Background: Tolvaptan has been used to adjust hyponatremia, and to increase urination in adult heart failure. However, little is known about its safety and efficacy in small children. No pharmacokinetics data is available in children with congenital heart disease (CHD). Purpose of this study was to clarify the pharmacokinetics and pharmacodynamics of tolvaptan in children with CHD.

Methods: Single arm and single dose prospective study was carried out. Patients younger than 10 years old, and who had water retention, which was difficult to control with conventional diuretic therapies were recruited. Pharmacokinetic data was obtained every 2 hours for 12 hours and at 24 hours of tolvaptan administration (0.15mg/kg), and pharmacodynamics data including urine output, urine and serum sodium concentration (Na) and osmolality were obtained during the first week of tolvaptan administration.

Results: There were 7 patients who completed the study. The mean age and body weight was 29.6 month (0-146 month) and 9.7 kg (2.4-29.8 kg). Three of 7 patients had single ventricle physiology. The maximum plasma concentration of tolvaptan was 41.1±33.7 ng/ml, time to reach the maximum plasma concentration was 3.1±2.3 hours, and terminal phase elimination half life was 3.5±1.5 hours. Urine output was increased from 4.5 ml/kg/h to 7.1±1.5 ml/kg/h at 4 hours (p=0.04, paired t-test), and urine osmolality was reduced from 331±150 mOsm to 197±40 mOsm (paired t-test, p=0.03) at 4 hours. Serum Na was unchanged, but urine Na tended to be reduced from 72±54 to 34±25 mEq/L at 4-8 hours after tolvaptan administration. (p=0.06, paired t-test) There was no creatinine, AST and ALT changes during the study period.

Conclusions: Pharmacokinetic data was obtained in patients with CHD for the first time. Tolvaptan was safe and effective to prevent Na excretion, and to increase urination in small children with CHD.