Can Fomepizole be Substituted by Abacavir in the Treatment of Methanol Poisoning?

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Methanol is metabolized into formaldehyde by alcohol dehydrogenase (ADH) in the liver and then, formaldehyde is converted to formic acid by aldehyde dehydrogenase. Formic acid is responsible for the characteristic signs and symptoms of methanol toxicity such as coma, seizure, visual disturbances, and metabolic acidosis with a high plasma anion gap [1–4]. Also, due to inhibition of mitochondrial cytochrome oxidase by formate, lactic acid accumulation can occur [5–11]. Two antidotes for methanol intoxication include ethanol and fomepizole since they both are competitive inhibitors of ADH [1, 12, 13].

Abacavir is used for treatment of human immunodeficiency virus (HIV) and acquired immune deficiency syndrome (AIDS). It is metabolized by alcohol dehydrogenase [14]. It has been shown that the metabolism of abacavir is completely inhibited by fomepizole in vitro [15]. Additionally, ethanol inhibits the metabolism of abacavir [16]. However, affinity of ADH for abacavir in comparison with methanol is not clear. Ghannoum and colleagues [17] presented an HIV-positive patient on the treatment with antiretrovirals, who had ingested more than 15-fold of the accepted lethal dose of pure methanol and had no signs and symptoms of methanol poisoning 11 h after the intake. None of the laboratory tests of the patient including arterial blood gases, measured osmolality, osmolal gap, and calculated anion gap was abnormal 5 and 11 h after the ingestion of methanol. Since methanol is rapidly absorbed after ingestion, its serum concentration usually reaches the peak level within 30 to 60 min [1], and the methanol-intoxicated patient generally

becomes symptomatic within 6 to 30 h post-ingestion [8, 9]. With this amount of pure methanol ingested, as the authors themselves suggested [17], their patient should have become symptomatic or at least have developed metabolic acidosis within this period of time (11 h). They hypothesized that from the antiretroviral drugs the patient was using, only abacavir might have had a strong competitive inhibiting role of ADH. They did not administer fomepizole to their patient. We hypothesize that abacavir may be a substitute for fomepizole in the treatment of methanol toxicity. To test this hypothesis, the affinity of abacavir for ADH in comparison with methanol should firstly be experimentally determined and if it is shown that it has a greater affinity for ADH compared with methanol, a multicenter randomized controlled trial study should be designed to compare fomepizole with abacavir in the treatment of methanol-poisoned patients. Albeit, the best opportunities for conducting this study are the mass poisonings with methanol that regularly occur in developed and developing countries [9, 18–21].

Concurrent use of fomepizole and ethanol is contraindicated in the treatment of methanol poisoning because it has been shown that fomepizole prolongs the half life of ethanol. On the other hand, it is not clear if abacavir has impact on the half life of ethanol. However, it has been shown that ethanol increases the abacavir plasma concentration and not vice versa [16]. Also, fomepizole is dialyzable and the frequency of its dosing should be increased during dialysis [12, 13] while abacavir is poorly removed by hemodialysis [22].

As AIDS and HIV infection are worldwide problems, abacavir—used for their treatment—is also available worldwide. In contrary, methanol poisoning is a rare toxicity that is seen in the form of isolated episodes and intentional ingestion, and sometimes occurs as single epidemics [9, 18–21]. Therefore, fomepizole is not widely stocked in some hospital pharmacy stocks in comparison

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with abacavir. Additionally, its high price and lack of availability in some countries should be borne in mind.

Conflict of Interest None.

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