Thérapie 2012 Novembre-Décembre; 67 (6): 523–527
DOI: 10.2515/therapie/2012075

Acute Indoramin Poisoning: a Review of 55 Cases Reported to the Paris Poison Centre from 1986 t o 2010

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Text received June 15th, 2012; accepted September 25th, 2012

Keywords:
seizures; dysrhythmias; ECG changes; QT; drug induced long QT syndrome; torsades de pointes; overdose; acute poisoning; indoramin

Abstract – Authors report a retrospective study of all cases of indoramin-only poisoning notified to the Paris poison Centre from 1986 to 2010. Fifty five cases of indoramin self-poisoning were included: 40 adults and 15 children. The mean supposed ingested dose was about 701 mg±464 mg. ECG showed a prolonged QTc interval (equal to or greater than 0.50 s) in 30% of patients. The lowest observed dose for prolonged QTc was 625 mg. This series includes two cases of seizures occurring around two hours after ingestion of 900 and 2 250 mg of indoramin. A review of the literature showed cardiac disorders, with a delayed mechanism of action up until 18 hours after ingestion. Therefore, rapid medical resuscitation and prolonged cardiac monitoring for at least 24 hours after ingestion of 625 mg are recommended.

Mots clés :
convulsions ; troubles du rythme ; modifications ECG ; QT ; syndrome QT d'origine médicamenteuse ; torsades de pointes; surdosage ; intoxication aiguë ; indoramine

Résumé – Intoxication aiguë par l'indoramine : une revue des 55 cas signalés au Centre antipoison de Paris de 1986 à 2010. Les auteurs rapportent une étude rétrospective de tous les cas de mono-intoxication par l'indoramine notifiés au Centre anti-poison de Paris de 1986 à 2010. Cinquante-cinq cas d'intoxication volontaire par l'indoramine ont été inclus. La dose moyenne supposée ingérée était de 701 mg ± 464 mg. L'ECG a mis en évidence un allongement de l'intervalle QTc (supérieur ou égal à 0,50 s) chez 30 % des patients. La dose la plus faible à l'origine d'un allongement de l'intervalle QTc était de 625 mg. Cette série comporte deux cas de convulsions survenues environ deux heures après l'ingestion de 900 et 2 250 mg d'indoramine. La survenue de troubles du rythme cardiaque retardés jusqu'à 18 heures après l'ingestion de 750 mg d'indoramine a été constatée dans une revue de la littérature. Par conséquent, une réanimation médicale rapide et prolongée, une surveillance cardiaque pendant au moins 24 heures après l'ingestion de 625 mg est recommandée.

Abbreviations: see end of article.

1. Introduction

Indoramin is a postsynaptic selective alpha 1-adrenoceptor antagonist; it also exerts antagonistic effects on H1 histamine and 5HT receptors. It is mainly used for the treatment of hypertension (25-100 mg twice daily), benign prostatic hyperplasia (50-100 mg, daily), and migraine.[1] It has been marketed in France, since 1985 and is also available in several other states of the European Union, in Brazil and South Africa. To our knowledge, no series of more than two cases of indoramin self-poisoning has been reported or published to date.[2-5] We present a retrospective study of cases reported to the Paris poison Centre from 1986 to 2006 and a review of the literature.

2. Methods

This study reviewed all cases of indoramin-only self-poisoning notified to the Paris poison Centre from 1986 to 2010. Adults and children (0-15 years) were analysed separately. All reported doses are supposed ingested doses (SID).

Hypotension was defined as systolic blood pressure <90 mmHg and bradycardia was defined as heart rate less than 60 beats per minute. From the QTc reported by the calling physicians, prolongation of corrected QT interval (QTc) was defined as QTc equal to or greater than 500 milliseconds (msec).[6,7]

Comparisons of supposed ingested doses in the two groups with and without prolonged QTc were performed, using the Mann and Whitney test.

3. Results

From 1986 to 2010, 55 cases of indoramin-only poisoning were observed in 40 adults and 15 children.

3.1. Adult cases

All 40 cases of indoramin overdosage in adults (30 females [75%] and 10 males [25%]) with a mean age of 28±12 years (range: 16-66 years; median age: 24 years) resulted from self-poisoning. The mean SID was 701 mg±464 (range: 100 to 2 250 mg; median dose: 625 mg); 30 patients (75%) ingested a packet or less (in France, indoramin is marketed in packets with the total quantity of 750 mg).

