A trial of deglycyrrhizinated liquorice in the treatment of duodenal ulcer

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SUMMARY A double-blind trial of deglycyrrhizinated liquorice was performed in 47 patients with active duodenal ulcer. Twenty-four patients received a placebo and 23 the trial medication (Caved-S) for one month. Both groups were clinically similar. No advantage of deglycyrrhizinated liquorice over placebo was found.

The introduction of liquorice extract and its active principle carbenoxolone and subsequent evidence of their efficacy in the treatment of gastric ulcers marked a significant advance in ulcer therapy (Doll, Hill, Hutton, and Underwood, 1962; Doll, Hill, and Hutton, 1965; Horwich and Galloway, 1965; Turpie and Thomson, 1965; Bank, Marks, Palmer, Groll, and van Eldik, 1967). This is a new class of drugs devoid of antacid activity which possibly enhance mucosal resistance. To avoid the sodium and fluid retention caused by whole liquorice extract and carbenoxolone, the latter was eliminated and a new preparation, deglycyrrhizinated liquorice (Caved-S) introduced. It did not cause sodium or fluid retention and was reported to be active in gastric ulcer (Tewari and Trembalowicz, 1968; Russell and Dickie, 1968), and more interestingly in duodenal ulcer in which carbenoxolone was not proved to be effective (Doll *et al*, 1962; Cliff and Milton-Thompson, 1970). In this article we report a double-blind trial of de-

glycyrrhizinated liquorice (Caved-S) in patients with duodenal ulcer.

Material and Methods

Included in the trial were patients from the clinic suffering from duodenal ulcer for at least six months. The patients had recent radiological proof of a deformed bulb or ulcer niche and had ulcer pains at the start of the study. Data on the subjects studied are given in Table I. The following tests were performed before and after the trial: blood count, urine analysis, blood urea, GO-transaminase, bicarbonate, sodium, potassium, and chloride. Patients were seen before and then one week, two weeks, and 30 days after the start of therapy. At each visit they were examined, interviewed, and the symptoms recorded using a standard questionnaire. Blood pressure and weight were also recorded. We personally examined and followed up all patients.

The study was double blind with patients receiving

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	Placebo Group (24)	Treated Group (23)
<i>Age</i>		
Mean (range)	43.4 (15-64)	38.9 (19-70)
<i>Sex</i>		
Male	17	15
Female	7	8
Average duration of disease (yr)	10.1	8.2
Previous complications (bleeding, perforation)	3	3
<i>Previous admissions to hospital</i>		
No. of subjects	10	11
No. of admissions	18	13
Smokers	12	14
Average duration of present attack (mth)	2.5	2.6
No. of subjects with attacks = 1 month	10	12
Eliminated from study	1	2

Table I *Patients studied*

coded tablets, the code being revealed only after completion of the study. Patients received two tablets three times a day after meals for 30 days and were instructed to chew them before swallowing. Each Caved-S tablet contained 380 mg deglycyrrhizinated powdered block liquorice, 100 mg bismuth subnitrate, 100 mg aluminium hydroxide gel, 200 mg magnesii carbonas levis, 100 mg sodium bicarbonate, and 30 mg powdered frangula bark. The placebo tablets were inert tablets of the same composition except that each contained lactose flavored with aniseed to simulate the taste of liquorice.

Patients were instructed to eat at least five meals a day and to take an antacid tablet as necessary for pain or heartburn and to record the number of tablets taken. The antacid (Lucol) contained 180 mg aluminium hydroxide and 60 mg magnesium hydroxide. No dietary restrictions were imposed. Fifty patients started the trial and 47 completed it. One patient developed pyloric stenosis after nine days of treatment and was operated on; another patient failed to appear for follow up. Both these patients belonged to the treated group. A patient of the placebo group stopped taking the coded tablets and changed medication during the trial period. Results of the trial were evaluated before revealing the code. The disappearance of pain during the trial was classified as a success while the persistence of pain was classified as a failure.

Results

Results of treatment are detailed in Table II. There were no significant differences between the two groups. There were no side effects attributable to treatment and, in particular, no fluid retention and no effects on blood pressure and electrolytes. Laboratory examinations remained normal through-

out the study. Constipation was improved during treatment in both groups.

Discussion

Gassman and Forster (1963) reported on the favourable effects of deglycyrrhizinated liquorice in patients with duodenal ulcer. Of 30 patients studied 'good' results were obtained in 17 and an 'improved effect' noted in another eight. 'All postprandial complaints completely disappeared within five to eight days after the use of an average of 40 tablets' in these patients as well as in some patients with gastric ulcer. No controls were studied and the trial was not blind. Russell and Dickie (1968) reported results of a double-blind trial in 16 patients with gastric ulcer and 32 patients with duodenal ulcer. An effect was noted in the gastric ulcer patients, while in duodenal ulcer patients the difference in the clinical improvement between the treated group and the control group 'was not statistically significant'.

