European Journal of Molecular & Clinical Medicine
ISSN 2515-8260 Volume 07, Issue 07, 2020

Hypoglycemia in a Child with Tramadol Poisoning

Dr. Shafath Ahmed[1], Dr. Sundari S[2]

[1]*Professor, Department of Paediatrics, Sree Balaji Medical College and Hospital.*
[2]*HOD, Department of Paediatrics , Sree Balaji Medical College and Hospital.*

1. INTRODUCTION

Tramadol is a synthetic centrally acting analgesic, which has two stereoisomers with dual mechanism of action-opioid and monoaminergic. Its major metabolite O-desmethyl tramadol (M1) has a weak affinity on the □-opioid receptors (MORs) as an agonist. The monoaminergic activity of tramadol acts synergistically on serotonergic and noradrenergic mechanisms of pain transmission. More specifically, tramadol enhances spinal pain inhibitory pathways by inhibiting neuronal re-uptake of serotonin (5-hydroxytryptamine [5-HT]) and noradrenaline, stimulating 5-HT release.[1] Tramadol poisoning is rare in children because it is not commonly used for children. Common presentations include respiratory and central nervous system (CNS) depression.[2] However, we highlight the case of a 4-year-old boy,who in addition to the above-mentioned presented with hypoglycemia.

2. CASE REPORT

A4-year-oldboywasreferredtoourpediatricemergency unit with the complaint of unintentionally ingesting 6 tablets of (200 mg tablets) tramadol an hour before presentation.Hewasgivenlemondrinkathomebefore presenting to the emergency unit. He vomited several times and convulsed twice on the way to the referring hospital and lapsed intounconsciousness

On examination, he was unconscious with Glasgow coma scale score of 3/15, and pupils were 1 mm in size bilaterally, respiratory rate of 19/min with oxygen saturationof85%(inroomair);thepulseratewas110b/ min,bloodpressure-90/60mmHg.Hewashypoglycemic with random blood sugar (RBS) of 2.0 millimoles/liter. Electrocardiogram showed normal sinus rhythm, and other laboratory investigations, which included full blood count,electrolytes,ureaandcreatinineandliverfunction tests werenormal.

Hypoglycemia and hypoxia were corrected with dextrose infusion (RBS-5.5 mm/L) andintranasal oxygen (SPO_2 96%)respectively. He regainedconsciousness 7 h after admission with no new seizures recorded.He was discharged home after 24 h to return for follow-up 72hlater.Noneurologicdeficitwasdocumentedonthe follow-upvisit.

3. DISCUSSION

Tramadolhydrochlorideisacentralactinganalgesicused for the control of moderate to severe pain in adultsand adolescents,butnotroutinelyrecommendedforchildren becauseitssafetyandefficacyinpatientsunder16years of age have not been established. However, pediatric therapeutic dose of 1-2 mg/kg/dose and a maximum dose of 8

mg/kg/dose or 400 mg/day are occasionally prescribed.[3,4]

Few cases of overdoses with tramadol have been reported. Ingested doses with some fatalities have ranged from 3 to 5 g with the lowest dose reported as between500and1000mginawomanwhoweighed
40 kg.[5] The International Association of Forensic Toxicologists reported blood levels in adults ranging from 0.1to 0.8 mg/L, 1-2 mg/L and greater than
2 mg/L represent therapeutic, toxic and lethal doses respectively.[6] However, we were unable to measure the serum concentration in the index case due to nonavailability of such services.

