A rarely described use of neostigmine in a case of acute anticholinergic poisoning

Une utilisation de la néostigmine peu décrite: l’intoxication volontaire à la tropatépine

Introduction
Anticholinergic poisoning can require administration of an antidote. The classical antidote used is the anticholinesterase, physostigmine [1]. Another anticholinesterase, neostigmine, has been less described for this indication [2]. Tropatepine (Lepticur®) is a synthetic molecule used in the treatment of Parkinson’s disease or to correct Parkinson syndromes induced by neuroleptic drugs [3]. This anticholinergic drug has side effects of xerostomia, difficulty focusing, ocular hypertension, micturition disorders, constipation, hallucination, confusion, mental disorders at recommended doses as well as in overdosage [4]. The latter, however, are rarely described, since this treatment is mainly used in Europe. The authors describe a case of acute anticholinergic poisoning with tropatépine, which responded well to antidote treatment using neostigmine.

Observation
A suicidal female patient of 17 years old usually treated with loxapine and tropatépine took 30 tablets of Lepticur® 10 mg (brand name of the molecule in France), i.e. 300 mg of tropatépine, as well as 8 g of paracetamol. Her parents drove her rapidly to the emergency department. Two hours post-ingestion, she was still asymptomatic and was given activated charcoal on the advice of the poison control centre. Four hours post-ingestion, she showed severe signs of atropinism: tachycardia, agitation, hyperthermia, mydriasis with confusion, and without seizures. One milligram clonazepam was injected intravenously as well as an antidote treatment of 0.5 mg neostigmine given by intravenous infusion, physostigmine being unavailable. This antidotal treatment was repeated 20 min later. During this 20 minutes second infusion, a marked clinical improvement of all symptoms was noticed. A relapse into these neurological signs (especially agitation, confusion and mydriasis) was noted 21 h post-ingestion. Therefore, a third dose of 0.5 mg of neostigmine was prescribed. Following this 20 minutes infusion, a clinical improvement with a decrease in neurological signs allowed the patient to be discharged 4 days after taking the tablets. Serum paracetamol levels taken at h4 post-ingestion were 50 mg/L, therefore below toxicity levels. The rest of the paraclinical tests were completely normal (without CPK elevation). Tropatépine blood levels were not measured.

Discussion
The clinical picture of this patient was characteristic of anticholinergic poisoning: tachycardia, agitation, hyperthermia, mydriasis and confusion. Central nervous system symptoms were preponderant, in accordance with pharmacological data, which suggests a greater affinity of tropatépine for the central nervous system [4]. After insufficient neutralizing and symptomatic treatments, antidote treatment was started. Its efficiency was notable in few minutes, even though three doses were necessary, with a clinical relapse, due to a short elimination half-life. A total of 1.5 mg was used, which corresponds to the usual prescribed dose [2]. The antidote response fast delays in this anticholinergic syndrome with hyperthermia and hypertonia but without CPK elevation allows us to eliminate a neuroleptic malignant syndrome. This demonstrates well the rapid pharmacokinetics of the antidote, which may need to be given in repeated doses. Neostigmine is a parasympathomimetic cholinesterase inhibitor used as an antidote in severe cases of anticholinergic poisoning, but also in the management of drug-induced ileus in poisonings [5]. Its indications as treatment for poisoning with tetrodotoxins [6], with snake bites [7,8], and even with imipramine [9], are more contested. To our knowledge, it has never been described with tropatépine poisoning. Only a single case of fatal tropatépine poisoning has been published, which was for a 76-year-old female patient [10]. This adverse progression may be explained by age, comorbidity, the fact that the quantities ingested were unknown and by the lack of antidote administration. It should be noted that the tropatépine blood levels of this patient were shown to be over six times higher than the normal limit (139 μg/l) [10].

Conclusion
It is important to be familiar with treatment indications for neostigmine, which is an efficient antidote for cases of severe anticholinergic poisoning. This antidote may now be offered in cases of tropatépine poisoning.

Disclosure of interest: the authors declare that they have no competing interest.

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Letter to the editor
References


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