angiotensin converting enzyme inhibitor intoxication: Naloxone to the rescue? Naloxone for ACE inhibitor intoxication☆



Martine Robert^a, David De Bels^{b,*}, Martin Chaumont^c, Patrick M. Honoré^b, Philippe Gottignies^d

^a Intensive Care department, Centre Hospitalier Régional de Namur, Namur, Belgium

^b Intensive Care Department, Brugmann University Hospital, Brussels, Belgium

^c Department of Cardiology, Erasme Academic Hospital, Brussels, Belgium

^d Intensive Care Department, Hôpitaux IRIS-Sud, Brussels, Belgium

ARTICLE INFO

Article history:

Received 1 March 2019

Accepted 27 March 2019

Keywords:

ACE inhibitors

Toxicology

Naloxone

Baroreflex

ABSTRACT

We report here the case of a patient with perindopril intoxication inducing severe bradycardia together with a profound hypotension. Initiation of a naloxone infusion completely resolved those symptoms. As a consequence, we could recommend as a first step the use of naloxone in order to prevent the use of more invasive therapeutic tools.

© 2019 Elsevier Inc. All rights reserved.

1. Introduction

Cardiovascular drugs represent only 4% of all drug intoxications. Angiotensin-converting-enzyme inhibitor (ACEI) intoxication range from mild to severe clinical forms. Classical treatment of ACEI intoxications includes activated charcoal, fluid administration and vasoconstrictive drugs. Naloxone has been used with some effect in captopril poisoning but is not recommended for routine use yet [1].

2. Case report

A 46-year-old Caucasian male patient was admitted to our hospital for perindopril, indapamide, diazepam and ethanol intoxication in undefined quantities. The patient was conscious (Glasgow scale 15/15), and hemodynamically stable (heart rate (HR) 77 bpm, blood pressure 130/90 mmHg, pulse oximetry 94% on room air). There was no relevant finding in his medical history. His physical examination was normal. Laboratory findings were unremarkable except for blood ethanol levels (3 g/L, normal limits 0 g/L).

During his one hour stay in the emergency department, the patient developed a severe bradycardia (Fig 1, nadir HR 22 bpm) triggering immediate cardiopulmonary resuscitation with rapid rate response before administration of any drugs (atropine or epinephrine). The patient was

transferred to intensive care under mechanical ventilation and sedation in a stable hemodynamic condition. The patient relapsed severe bradycardia associated with hypotension two more times necessitating atropine and epinephrine administration this time. After a contact with the Poison Center, an intravenous bolus of naloxone (2 mg) was administered, which immediately reversed bradycardia and normalized blood pressure. In order to maintain hemodynamic parameters in a normal range a continuous intravenous infusion of naloxone (0.04 mg/kg/h) was introduced. The latter treatment was stopped after 10 h because of a medical shift change. A severe bradycardia (Fig 1, nadir HR 38/bpm) immediately followed the naloxone cessation and required immediate resumption of the treatment (0.04 mg/kg/h) for 24 h. This subsequently restored a normal HR (Fig 2). Thereafter, the patient did not relapse his bradycardia. He was extubated on day 3 and discharged from ICU on day 6. Follow-up at three months was uneventful.

3. Discussion

Perindopril, a widely used ACEI [2], is a prodrug with a half-life of 17 h which has an effect on blood pressure 2–5 h after ingestion. This time frame could explain normal blood pressure on patient's admission. Bradycardia is a very rare secondary effect of ACEI and has only been described in its first utilization [3]. Modification of baroreflexes, parasympathetic activation, or discontinuation of angiotensin II-mediated vagal inhibition have been proposed as potential mechanisms to explain the lack of compensatory tachycardia following ACEI induced blood pressure fall. In vitro, ACEI inhibit enkephalinase and thus increase endogenous opioids, themselves reducing baroreflex sensitivity [4]. A study has demonstrated a higher baseline HR in healthy volunteers

☆ No Funding was sought for this article. The case has not been presented outside the hospital.

* Corresponding author at: ICU, Brugmann University Hospital, 4 Place A Van Gehuchten, 1020 Brussels, Belgium.

E-mail address: david.debels@chu-brugmann.be (D. De Bels).

