SUCRALFATE

Pages with reference to book, From 105 To 107

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During the study of sulfated polysaccharides a compound \'sucralfate\' was developed[1]. It is a complex. salt of sucrose sulphate and aluminium hydroxide, which is poorly soluble in water and minimally in dilute acids and alkalies. When dissolved in stomach contents, after releasing aluminium salt it becomes strongly negative and combines with mucin to form a viscous suspension that binds with normal as well as defective mucosa. It binds pepsin but lacks anti-ulcer efficacy[1,2]. A combination of different actions enables sucralfate to prevent mucosal injury, these are its antipeptic effect, acting as a physical barrier, increasing the production, viscosity hypophobicity and aluminium, carbohydrate content of mucosa making it more acid resistant. It also promotes prostaglandin mediated and independent bicarbonate output from gastric and duodenal mucosa. Its effect on tissue growth regeneration and repair is also contributory[1-4]. Sucralfate has been reported as a safe drug during last 10 years of its use[5,6]. No systemic toxicity, teratogenicity or tumour producing effect have been reported, except hypophosphatemia and aluminium intoxication in patients with renal defect[7,8]. Although plasma aluminium levels in normal individuals are not increased in first 12 months of drug therapy, but in patients undergoing renal dialysis do show a substantial dose dependent rise in levels[9,10]. Therefore, it should be carefully used in ulcer patients with renal insufficien[7,9,10]. Most common side effect is constipation, observed in 1-3% patients, others occurring in 0-5% are dry mouth, nausea, vomiting, headache, urticaria and rash[11,12]. Absorption and bioavailability of some commonly used drugs like tetracycline[13] aminophylline[13], theophyline[14,15], ciprofloxacin[16,17], norfloxacin[18,19], phenytion[13,20] and digoxin[13] are effected when given with sucralfate, but in case of tetracycline, phenytoin and digoxin, this effect can be counteracted by giving 2 hours before sucralfate intake[13]. Its interaction with H2 receptor antagonist has not yet been studied completely, but the effect of combined therapy with antacids in animals has shown reduced binding of sucralfate to gastric mucosa[21]. Many trials have been conducted to assess the efficacy of sucralfate in the treatment of acute duodenal ulcers and long term therapy against relapses. Five randomised, double blind, placebo controlled studies in 23 patients on sucralfate therapy showed healing rate of 34%, 77%, 60%, 82% and 72% at 2, 4, 6, 8 and 12 weeks. In all sucralfate was better than placebo[22-26]. When compared with cimetidine in six, randomised double blind, controlled studies, healing rates at 4 weeks were 73% and 72% with sucralfate, 76% and 74% with cimetidine. In another study both drugs showed almost equal healing rate of 85% at 8 weeks with ig qid of sucralfate and 300 mg qid of cimetidine[27-32]. Effect of smoking on ulcer healing was reported in a Canadian study which showed a significantly lower healing rate in smokers than in non-smokers, after 4-8 weeks of anti-ulcer therapy[33]. Lam et al[34], reported that duodenal ulcer healing is not delayed in smokers when treated with sucralfate and H2 antagonist. There are some controversies about the role of anti-ulcer drugs in reducing the relapse of duodenal ulcer. Many studies support the possible advantage of sucralfate over H2 receptor antagonist but the idea has not yet been confirmed by any specific study[35]. Sucralfate as a maintenance therapy (ig bd) to prevent ulcer relapse has been approved by FDA[36]. One of five randomised, placebo controlled, double blind 12 month trial[10,37,38] showed 27% recurrence rate of duodenal ulcer with sucralfate as compared to 81% with placebo. In another similar study of 122 patients[39] where endoscopy was done monthly, by 4 months, a relapse of 36% and 55% was seen with sucralfate and placebo respectively. In a Japanese study[40], when sucralfate was compared with cimetidine almost similar results were observed at one

year, i.e., 60% with 400 mg/day of cimetidine and 58% with 2 g/day of sucralfate. Gastric ulcer healing is also higher with sucralfate than placebo, but it is of no use in gastric ulcer associated with duodenal ulcer[41,42]. When compared with cimetidine in four trials similar results have been observed at 4,8 and 12 weeks and same was reported for ranitidine but sucralfate showed better results than low dose antacids after 4 and 8 weeks of therapy[30,43,44]. The role of sucralfate in the prevention of gastric ulcer recurrence is debatable, many studies show a beneficial effect but still it is not recommended due to lack of placebo controlled studies. Comparison to cimetidine showed lower rates of endoscopically determined relapses at 12 month with sucralfate than cimetidine but in a small study ranitidine showed even better results than sucralfate, when endoscopy was done at 6 weeks or at recurrence of symptoms[45]. Patients with bleeding peptic ulcer get episodic bleeding which stops spontaneously. There is no specific therapy for the bleeding episode but benefit lies in long term maintenance therapy with sucralfate and other anti-ulcer drugs[46]. No placebo controlled study is done to assess the efficacy of sucralfate in bleeding stress ulcer. The claim is based only on comparative studies with antacids and Ff2 antagonist which show similar results for all 3 groups, so its role in stress ulcer is still controversial[47,48]. Patients in ICU with indwelling stomach tube, receiving antacids and specially during mechanical ventilation develop nosocoinial pneumonia. According to hypothesis based on previous studies due to rise in gastric pH, gram negative flora increase in stomach and their aspiration leads to pneumonia. Benefit of sucralfate in such patients is supposed to be due to its lack of effect on gastric p11, but no studies have established its advantage over H2 receptor antagonist[49,50]. In patients with duodenal ulcer receiving NSAIDs, sucralfate plays a part in healing of duodenal ulcer and relieving dyspeptic symptoms, but it has no role in preventing NSAID associated duodenal or gastric ulcer and their complication[51-54]. More than 20 placebo controlled clinical trials have shown its advantage in GOR and nonresponsive oesophageal disease but no effect on post sclerotherapy oesophageal ulcers[55-58]. As a topical treatment of stomatitis or proctitis induced by chemotherapy or radiation, its value has been proved by different studies[59,60]. Its role as sucralfate enema in inflammatory bowel disease, healing of decubitus ulcers on inflamed perianal skin and gastric bleeding prevention in patients on high dose steroids are subjects for further studies.

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