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Case Report

Expanding Indications of Flexible Ureteroscopy in Renal and Ureteral Stones

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Abstract

Propylene Glycol toxicity is well known complication of Lorazepam infusion used in critical care settings as it is used as solvent for Lorazepam. Multiple case reports have been reported in the past about this complication of Benzodiazipine infusion. This iatrogenic complication is dose independent and has been reported in therapeutic as well as high doses especially if infused over a short period of time and in the backround of renal dysfunction.

Case

54 years old man with medical history of Hypertension and chronic alcohol abuse presented to the emergency department after multiple falls at home and possible convulsions. He was complaining of tremulousness, vomiting and abdominal pain. He used to drink one pint of alcohol on a daily basis, his last drink was 2 days before presentation. He was admitted to the ICU with the impression of alcohol withdrawal and possible delirium tremens. His initial set of labs was significant for creatinine 1.1, albumin 4.2, ALT 68, AST 95, ALP 48, total bilirubin 2.3 and direct bilirubin 0.4, lactic acid 2.6 and alcohol level of <10. He was started on Thiamine, Folic acid, Multivitamin, Intravenous (IV) fluids and IV Lorazepam pushes. He was later started on IV Lorazepam drip for alcohol withdrawal symptoms. He was given continuous IV Lorazepam infusion for 5 days. Initial serum osmolality was 286.1, serum creatinine of 0.7, serum bicarbonate of 24 on day 1 of IV Lorazepam infusion. On day 2, the creatinine level worsened to 1.2, serum bicarbonate of 18 and serum osmolality of 267.2. On day 3, the serum creatinine worsened to 1.9, serum bicarbonate of 17 and serum osmolality of 280.9. On day 4, the serum creatinine worsened further to 1.9, serum bicarbonate of 13 and serum osmolality of 281.6. On day 5, the serum creatinine worsened to 2.4, serum bicarbonate of 12 and calculated serum osmolality of 280.1. Serum osmolality was checked on day 5 which came back as 285. IV Lorazepam infusion was stopped on day 5. However, the metabolic abnormalities and renal function continued to deteriorate. The creatinine worsened to 2.9 on day 6. The calculated serum osmolality was 293.5, 299.2 and 301.8, 301.3 with calculated osmolar gaps of 8.5, 14.2, 16.8, 16.3 on day 6, 7, 8 and 9 respectively. The renal function returned to baseline (serum creatinine 1.0) 8 days after stopping IV Lorazepam infusion. Serum bicarbonate level also improved to normal level along with serum osmolar gap. The trend of renal function has been shown in (Table 1).

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 8	Day 10
S. Creatinine	0.7	1.2	1.9	1.9	2.4	2.9	1.0	0.9
BUN	14	4	8	10	15	24	13	8
S. Bicarbonate	24	18	17	13	12	12	17	27

After stopping IV Lorazepam infusion, patient was managed with initally with IV midazolam drip which was discontinued after 1 day. Patient was also later on managed with Chlordiazepoxide. Patient alcohol withdrawal symptoms improved and later on, he was discharged.

Patient suffered acute kidney injury, high anion GAP metabolic acidosis and high osmolar gap in the setting of continuous IV Lorazepam infusion, the common picture of Propylene Glycol toxicity. These findings resolved after IV Lorazepam infusion was stopped. We did not measure the propylene glycol levels in this case. However, the sequence of events and the subsequent resoluation of acute renal failure and metabolic abnormalities can be best explained by Propylene glycol toxicity in the settting of continuous IV Lorazepam infusion.

Discussion

Propylene Glycol is the solvent used for intravenous administration of Lorazepam and Diazepalm. Both of these medications are frequently used in critical care settings for sedative purposes and can lead to the development of Propylene Glycol. Underlying renal and hepatic dysfunctions are risk factors for Propylene Glycol toxicity although it has been reported in patients with normal renal and hepatic functions [1], as is our patient who had normal baseline renal and hepatic panel. Propylene Glycol Toxicity is characterized by hyperosmolarity and high anion gap metabolic acidosis, often accompanied by acute kidney injury and if severe can progress to multisystem organ failure [2]. The possible mechanism of Propylene Glycol toxicity is accumulation of toxic metabolites. It has been reported that Propylene Glycol can cause severe lactic acidosis with out any derangement in renal function [1]. Metabolic acidosis caused by Propylene Glycol is mainly due to L- and D-Lactic acidosis which are acid metabolites of Propylene Glycol. Some case of acute tubular necrosis possible secondary to Propylene Glycol toxicity has been reported [3]. It has been reported with normal, low and high dose infusions [4].

Prevention is better than cure. Propylene Glycol toxicity can be avoided by avoiding Propylene Glycol containing medications, Of Benzodiazipines, Midazolam is the one which does not have Propylene Glycol as solvent and can be used where ever possible. If Lorazepam has to be used, it can be used as injections istead of continuous intravenous infusion. For patients on continuous intravenous infusion there should be careful monitoring of basic metabolic profile. In whom Propylene Glycol toxicity is suspected, infusion should be stopped and osmolar gap should be measured as it can be used as surrogate marker for serum propylene glycol concentration [5]. Therapy for Propylene Glycol toxicity is mainly to stop intravenous infusion [6]. In cases where there is no improvement in clinical and metabolic profile hemodialysis is another option [7].

Conclusion

Lorazepam infusion is commonly used medication in ICU patients, which is accompanied by Propylene Glycol as solvent. Although it is usually considered safe medication, but clinitions always keep in mind that it can be complicated with Propylene Glycol toxicity especially in the back ground of deranged hepatic and renal function. Where ever is possible other agents should be used, if it is used, there should be close monitoring and low suspicion for Propylene Glycol toxicity and low threshould of stopping IV infusion.

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