

Abstract

The 24-hr LD50 of colchicine in newborn rats is 0.24 mg/kg, which is about 1/10 that observed in the adult. The 24-hr LD50 of colchicine was relatively constant in rats over 25 days of age. In an attempt to determine the mechanism of the increased sensitivity of the newborn rat to the toxic action of colchicine, the distribution of 3H after the administration of 3H-colchicine (0.1 mg/kg) was measured in 10- and 35-day-old rats. The concentration of 3H was higher in all tissues of the newborn than the adult after ip administration, suggesting an immaturity in the pathway for colchicine elimination. After iv administration, radioactivity disappeared much more slowly from the plasma of the newborn rat than from the adult. This was due to a lower capacity of the liver of the newborn to concentrate colchicine and to excrete it into the bile. Development of the hepatic excretory mechanism responsible for excretion of colchicine occurred at the same age as did the increase in LD50. These results suggest that colchicine is more toxic in the newborn because the drug remains in the body for a longer time due to immaturity of the liver excretory process.