

**EXTENDED RELEASE AZITHROMYCIN INDUCED DIZZINESS**

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**Summary**

Extended release azithromycin has been approved about five years back. In this case series we report the occurrence of dizziness with extended release single dose 2gram formulation in patients who did not report such an adverse effect with conventional daily 500mg of Azithromycin.

**Key words:** Extended release azithromycin, dizziness.

**Introduction**

Azithromycin a 15-atom lactone macrolide ring revolutionized antibiotic care by decreasing duration of treatment from 7-14 days to 1-5 days with comparable efficacy. Azithromycin extended release, a novel single dose administration formulation, was approved by FDA in June 2005.<sup>[1]</sup> It is currently approved for community acquired pneumonia and acute bacterial sinusitis.<sup>1</sup> Azithromycin extended release is incorporated into sustained release microspheres which are 200µm in diameter and release the drug through pores. Alkalinizing agents (sodium phosphate tribasic and magnesium hydroxide) are incorporated in microspheres to delay initial release of drug in stomach and thereby decreasing the gastrointestinal side effects. The factors considered to design this extended release 2g single dose formulation were improving gastrointestinal tolerance, minimizing loss of bioavailability and masking bitter taste of azithromycin.<sup>[2]</sup> This so called front loading of the dose early in the course of infection maximizes drug exposure when bacterial burden is highest.<sup>[3]</sup> Also the advantage of single dose azithromycin administration is to ensure that patient complete their prescribed course of therapy. Further for some conditions it can be directly observed therapy<sup>[4]</sup>. Regarding safety profile, a study comparing the pharmacokinetics of azithromycin following a single oral dose of extended release and immediate release formulations has shown that two have similar safety profile<sup>[5]</sup>.

### **Case Reports**

Here we are reporting three cases in which dizziness was seen secondary to single dose of two gram azithromycin extended release.

Case 1: A 37-year-old hypertensive male, who was well controlled on Ramipril 5mg per day, took azithromycin 2 gram suspension for bacterial sinusitis. After two hours he had weakness, nausea, diaphoresis, lightheadedness and then became unconscious. On examination the pulse was feeble and blood pressure was low. Once the patient was put in horizontal position, volume of pulse increased, pallor disappeared and he regained consciousness in approximately 30 seconds. During this episode there were no signs and symptoms suggestive of seizure activity. The ECG done later did not reveal any abnormality. After this episode dizziness persisted for 4 to 5 hours. There was no history suggestive of cardiac or neurological illness in the past.

Case 2: A 36-year-old male diabetic with well controlled blood glucose levels on metformin 500 mg twice daily developed dizziness after two hours of taking azithromycin 2 gram suspension and he could not maintain balance. Blood biochemistry and ECG was normal. These symptoms persisted for 4-5 hours prior to complete recovery.

Case 3: A 59-year-old female with no co morbid illness took azithromycin 2 gram suspension for the treatment of bacterial sinusitis and within one and a half hours she developed severe dizziness. The symptom persisted for 3-4 hours interfering in her routine daily activities. All the routine investigations were within normal limits. She recovered completely and with no residual effects.

### **Discussion**

All the three patients had taken conventional 500mg of Azithromycin for 3 days before but did not get any untoward incident however it was only after administration of 2 gram extended release preparation of azithromycin that they developed dizziness. Liu et al in a study comparing single dose azithromycin extended release with 3-day azithromycin immediate release found that front loading with azithromycin single dose achieved three-fold higher azithromycin exposure in serum and WBC during first 24 hours after the start of dosing [6]. Most probably in the three cases mentioned above the dizziness can be secondary to high plasma concentration of azithromycin. With azithromycin microsphere formulation most of the adverse events occur on the day of administration and are resolved within 2 days [2]. In all the cases mentioned above the adverse events were seen on the day of administration of drug.

### **Conclusion**

These case series highlights that dizziness can develop even in patients who did not experience such an event with conventional azithromycin. So it becomes imperative for physicians prescribing 2 gram extended release single dose of azithromycin to caution the patients against this side effects and warn them regarding activities that require physical co-ordination and alertness at least on first two days.

**References**

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