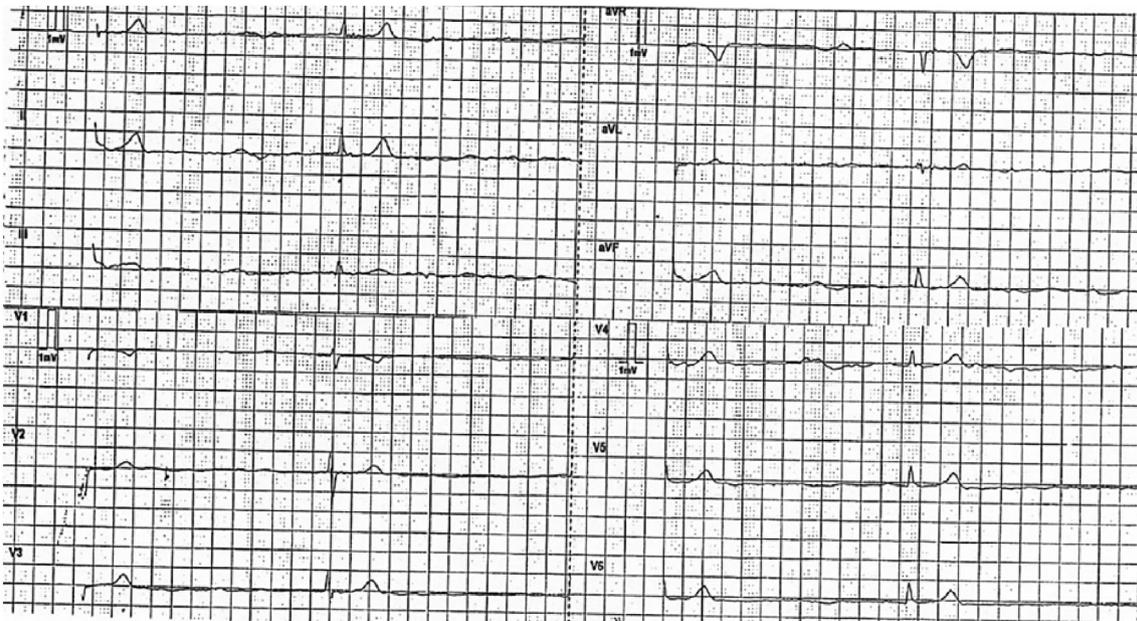


Fig. 1. ECG showing severe bradycardia.

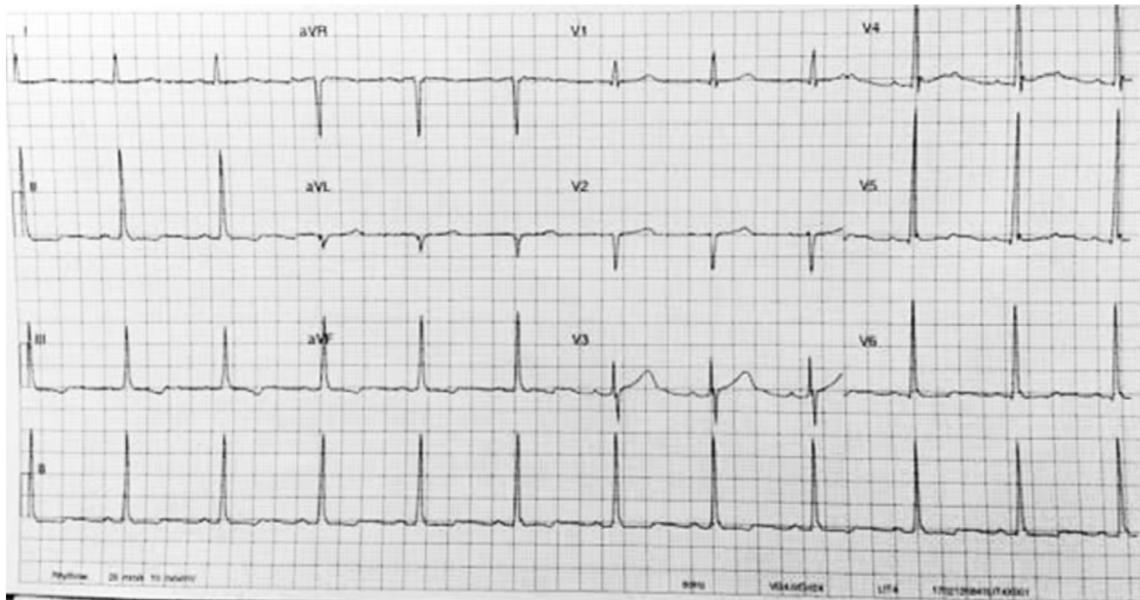


Fig. 2. ECG after naloxone administration.

treated with naloxone plus captopril in comparison to the group that received captopril alone [5]. This suggests that using opioid antagonists such as naloxone is an interesting therapeutic option in case of ACEI intoxication [6].

To the best of our knowledge, this is the first case reporting a successful treatment by naloxone of a bradycardia together with a severe hypotension induced by a perindopril intoxication. The use of naloxone as a first step approach in this type of intoxication might prevent (if the patient is a responder) the use of a more important therapeutic arsenal including external pace-maker, vasopressive support just to cite a few.

References

- [1] Lip GY, Ferner RE. Poisoning with anti-hypertensive drugs: angiotensin converting enzyme inhibitors. *J Hum Hypertens* 1995;9(9):711.
- [2] Kellow NH. The renin-angiotensin system and angiotensin converting enzyme (ACE) inhibitors. *Anaesthesia* 1994;49(7):613–22.
- [3] Semple PF, Thoren P, Lever AF. Vasovagal reactions to cardiovascular drugs: the first dose effect. *J Hypertens* 1988;6(8):601–6.
- [4] Rubin PC, Millar JA, Sturani S, Lawrie C, Reid JL. The influence of naloxone on the circulatory effects of captopril. *Br J Clin Pharmacol* 1984;17(6):713–7.
- [5] Ajayi AA, Campbell BC, Rubin PC, Reid JL. Effect of naloxone on the actions of captopril. *Clin Pharmacol Ther* 1985;38(5):560–5.
- [6] Varon J, Duncan SR. Naloxone reversal of hypotension due to captopril overdose. *Ann Emerg Med* 1991;20(10):1125–7.