



PIC QUESTION OF THE WEEK: 2/20/06

Q: Has mesalamine been implicated as a cause of renal disease?

A: Mesalamine, also known as 5-aminosalicylic acid (5-ASA) and mesalazine (in Europe), is labeled for the treatment and maintenance therapy of ulcerative colitis and has also been used extensively for acute and chronic management of Crohn's disease. The drug is available for topical use as rectal suppositories and enemas. In addition, there are a number of additional oral dosage forms of mesalamine (Pentasa®; Asacol®) and its analogs (olsalazine-Dipentum® and balsalazide-Colazal®) used in inflammatory bowel disease (IBD). Oral absorption of mesalamine ranges from 20-30% and a similar rate of systemic absorption occurs with rectal dosage forms. Renal elimination of the drug and its acetylated metabolite ranges from 20-30%. The majority of orally administered mesalamine is eliminated in the feces and the amount is proportional to dosage. Because of its limited absorption, adverse systemic effects have generally been considered minimal. There have, however, been case reports of pericarditis, hepatitis, gout, thrombocytopenia, peripheral neuropathy, etc. associated with administration of mesalamine. A number of reports of nephrotoxicity (interstitial nephritis, nephrotic syndrome, etc.) have also been attributed to the drug. A causal relationship between use of mesalamine and renal complications is difficult to establish because renal disease is considered by some to be an extra-intestinal manifestation of IBD. Two recent studies have evaluated the possible link between mesalamine and renal disease in patients with IBD. The first study compared the incidence of renal events (acute and chronic glomerulonephritis, nephrotic syndrome, and other types of nephritis/nephropathy) in three cohorts. These consisted of patients with IBD receiving mesalamine or sulfasalazine; a group with IBD not prescribed mesalamine; and a cohort getting mesalamine (for rheumatoid arthritis-RA), but without IBD. A reference cohort was also included. Results revealed that a total of 130/19,025 patients (0.17 cases per 100 patients per year) in the IBD/mesalamine cohort developed renal disease. In comparison, the rates in the IBD/no mesalamine and mesalamine-RA groups were 0.25 and 0.29 respectively. The reference group rate was 0.08. Another study evaluated the effects of mesalamine on renal function in 153 patients with Crohn's disease. The mean decline in creatinine clearance over an eleven year period was only 0.3 ml/min/year. In addition, there were no cases of interstitial nephritis or other types of renal disease. Based on these studies, it would appear that patients undergoing treatment with mesalamine have a minimal risk of renal disease. This risk may be partially attributable to the underlying IBD. Most authors still recommend that patients receiving mesalamine have their serum creatinine levels monitored every 3-4 months for the first year and once yearly thereafter.

References:

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