BELGIAN POISON CENTRE, BRUSSELS, BELGIUM

A CASE OF INADVERTENT INGESTION OF CINACALCET BY A 1-YEAR-OLD CHILD

VAN PELT H (1), DE RIDDER J (2), MOSTIN M (1). 1. BELGIAN POISON CENTRE, BRUSSELS; 2. AZ TURNHOUT, BELGIUM.

INTRODUCTION

Cinacalcet is a calcimimetic drug used in patients with end-stage renal disease with secondary hyperparathyroidism (pathophysiology see fig.1 (ref.1)) who are on dialysis. The main effect is a decreased calcium level in the blood. High calcium together with a risen parathormone (PTH) and phosphorus leads to osteitis fibrosa, metastatic calcifications and an increased risk of mortality.

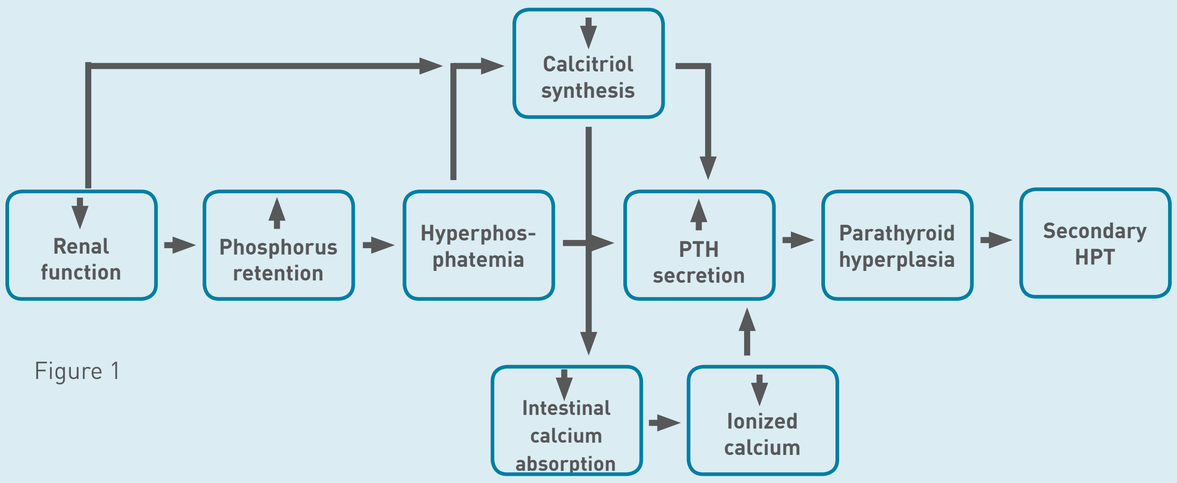

Figure 1

The main effect of a declined renal function is a rise of phosphorus. This stimulates the production of parathormone and inhibits the conversion of 25(OH) VitD to its active form 1,25(OH)VitD (calcitrol). Less calcitrol leads to lower calcium concentrations, which also stimulates the production of PTH. This chronic effect gives way to a secondary hyperparathyroidism with a rise in calcium.

Cinacalcet acts as a allosteric modulator of the calcium-sensing receptors (CaRs) of the parathyroid gland, thereby directly targeting the molecular mechanism by which calcium modulates PTH secretion. Cinacalcet suppress PTH secretion by increasing the sensitivity of CaRs. By directly activating the CaRs, a reduction in PTH release occurs without a concomitant increase in extracellular calcium. Cinacalcet is also used in carcinoma of the parathyroid glands and primary hyperparathyroidism.

