

Side Effects of Cimetidine

Pages with reference to book, From 159 To 160

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Cimetidine, an H₂ receptor antagonist, is widely used in the treatment of duodenal ulcer, Zollinger-Ellison Syndrome (Binder et al., 1978; Winship, 1978; Ippoliti et al., 1978; Gray et al., 1978; Lc Canthy, 1978) benign gastric ulcer, gastric erosions and oesophagitis (Freston, 1979; Frost et al., 1977; Englert et al., 1978). In human beings it has a circulating half life of disappearance of 123±12 min (Burland et al., 1975). Complete absorption occurs on oral ingestion, in 80-90 min. Seventy percent is excreted in urine (Regan et al., 1977), 10% in stool (Griffiths, 1977) and inactivated mainly by the liver (Griffiths et al., 1977). Its main toxic effects are due to its action on widely distributed H₂ receptors, or due to idiosyncrasy, in some instances, mechanism of side effects is not well understood.

Hepatotoxic effect are slight rise in serum transaminases (<100 mu/ml) without any signs of hepatic dysfunction, focal necrosis and cholestasis reported in 5 children by Spence et al (1977), who observed higher levels of Cimetidine in bile than in portal or systemic venous blood implying active transport of drug from portal blood to hepatic bile.

Effect of Cimetidine on fasting serum gastrin levels is not well established (Bank et al., 1977; Richardson, 1978).

Rebound in acid secretion or ulcer activity after discontinuance of Cimetidine is not known (McGuigon, 1981) and if given for longer duration effectively reduces frequency of ulcer recurrences (Blackwood et al., 1978).

Cimetidine is recommended in treatment of benign gastric ulcer and not in malignant (Elder et al., 1979) where its role is debatable. Nitrosation of the drug has been observed in vitro (McGuigon, 1981) but whether it occurs in vivo and these nitrosated compounds are carcinogenic in experimental animals or in human beings is not well established. Marked structural similarity has been reported by Elder et al (1979) between these potential nitroso derivatives of Cimetidine and N-Methyl N-Nitroso-N-nitrosoguanidine (MNNG) which in some species behaves as direct local acting gastric carcinogen (Sugimura and Fujimura 1967).

Vitamin B₁₂ malabsorption by Cimetidine has not yet been observed (McGregor et al., 1977) probably because Cimetidine reduces only the volume of gastric secretion and not the concentration of gastric juice intrinsic factor (Sharpe et al., 1979).

As an H₂ receptor antagonist Cimetidine may act as a local immuno-inhibitory agent and stimulate H₂ receptor bearing suppressor T-Lymphocytes (Weinstein and Melmon, 1976; Rocklin, 1978) or interfere with the inhibitory effect of histamine and thus augment cell-mediated immune response (Avella et al., 1978). Lymphocyte transformation is enhanced in normal subjects receiving cimetidine (Smith et al., 1979). McGregor (1977) observed no alteration in leucocyte migration inhibition with a variety of autoantibodies and serum immunoglobulin in patients on Cimetidine. Clinically no adverse effect due to this phenomenon has been reported so far (McGuigon, 1981). Cimetidine may also block the receptors in central nervous system and causes mental confusion, somnolence, lethargy, restlessness, disorientation, agitation, hallucination, focal twitching, seizures, flushing, sweating or unresponsiveness of speech. These symptoms were observed only in a small group of patients (Agarwal, 1978; Wood et al., 1978; Bacigalupo et al., 1978; Levine, 1978; Van Rajthave Awam, 1979; Arneson, 1979; Schentag et al., 1979) and are more marked in elderly or very young patients, in patients with hepatic and or renal dysfunction and are dose related (McGuigon, 1981).

Leucopenia and granulocytopenia occurs in patients receiving cimetidine (Johnson et al., 1977; Corbett and Holdsworth, 1978; James and Prout, 1978; Freston, 1979). These effects are temporary and rare and can also be due to other drugs given simultaneously or other intercurrent diseases (Johnson et al.,

1977, McGuigon, 1981).

Endocrine abnormalities like gynecomastia, elevation of serum prolactin, galactorrhoea, loss of libido, impotence and reduction in sperm count in males are occasionally seen (Bateson et al., 1977; Daubresse et al., 1978; Majumdar et al., 1978; Spiegel et al., 1978; Rowley Jones, 1978; Peden et al., 1979; Barber, 1979; Spence and Celestin, 1979).

Cimetidine at present has no place in the treatment of acute Pancreatitis (Meshkinpour et al., 1979); The only renal abnormality so far observed is slight rise in serum creatinine rarely exceeding 2 mg/100 ml (Dubb et al., 1978).

Severe toxic effects are rare and if used dis-criminately Cimetidine may prove to be a very useful discovery.

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