Gut, 1968, **9**, 5-6

Carbenoxolone sodium

There is now considerable support[1,2,3] for the original observation[4] that carbenoxolone will promote the healing of gastric ulcers, but our understanding of the mode of action and metabolic effects of the drug remains poor. Carbenoxolone does not seem to alter the normal processes of tissue growth and repair as judged by conventional histology[5] or by electron microscopy.[6] An effect upon mucosal resistance through alterations in the quality or quantity of gastric mucus has been suggested, but such an action has yet to be shown unequivocally in man.

Treatment with carbenoxolone is frequently complicated by fluid retention and by electrolyte disturbances, notably sodium retention. Hypokalaemia can also occur, but it is uncertain whether this is due to redistribution of the ion between the intracellular and extracellular compartments[7] or to a loss of total body potassium.[8] Administration of the aldosterone antagonist spironolactone will prevent the development of side effects, but it also blocks ulcer healing.[9] Reduction of the dose of carbenoxolone will reduce the frequency of side effects,[10] but does not always abolish them,[11] and the ulcer healing rate also falls. A variant of carbenoxolone which is devoid of effects on fluid and electrolyte balance is therefore clearly needed. The administration of a thiazide diuretic will prevent fluid retention without impairing ulcer healing,[9] but the risk of disturbances of potassium balance must be increased.

Peak blood levels of carbenoxolone are achieved extremely quickly after oral administration of the drug,[12] suggesting that a large proportion is absorbed from the stomach. Little may therefore enter the duodenum, which could explain why carbenoxolone in tablet form is ineffectual in duodenal ulcer.[4] To overcome this hypothetical disadvantage a positioned release preparation has been made containing carbenoxolone with other ingredients in a capsule designed to burst in the gastric antrum and liberate its contents into the duodenum. Initial clinical experience in a double-blind controlled trial suggested that the preparation was indeed of value in duodenal ulcer,[13] and this result has been supported by those obtained in two open trials in which the capsules were compared with anticholinergic and alkali preparations.[14,15] However, in another double-blind trial the preliminary results have suggested that the Duogastrone capsules were no more effective than the dummy preparation.[16] In addition studies of the behaviour of radioopaque capsules under the clinical conditions of use showed that they rarely entered the antrum, but tended to float and burst in the fundus of the stomach (a finding which might be predicted from the low specific gravity of the capsule).

Glycyrrhizinic acid extracted from liquorice is the basic substance used in the production of carbenoxolone. It has been suggested, however, that liquorice from which the glycyrrhizinic acid has been removed is not only free of the known side effects of carbenoxolone or glycyrrhizinic acid but remains effective in the treatment of peptic ulceration. In a clinical trial described in this issue[17] duodenal ulcer patients treated with a deglycyrrhizinated liquorice and alkali preparation were found to lose their symptoms more rapidly than those given a dummy

tablet which contained an identical amount of alkali. A limited investigation was also carried out in gastric ulcer; in five of six patients treated for four weeks the ulcer healed completely, including two of extremely large size, both being initially of more than 450 sq mm in profile area on barium meal examination before treatment. Three of the patients had previously been treated for four weeks with dummy tablets without any change in ulcer size and in two the ulcers were then observed to heal during treatment with the test preparation.

The conflicting results obtained with Duogastrone may in part be due to the comparatively small numbers of patients treated—less than 40 in each of the trials—and also to the difficulty in assessing the progress of duodenal ulcer. Further studies both of this preparation and of the deglycyrrhizinated liquorice (Caved-S) are needed before they merit general use. The results obtained in gastric ulcer with deglycyrrhizinated liquorice are clearly too few and too unusual for any reasoned judgement of its value to be possible.

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