

A dose escalation study to determine the safety and efficacy of fructose 1, 6-diphosphate (FDP) in treating yellow oleander-induced cardiac toxicity

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Objective: The principle objective is to find the lowest dose of FDP that has a beneficial effect on yellow oleander-induced cardiac toxicity in human. **Background:** Cardiac glycoside toxicity is one of the most common causes of drug-induced toxicity and is the most common type of plant poisoning in Sri Lanka and some other South Asian countries (1, 2). The only current antidote (Digoxin Fab antibody fragments – DigiFab – KaneruTab) is effective but extremely expensive. Fructose-1, 6-diphosphate (FDP) has been shown to treat cardiac toxicity in animal studies of oleander poisoning and has been used intravenously in a large number of human studies. It has the advantages of being cheap and low human toxicity. **Method:** We have conducted a multi-centre phase II dose escalation study in the General hospitals of Polonnaruwa and Chilaw for the period of 16 months (April 2006 to July 2007). Patients presenting with significant cardiotoxicity after ingestions of oleander seeds were recruited to this study. Informed consent was obtained from all patients. Patients were randomly allocated to four dose levels doubling at successive dose levels (30, 60, 125, and 250 mg/kg). In each dose level two patients received placebo and six patients received active treatment. Blood samples, serial ECG and continuous holter readings were obtained. **Results:** We have recruited 32 patients; 20 were female (62.5%). Median age and number of oleander seed ingested were 25 years (IQR 18-34) and 3 seeds (IQR 2-5) respectively. Median time from ingestion to starting of the FDP/placebo was 12 hours (IQR 6-19.5). Holter reading was obtained ((mean duration 121. 25 minutes) from all the patients and sent to our collaborators in Australia for interpretation. There were two deaths (6.25%, 95% CI 1.1-19.2); one in each study groups. Both these patients died due to cardiac arrest. FDP was tolerated well in our patients. None of them develop major adverse effect or allergic reactions to FDP. Two patients develop transient hypotension on completion of bolus infusion of FDP which responded to fluids and ionotropes. **Conclusion:** This study does confirm that FDP even at a higher dose of 250 mg/kg in severe cardiac toxic patients is safe. FDP may be effective in reducing deaths on oleander toxicities. However further studies are needed to confirm our preliminary findings. **References:** 1. Eddleston M et al. Epidemic of self-poisoning with seeds of the yellow oleander tree (*Thevetia peruviana*) in northern Sri Lanka. *Trop. Med Int. Health* 1999; 4(4):266-73. 2. Bose TK et al Cardiovascular effects of yellow oleander ingestion. *J. Indian Med Assoc.* 1999; 97(10):407-10