Tewari and Trembalowicz (1968) reported excellent results in 48 patients with duodenal ulcer and in six patients with gastric ulcer in a double-blind trial. The clinical effect is reported for both ulcer types together. Results were 'good' or 'improved' in 25 of 28 treated patients versus eight of 26 controls. In 15 patients with duodenal ulcer the therapy was crossed over after four weeks and again much better results were reported in the treated group with 12 out of 15 'improved' versus three out of 15 controls. Mills and Damrau (1969) report a double-blind crossover trial including 22 patients with duodenal ulcer. The patients were treated for four weeks with a crossover at two weeks. Only 18 of the 22 patients had pain at the start of the trial. Relief of pain was obtained in 78% of treated patients and in 33% of the placebo group.

Symptom	No. with Symptoms	Symptom Relieved	Average Time to Relief (dy)
<i>Pain</i>			
Placebo	24	11	15.2
Caved-S	23	12	18.8
<i>Nocturnal pain</i>			
Placebo	21	14	13.4
Caved-S	21	16	15.9
<i>Heartburn</i>			
Placebo	19	9	14.7
Caved-S	16	7	19.0
<i>Nausea</i>			
Placebo	14	9	15.7
Caved-S	14	9	12.8
<i>Vomiting</i>			
Placebo	5	2	7.0
Caved-S	6	4	15.5

Table II Results¹

¹The average consumption of antacid tablets in 30 days was 107 in the placebo group and 91 in the treated group.

In our study no significant differences were found between the placebo and the treated groups.

The differences between the reported results are not easy to explain. Crossover trials in patients with duodenal ulcer are not easy to evaluate. In particular, it is not clear how after one month of reportedly successful therapy with complete relief of symptoms another drug (placebo) can be evaluated using clinical criteria. Even if the placebo is used first, the attack may be expected to subside within a month in part of the group.

In view of the conflicting reports more studies will have to be performed before a therapeutic effect can be attributed to deglycyrrhizinized liquorice in patients with duodenal ulcer.

It is not clear whether our results reflect on the efficacy of liquorice extract after the removal of carbenoxolone or merely on its efficacy in duodenal as contrasted to gastric ulcer. In common with others we found no side effects attributable to treatment with deglycyrrhizinized liquorice.

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References

- Bank, S., Marks, I. N., Palmer, P. E. S., Groll, A., and Eldik, E. van. (1967). A trial of carbenoxolone sodium in the treatment of gastric ulceration. *S. Afr. Med. J.*, **41**, 297-300.
- Cliff, J. M., and Milton-Thompson, G. J. (1970). A double-blind trial of carbenoxolone sodium capsules in the treatment of duodenal ulcer. *Gut*, **11**, 167-170.
- Doll, R., Hill, I. D., and Hutton, C. G. (1965). Treatment of gastric ulcer with carbenoxolone sodium and oestrogens. *Gut*, **6**, 19-24.
- Doll, R., Hill, I. D., Hutton, C. F., and Underwood, D. J., II. (1962). Clinical trial of a triterpenoid liquorice compound in gastric and duodenal ulcer. *Lancet*, **2**, 793-796.
- Gassmann, R., and Forster, G. (1963). Erfahrungen mit dem Succus liquiritiae-präparat Caved-S bei der Behandlung von Ulzern des Magen-Darm-Tractes. *Ther. Umsch.*, **20**, 306-312.
- Horwich, L., and Galloway, R. (1965). Treatment of gastric ulceration with carbenoxolone sodium: clinical and radiological evaluation. *Brit. med. J.*, **2**, 1274-1277.
- Mills, D. H., and Damrau, F. (1969). Deglycyrrhizinized glycyrrhiza in treatment of peptic ulcer; double-blind crossover clinical trial in 40 cases. *Int. med. Dig.*, **4**, 36-44.
- Russell, R. I., and Dickie, J. E. N. (1968). Clinical trial of a deglycyrrhizinized liquorice preparation in peptic ulcer. *J. Ther. clin. Res.*, **2** (1), 2-5.
- Tewari, S. N., and Trembalowicz, F. C. (1968). Some experience with deglycyrrhizinized liquorice in the treatment of gastric and duodenal ulcers with special reference to its spasmolytic effect. *Gut*, **9**, 48-51.
- Turpie, A. G. G., and Thomson, T. J. (1965). Carbenoxolone sodium in the treatment of gastric ulcer with special reference to side-effects. *Gut*, **6**, 591-594.