Ramipril – How toxic is it?

Dagmar Prasa (1), Jutta Trompelt (2), Sonja Groß (2), Andreas Vagt (3), Eva-Carina Heier (4), Wolfgang Klumb (5), Uwe Stedtler (6), Elke Färber (7), Cornelia Reichert (8), Claudia Zatloukal (9), Dieter Genser (9), Mandy Gollmann (1)

1) Poisons Information Centre Erfurt, Germany, 2) Poisons Information Centre Mainz, Germany, 3) Poisons Information Centre Berlin, Germany, 4) Department of Clinical Toxicology and Poison Control Centre Munich, Klinikum rechts der Isar, School of Medicine, Technical University of Munich, Germany, 5) Poisons Information Centre Bonn, Germany, 6) Poisons Information Centre Freiburg, Germany, 7) Poisons Information Centre Göttingen, Germany, 8) National Poisons Centre, Tox Info Suisse, Associated Institute of the University of Zurich, Zurich, Switzerland, 9) Poisons Information Centre Vienna, Austria

Objective

Ramipril is an angiotensin-converting enzyme inhibitor, widely used in the management of hypertension and heart failure. Hence, overdose of ramipril is a frequent cause of enquiries in Poisons Information Centres. Its toxicity seems to be relatively low, but available information is limited. The aim of the study was to assess the acute toxicity of ramipril.

Method

Retrospective analysis of acute overdoses of ramipril reported to nine Poisons Information Centres in Germany, Austria, and Switzerland between 1999 and 2021. Inclusion criteria were single substance ingestion, defined dose, and documented follow-up for at least 8 hours. Severity of symptoms was assessed according to Poisoning Severity Score.

Case series

Patients and dose

A total of 141 cases met the inclusion criteria. Patients involved were 71 children (<14 years), 5 adolescents (14-≤18 years), and 65 adults (>18 years).
Doses ranged from 1.25 to 85 mg (0.08-1.7 mg/kg) in children, 10 to 495 mg in adolescents, and 5 to 1000 mg in adults. (Table 1).

Table 1: Cases of exposure to ramipril

Age group	Number of cases	Age (years) median (range)	Dose (mg) Median (range)
Baby (< 1 year)	5	0.83 (0.1 - 0.93)	4 (1.25 – 5)
Toddler/Preschool (1 - < 6 years)	56	2 (1 - 5)	5 (1.25 – 15)
Schoolchild (6 - < 14 years)	10	11 (7 - 13)	5 (1.25 – 85)
Adolescent (14 - < 18 years)	5	16 (15 - 17)	100 (10 – 495)
Adult (≥ 18 years)	65	57 (18 - 96)	100 (5 – 1000)

Clinical effects

Common clinical features in overdose were hypotension (30.9 %), fatigue (14.5 %), dizziness (12.7 %), vomiting (12.7 %), headache (9.1 %), and tachycardia (9.1 %). Less frequent were somnolence (5.5 %), syncope (3.6 %), and bradycardia (3.6 %).

Severity of poisoning

62 % (n=88) of all patients remained asymptomatic, 32 % (n=45) developed only mild symptoms. In 4 % of all cases moderate symptoms were observed (one toddler, one adolescent, three adults). The toddler developed moderate hypotension (75/39 mmHg) after ingestion of 10 mg (0.42 mg/kg).

Severe toxicity was only seen in adults (n=3), after ingestion of at least 250 mg. They developed severe hypotension (minimum 40 mm Hg systolic) and bradycardia (minimum 30 bpm). The lowest dose causing moderate symptoms was 150 mg in adolescents and adults. Adults tolerated up to 1000 mg without any toxicity. In children asymptomatic cases were observed after ingestion of a maximum dose of 15 mg (1.36 mg/kg).

Table 2: Dose of ramipril and severity of symptoms

Age group	Dose range in mg which causes effects (case number)			
	PSS: none	PSS: minor	PSS: moderate	PSS: severe
Baby	1.25 – 5 (n = 5)	-	-	-
Toddler/Preschool	1.25 – 15 (n = 43)	2.5 – 10 (n = 12)	10 (n = 1)	-
Schoolchild	1.25 – 10 (n = 6)	5 – 85 (n = 4)	-	-
Adolescent	495 (n = 1)	10 – 100 (n = 3)	150 (n = 1)	-
Adult	10 – 1000 (n = 33)	5 – 900 (n = 26)	150 – 1000 (n = 3)	250 – 600 (n = 3)

References

Balit CR, Gilmore SP, Isbister GK. Unintentional paediatric ingestions of angiotensin converting enzyme inhibitors and angiotensin II receptor antagonists. J Paediatr Child Health 2007;43(10):686-8.

Corresponding author: prasa@ggiz-erfurt.de

Conclusion

Most exposures in this study resulted in no or only mild symptoms (94 %). Severe symptoms occurred in only three exposures, confirming past experience that severe toxicity is rare. There is no clear correlation between dose and severity of symptoms. Data from this study support the assumption of Balit et al., that children can be observed at home after ingestion of up to 5 mg ramipril.