Correspondence

Malignant Colo-jejunal Fistula- A Rare Internal Fistula

Sir,

Small bowel fistula can be classified as internal, external and mixed. In internal gastro-intestinal fistulas a communication exists between segments of intestine or with any other hollow viscus, whereas in external gastro-intestinal fistulas intestine communicates with skin of abdominal wall. The mixed variety involves both internal and external communications often through an abscess cavity. Most of small intestinal fistulas (75-80%) occur as complication following surgery; rest (20-25%) includes spontaneous type.1-3 The principal causes of entero-enteric fistula in order of frequency are Crohn’s disease, diverticular disease, colo-rectal malignancy, radiation enteritis, tuberculosis and actinomycosis.2 The internal gastrointestinal fistulas include gastro-colic, duodeno-colic, entero-colic, entero-enteric, colo-vaginal and colo-vesical. Most common ileo-colic fistula is to sigmoid colon.1-3

Eighty five years female presented with constipation for three months followed by loose watery stools, 4-6 per day, small quantity, with crampy pain and streaky blood occasionally. She used to pass stool after 10-15 minutes taking oral feeds. Her weight was 38 kg, had mild pallor and was dehydrated. Hemoglobin was 7gm% with dimorphic anemia. Serum biochemistry was normal. On small bowel barium studies, there was rapid passage of contrast from small bowel and small amount of barium was noted in sigmoid colon. Barium enema studies showed a narrowing at recto-sigmoid junction with passage of contrast directly to jejunal loops from sigmoid colon (Fig. 1). Colonoscopy revealed a growth at recto-sigmoid junction which was proved to be adenocarcinoma on histopathology. CT scan for abdomen showed a thickened wall of sigmoid colon with infiltration in mesentery and loops of small bowel (Fig. 2). She was advised surgery and chemotherapy but refused.

The exact incidence of internal fistula in large bowel carcinoma is unknown. Malignant entero-enteric fistulas are usually from ileum or jejunum to colon and primary is frequently in sigmoid colon.2 However in malignancy obstruction and perforation are more common than fistulization.3 In entero-enteric fistulas, if a small length of bowel is by-passed, it may remain completely asymptomatic; there can be significant metabolic and nutritional deficiencies if longer lengths of bowel are by-passed.1-3 Bacterial overgrowth, mechanical by-pass and choleretic effects of conjugated bile acids entering colon, all contribute to diarrhea. Poor intake, impaired absorption because of in-formed by-pass, and catabolic sepsis lead to weight loss.1-2 Small bowel barium examination will show premature filling of distal colon and rectum. When underlying diagnosis is unknown, malignancy and diverticular disease may be excluded by barium enema. If there is any doubt about nature of colonic pathology, colonoscopy and biopsy can be done.2 Barium enema is most accurate as it can
Fenofibrate can Increase Serum Creatinine Levels in Renal Insufficiency

Sir,

Fenofibrate is widely used to treat hypertriglyceridaemia. It acts by increasing the expression of the LPL gene, while decreasing expression of apo-C III (a powerful inhibitor of LPL activity). Recent studies have shown that fenofibrate may cause a moderate reversible increase in serum creatinine levels. It has not been clearly studied whether the increased creatinine levels reflect a fenofibrate induced alteration of renal function or whether fenofibrate interferes with tubular handling of creatinine. Moreover there is no Indian data on this aspect.

A retrospective study was therefore done by us at Dr. Mohans’ Diabetes Specialities Centre and Madras Diabetes Research Foundation, Chennai. Medical records of diabetic subjects with no prior renal insufficiency who were given fenofibrate and followed for a minimum period of 3 years were studied. There was no significant increase of creatinine levels: 10 out of 50 patients (20%) had slight increase of creatinine in the range of 0.2 – 0.4 mg/dl, which however came down to normal with the continued use of fenofibrate.

We also studied 50 diabetic subjects with nephropathy who had received fenofibrate therapy for hypertriglyceridermia. This study revealed that 28 out of 50 patients (56%) had a marginal rise in creatinine levels even in the absence of other conditions, which may have affected the glomerular filtration rate. Liver enzymes remained unchanged.

It has been shown that fenofibrate induced changes in creatinemia induced by creatinine level measured by the Jaffe Technique were strongly correlated to those measured by HPLC (High Pressure Liquid Chromatography). A study done by Hohelart et al, prospectively examined the effect of two weeks fenofibrate (200mg) treatment on renal function in 13 hyperlipidemic patients with normal renal function or mild to moderate renal failure (creatinine clearance = 110 to 30 ml/min). This study showed that fenofibrate therapy significantly increases creatinine level in patients with mild to moderate renal failure but does not alter renal hemodynamics or the glomerular filtration rate. The increase in creatinine level is not due to an inhibition of tubular excretion of creatinine, since no changes in creatinine clearance were observed (69 ± 8 vs 68 ± 8 ml/min), but it appears to be associated with a parallel increase in urinary excretion of creatinine.

Another study by Broeders et al, reported on 27 patients who developed renal dysfunction when treated with a fibric acid derivative. The specific agents used in that study were fenofibrate and bezafibrate.

One possible explanation for these diverse effects of fibric acid derivatives could be that fibrates, such as fenofibrate, ciprofibrate and bezafibrate, impair the generation of vasodilatory prostaglandins, probably because of the activation of peroxisome proliferator-activated receptors (PPARs), which can down-regulate the expression of the inducible COD-2 enzyme.

We conclude that fenofibrate therapy does not affect creatinine levels in those without renal disease. However, it is better to withhold fenofibrate in those with established renal disease. If it is used, physicians should be aware that they can expect a marginal rise in creatinine levels which is most likely reversible on stopping the drug.

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Received : 12.12.2005; Accepted : 24.1.2006

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