Apart from its analgesic effect, tramadolhydrochloride may produce a constellation of symptoms such as dizziness, somnolence, nausea, constipation, sweating and pruritus similar to those of other opioids, but in contrast to morphine, tramadol rarely causeshistamine release. At therapeutic doses, tramadol hydrochloride has no effect on heart rate, left-ventricular function or cardiac index. Constipation and respiratory depression are less common but may occur in overdose as was reported in the index case. Tramadol may increase the risk of seizures especially in those with a history of epilepsy,butisrarely associated with idiopathicseizures exceptatveryhighdoses[1]aswaswitnessedinthiscase. Previous reports have shown that tramadol-induced seizure is dose dependent. However, there is no direct correlation of blood concentration to occurrence or severityofseizure.[7]Tramadoloverdosecanalsopresent withfeaturesofserotoninsyndrome,whichispotentially life-threatening especially when used concomitantly withserotonergicdrugsandwithdrugswhichimpairthe metabolism of tramadol. However, there was no such associationinthecaseunderdiscussion.Hypoglycemia is an uncommon presentation of tramadol toxicity; thoughtherehavebeenafewreportedcasesinadults:[8] thecaseofhypoglycemiainasuicidal54-year-oldwoman, with a past history of partial hepatectomy following hepatic metastasis of gastrointestinalstromal tumour, who ingested 3,000 mg of tramadol.[9] The French pharmacovigilance (Adverse Drug Reports) databasealsoreported2casesofhypoglycemiafollowing tramadol poisoning, one in an 88-year old nondiabetic woman and the other in an 8-year-old diabetic girl.[10] However, unlike our patient, these patients had other co-morbidities which affected the control of glucose metabolism with the risk of hypoglycemia. Studies in rats have shown that activation of MOR, which is the principaltargetoftramadolfoundmainlyinCNSandliver hepatocytes results in an increased glucose utilization and/or reduction of hepatic gluconeogenesis probably through a noninsulin-mediated mechanism causing hypoglycemia.[11] Furthermore, serotonin increases insulin concentration in mice; induce endorphin releaseandstimulatemuscleglucoseutilizationthrough theactivationofMORsbyamechanismwhichisneither dose nor insulin-dependent. However, a few cases of hypoglycemia associated with selective serotonin re-uptake inhibitor treatment have been reported.[12] However,whatisnotclearistherolethisplayedinthis case since other clinical features of serotoninsyndrome wereabsent.

Treatment of the index case was mainly supportive.We avoidedgivingnaloxone,fearfulthatitmightaggravate the seizure. However, he was closely monitored, and he improved remarkably without any neurologic complications.

4. CONCLUSION

Hypoglycemia may occur in patients with tramadol overdoseandthoughitisnotverycommon,physicians shouldbeonthelookoutforitinanypatientwithacute tramadolpoisoning.

5. REFERENCES

[1] Schug SA, FfpmanzcaF, Lim A. Tramadol, Prescriber Update 2000;20:26-30.
[2] Shadnia S, Soltaninejad K, Heydari K, Sasanian G, AbdollahiM. Tramadol intoxication: A review of 114 cases. Hum Exp Toxicol2008;27:201-5.
[3] ViitanenH,AnnilaP.Analgesicefficacyoftramadol2mgkg(-1)for
[4] paediatric day-case adenoidectomy. Br J Anaesth2001;86:572-5.
[5] Nikanne E, Kokki H, TuovinenK. Postoperative pain after adenoidectomy in children. Br J Anaesth1999;82:886-9.
[6] Tramadol Hydrochloride. Available from: http://www.drugs.com/pro/tramadol-tablets. [Last accessed on 2014 Jul10].
[7] PothiawalaS,PonampalamR.TramadolOverdose:ACaseReport. Proceedings of Singapore Healthcare. Vol. 20. 2011. p.3.
[8] TaghaddosinejadF, Mehrpour O, Afshari R, Seghatoleslami A, Abdollahi M, Dart RC. Factors related to seizure in tramadol poisoninganditsbloodconcentration.JMedToxicol2011;7:183-8.
[9] Tramadol Toxicity and Treatment, Toxic Update BC Drug and Poison Information Centre. 2010;6. Available from: http:// www.dpic.org/sites/default/files/10_v6_i1_Tramadol.pdf.[Last accessed on 2014 Jul08].
[10] MugunthanN,DavorenP.Dangerofhypoglycemiaduetoacute tramadol poisoning. EndocrPract2012;18:e151-2.
[11] GrandvuilleminA,JolimoyG,Authier F, DautricheA,Duhoux F, Sgro C. Tramadol-induced hypoglycemia 2 cases. Presse Med 2006;35:1842-4.
[12] Cheng JT, Liu IM, Chi TC, Tzeng TF, Lu FH, Chang CJ. Plasma glucose-lowering effect of tramadol in streptozotocin-induced diabetic rats. Diabetes2001;50:2815-21.
[13] BourneC,GouraudA,DaveluyA,GrandvuilleminA,AuricheP, DescotesJ,*etal*.Tramadolandhypoglycaemia:comparisonwith otherstep2analgesicdrugs.BrJClinPharmacol2013;75:1063-7.