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Letter to the Editor

Rhabdomyolysis and myoglobinuria following bisphosphonate infusion in patients with Duchenne muscular dystrophy

We read with interest the recent article by Ivanyuk et al. [1] who presented two cases of suspected Zoledronate induced rhabdomyolysis with myoglobinuria in boys with Duchenne Muscular Dystophy (DMD). Since 2014, 13 patients affected by DMD and steroid induced osteoporosis have been treated at our centre with intravenous Zoledronate. All had a BMD *Z*-score of −2.0 standard deviations or less with severe or symptomatic vertebral compression fractures and were treated in line with recent guidelines [2]. Two of the treated patients developed confirmed rhabdomyolysis with myoglobinuria following their first Zoledronate infusion, resulting in a prolonged hospital stay. They were managed with supportive therapy including analgesia, antipyretics, antiemetics and intravenous fluids and both made a full recovery within a week. No alternative explanation was found for their clinical presentation and the temporal nature of events implicates Zoledronate as the cause.

Our first case was an 11-year-old patient, with symptomatic vertebral compression fractures who received a half dose of Zoledronate (0.025 mg/Kg). 20 h post infusion he developed leg cramps, loin pain, significant pyrexia and tachycardia. Blood tests revealed raised inflammatory markers, with C-reactive protein (CRP) of 99.7 mg/L and an acutely elevated Creatinine Kinase (CK), (92,179 iu/L – day 1, 14,412 iu/L – day 6). He was mildly hypocalcaemic on day 1 (2.12 mmol/L) and hypophosphataemic on day 2 (0.8 mmol/L). His urine was positive for myoglobin, although renal function was not affected. Clinicians suspected an acute inflammatory reaction to Zoledronate with rhabdomyolysis. No alternative cause for his symptoms was identified. He recovered following supportive management.

Our second case was a 15-year-old, who received 0.05 mg/kg of Zoledronate for multi-level symptomatic vertebral fractures. Seven hours after infusion the patient developed right sided hip/abdominal pain, vomiting, significant pyrexia, tachycardia and tachypnoea. Blood tests showed an elevated CRP (244 mg/L), CK (peak 12,204 iu/L – day 1, 4079 iu/L – day 3) and lactate (4 mmol/L day 2) with mild renal derangement. As in the first patient, urinary myoglobin was positive. He also made a full recovery with supportive therapy. Calcium and phosphate levels were not checked at the time as there was no specific clinical indication to do so.

Both patients were taking 18 mg Deflazacort once daily for treatment of DMD and were on prophylactic Vitamin D supplementation. Normal renal function, Vitamin D and bone profile was confirmed prior to infusion and both received prophylactic calcium supplementation for 5 days post infusion as per hospital protocol. Both have subsequently received a second infusion of Zoledronate with no adverse reaction.

Our cases show strong similarities to those reported in this journal previously and add weight to the growing concern around serious side effects of bisphosphonates, in particular in those with DMD. We have critically demonstrated biochemical confirmation of Zoledronate induced rhabdomyolysis with myoglobinuria in two patients with DMD. In line with Ivanyuk and colleagues we urge that clinicians prescribing bisphosphates to patients with DMD warn them to seek urgent medical attention if they develop muscle cramps or discoloured urine. Medical professionals should be alert to this complication and in any patients presenting with these symptoms following infusion of bipshosphonates renal function, bone profile, CK and urine myoglobin should be checked.

In both our cases, we completed British National Formulary (BNF) “Yellow Cards” to report them as suspected adverse reactions to the UK Medicines and Healthcare products Regulatory Agency (MHRA). We call for rhabdomyolysis and myoglobinuria to be listed as potential side effects of Zoledronate, in drug compendiums such as the British National Formulary for Children (BNFc) [3].

References

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