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Letter to Editor

Pharmacology Section

Risk of Cardiovascular Effects with Azithromycin

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Dear Editor,

Macrolides, a class of antibiotics produced by strains of *streptomyces* have a complex chemical structure being linked to one or more sugars (cladinasone and desosamine) and act by inhibiting protein synthesis [1]. Most commonly used macrolides are azithromycin, erythromycin, clarithromycin, and roxithromycin. The most common adverse effects of macrolides are diarrhea, abdominal pain, vomiting, severe skin reactions and other gastrointestinal problems [2].

Previously, azithromycin has been reported to be a broad spectrum macrolide antibiotic free from cardiac toxicity [3]. It is the first macrolide antibiotic belonging to the azalide group derived from erythromycin by adding a nitrogen atom to the lactone ring [4]. Azithromycin differs from other antibiotics in its unusual pharmacokinetic properties. It is rapidly accumulated in cells and tissues, particularly in blood leucocytes and is slowly released from the sites with a half life of 40h [5].

In the recent past azithromycin has been shown to possess proarrhythmic effects [6]. There are seven reports of QT interval prolongation in patients with normal QT intervals prescribed a five day course of azithromycin [5]. A recent article mentions that compared to other antibiotics like amoxicillin, ciprofloxacin and levofloxacin, the risk of cardiovascular death is more with azithromycin [7]. The United States Food and Drug Administration (US FDA) warns that azithromycin may cause abnormal changes in the heart's electrical activity leading to fatal arrhythmias [8]. This communication is based on the findings of a study [7] by medical researchers as well as another study reported by one of the manufacturers of azithromycin that assessed the arrhythmogenic potential for the drug [8]. This applies only to patients with prolonged QT intervals, low levels of blood potassium or magnesium, and a slower heart rate than normal. The possible mechanism of macrolide induced QT prolongation is inhibition of repolarization of cardiac cells through potassium channels [9,10]. The macrolide antibiotics erythromycin, clarithromycin and azithromycin show similar QT prolongation but have divergent proarrhythmic potential [11]. Administration of azithromycin to healthy human subjects resulted in acute stimulation of neutrophil degranulation and phagocytosis associated respiratory burst [12]. Patients with prolonged QT intervals need to obtain advice from their healthcare professional before starting treatment with azithromycin. Health care professionals need to have information about their patient's family history, QT intervals, abnormal heart beat, and bradyarrhythmias before starting treatment with azithromycin.

The evidence shows that azithromycin not only produces cardiac arrest in patients with prolonged QT interval, but also affects healthy human subjects when azithromycin is taken for more than 4 days. If treatment is required for a longer duration, it is better to use other antibiotics like amoxicillin or ciprofloxacin. Azithromycin should be a priority candidate for pharmacovigilance and adverse drug reaction monitoring. In addition, large scale studies (if possible multicentric) covering large populations are needed to evaluate the exact clinical impact of these preliminary findings considering the large scale use of azithromycin and other macrolides.

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