No medical follow-up was available for four patients. The most commonly observed symptoms in the remaining 36 patients were drowsiness in 25 (69%) cases, hypotension in seven (19%) cases, sinus bradycardia in four (11%) cases, and seizures in two (6%) cases.

Hypotensive patients had a systolic blood pressure between 80 to 90 mmHg and patients with bradycardia had a heart rate between 35 and 40 bpm.

The time to onset of seizures was two hours and three hours in the two patients with this symptom, corresponding to the time of their first medical examination. In the first case, the patient presented only one episode of seizures lasting a few minutes that rapidly resolved with diazepam. The other patient experienced three consecutive episodes of seizures over a period of 30 min that required repeated administration of phenobarbital and benzodiazepines.

Electrocardiogram (ECG) recordings were performed in 27 patients; a prolonged QTc was reported by the treating physicians in eight cases (30%). The mean QTc of these eight patients was 530 msec (range: 500 to 590 msec, median: 510 msec). The mean supposed ingested doses in the two groups with and without prolonged QTc were 1 036 mg (range: 625 to 2 250 mg, median: 750 mg) and 732 mg (range: 250 to 1 500 mg, median: 600 mg) respectively (p=0.13).

In this study, the lowest SID (LSID) in a symptomatic patient was 225 mg. LSID for drowsiness, hypotension, bradycardia, seizure, and prolonged QTc were 225, 250, 250, 900 and 625 mg, respectively. The time to onset of prolonged QTc interval could not be determined in any of the cases, but the time to the complete return of a normal ECG was precisely determined in only three cases and was 12 to 24 hours.

Plasma indoramin concentration was measured in three cases and the results are shown in table I. Plasma half-life could be calculated in case 3 (table I); it was 7.4 hours.

We have complete information on 33/40 of the patients and they were all hospitalized. The mean length of hospital stay was 33±16 hours (range: 8-72 hours). Decontamination was performed for 31 patients. Six patients (19%) were only treated by gastric lavage, 18 (58%) had gastric lavage followed by activated charcoal administration, five (16%) only received activated charcoal, another patient was only given Ipecac syrup and the remaining patient did not receive any digestive decontamination due to late presentation to the emergency department.

All 33 patients were observed clinically and treatment was required in only six cases (18%): three received respiratory assistance; two were treated for seizures; one was treated with atropine for bradycardia; three hypotensive patients were treated by intravenous fluids and one patient received dopamine; one patient received noradrenalin, one patient with prolonged QTc received magnesium sulphate and potassium supplementation for prevention of torsade de pointes.

The outcome was known for 33 patients: all made a complete recovery.

3.2. Paediatric cases

The 15 paediatric patients all accidentally ingested indoramin. They were four girls (27%) and eleven boys (73%) with a mean age of 30±14 months (range: 15 to 72 months). The mean SID was 61±47 mg (range: 13-200 mg; 1.9-14.3 mg/kg). None of the children were symptomatic. Also, plasma indoramin was undetectable 1.5, 6 and 16 hours after the ingestion (SID) of 200 mg (14.3 mg/kg).

4. Discussion

To our knowledge, only five cases of human acute poisoning with indoramin had been previously published (see table II). We report on 55 new cases.

The main limitation of this study is a common one to all Poison Centre studies: the notifications are made voluntary; therefore not all cases are reported. Another commonly reported limitation of such studies is the possible inaccuracy of the reported ingested doses (but this is true for studies from any sources and emphasises that the overdosage should be analytically documented whenever it is possible).

Polyintoxication cases with indoramin ingestion were excluded from this study, to be sure that the observed effects were only due to indoramin.

All poisoned children in our series remained asymptomatic, probably because of the very small quantities actually ingested and in one case, serial plasma indoramin showed that the child had not actually taken indoramin.

Adult patients were young and three out of four are women; four of the five published cases also concerned female patients. This female predominance is higher than that usually observed for voluntary acute poisoning in France,[8] probably because indoramin is only used for the treatment of migraine in this country, and the prevalence of migraine is threefold higher in women than in men.[9]