CASE REPORT

A 1-year-old girl weighting 10 Kg accidently took one 30 mg pill Cinacalcet (Mimpara®/ Sensipar®) after playing with the pill organizer of her grandmother. Approximately 2,5 hour after the ingestion, she started to vomit and became lethargic. The parents contacted the poison centre, which advised to go to the nearby hospital. On admission she was falling asleep repeatedly. While waking her up, she started to cry and was agitated. The other clinical parameters were normal. A blood gas analysis on arrival showed an ionized calcium of 1.16 mmol/L (1.15-1.29) with a pH of 7.30 (7.38-7.42) and a lactate of 2.4 mmol/L (< 1.3). The light acidosis might be caused by difficulties taking blood with small children. The normal calcium can in fact be lower while it is known that an acidosis can rise the ionized calcium. The poison centre advised to follow the level of calcium repeatedly while Mimpara can lower the calcium concentration. A serum analysis 4 hours after ingestion showed a total calcium of 2.33 mmol/L (2.20-2.70) with a slightly elevated total protein of 75 g/L (54-70) and a leucocytosis of 22.190 109/L (5.000-15.000). The other laboratory tests were normal. A screening for drugs in urine was negative. An infusion with calcium-gluconate was started. 10 mL calcium-gluconate was diluted with 40 ml physiologic solution and given at an infusion speed of 10 mL/hr. Serum analysis 7 hours after ingestion showed a total calcium of 2.18 mmol/L (2.20-2.70). The speed of the infusion was changed to 5 mL/hr. After 21 hours the serum calcium was 2.25 mmol/L. The infusion with calcium was subsequently stopped. The girl left the hospital 2 days after admission in good clinical condition. Cinacalcet concentrations were determined in the serum samples of 4, 7 and 21 hours after ingestion. The results (figure 2) were respectively 129, 84 and <10 ng/mL (paediatric median peak value single 15 mg dose: 7.26 ng/mL (1.8-17.4)).

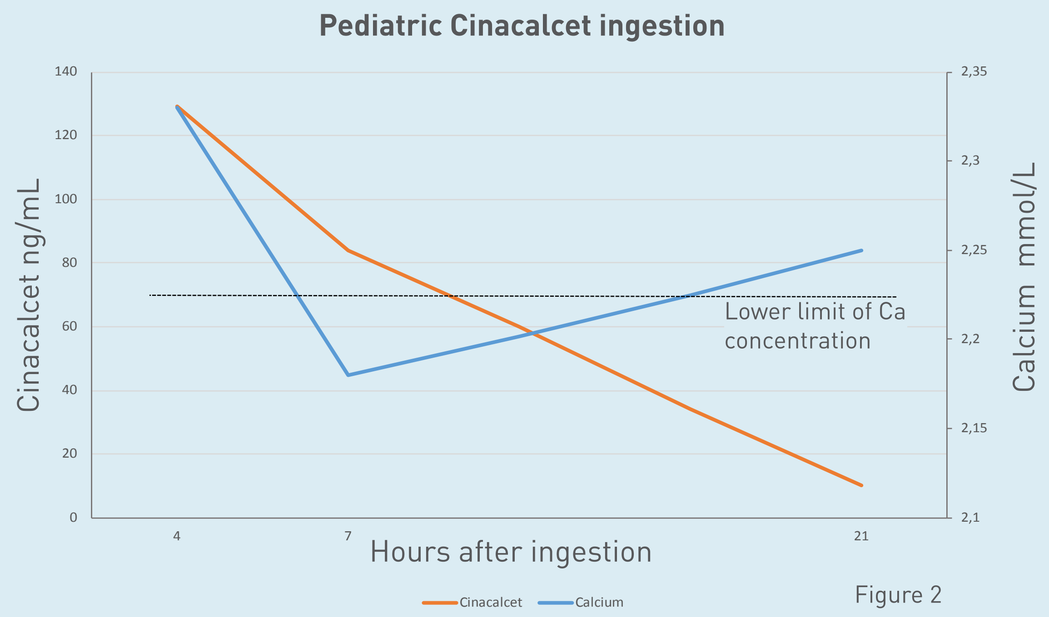

Figure 2

DISCUSSION

A dose of 30 mg Cinacalcet taken by a 1-year-old child weighting 10 Kg gives a very high concentration 4 hours after ingestion. The paediatric median peak value with a single 15 mg dose was 7.26 ng/mL (1.8-17.4)) with 12 children aged 6 to 17 years. The peak value in adults is reached 2 to 6 hours after ingestion. The first dosage of Cinacalcet from this child was measured just around this peak value. The concentration of calcium taken 3 hours after this first dosage showed a level below the lower limit despite an infusion with calcium. This infusion might have prevented an even lower calcium with all of its consequences.

CONCLUSION

To our knowledge there are no published case reports of overdoses with Cinacalcet. Haemodialysis patients have been given doses titrated up to 300 mg daily (Mimpara SPC, 2013). The Swedish Poison Centre (Hulten P, personal communication) had a call for a 74-year-old woman who took an overdose of 420 mg Cinacalcet, with an ionized calcium value of 1.16 mmol/L (1.14-1.32). She had no major symptoms. In our case we observed a low calcium despite an infusion of calcium-gluconate. Till more information is available we advise a close medical observation for any paediatric ingestion.

REFERENCES

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