

Embryotoxic effects of pyrimidine analogs on developing rat foetuses.

Lobo SW (1), Kumar S (2).

1. Department of Anatomy, Melaka Manipal Medical College, Manipal, India. 2. Department of Anatomy, Banaras Hindu University, Uttar Pradesh, India.

Objective: To observe the embryotoxic effects of anti-neoplastic drug, 5-Fluorouracil administered in early and late phases of gestation. **Methods:** A single dose (30mg/kg body weight, intra-peritoneally) of an anti-neoplastic drug, 5-Fluorouracil (5-FU), was administered to pregnant female rats on the 4th and 12th days of gestation. On the 19th day of gestation all the animals were anesthetized by administering ether anesthesia and the foetuses were delivered by uterotomy. The number of alive and dead fetuses was recorded. Each live foetus was dried on a blotting paper, weighed and subsequently, the foetal weight, crown rump length, and tail length were measured. Each foetus was examined carefully for various congenital anomalies. **Results:** Administration of 5-FU during early and late phases of pregnancy resulted in mortality, growth retardation and various malformations. Mortality rate was found to be 15% in the 4th day treated group and 18.4 % in the 12th day treated group, whereas the viability was about 95% in the control group of foetuses. Anthropometric measurements like foetal weight, crown-rump length and tail length showed reduction in both the treated groups, the effects being more marked in the 12th day treated group. The foetal limbs of the 12th day treated group revealed shortening of the humerus and femur in the forelimbs and hind limbs respectively, and various defects of the digits of the foetuses. Phocomelia was observed in 30.39% of the 12th day treated group. The foetal limbs of the 4th day treated group also revealed shortening and defects of the digits, but no phocomelia was observed. Abnormalities like cleft palate, micrognathia and microcephaly were also observed in the 12th day treated foetuses. **Conclusion:** Therapeutic exposure of the mother to anti-neoplastic agents like 5-FU during pregnancy may present a risk to the growing foetus. If such agents are administered in the early phases of pregnancy, they impair embryogenesis, and induce malformations, and if given in subsequent phases of pregnancy, cause gross malformations in the foetus and be potentially lethal. **References:** 1. Chabner BA, Amrein PC, Druker BJ et al. Antineoplastic agents. In: Brunton LL, Lazo JS, Parker KL (eds). Goodman and Gillman's The Pharmacological Basis of Therapeutics. 11th Edition. New York: Mc Graw Hill 2001: 1342-43. 2. Hasken CM & Rosen L, eds. Anticancer drugs. In: Haskell cancer treatment. 5th Edition. Philadelphia: W.B. Saunders Company 2001: 151. 3. Myers CE, Diasio R, Eliot HM, Chabner BA. Pharmacokinetics of the fluoropyrimidines: implications for their clinical use. *Cancer Treat Rev* 1976; 3: 175-83.