United States Patent Office 2,868,693 Patented Jan. 13, 1959

2,868,693

PEPTIC ULCER-TREATING COMPOSITIONS CONTAINING GLUTAMINE

William Shive and Joanne M. Ravel, Austin, Tex.

No Drawing. Application July 16, 1956
Serial No. 597,893

2 Claims. (Cl. 167—55)

This invention relates to pharmaceutical preparations and particularly to one for the treatment of peptic ulcers. The invention also involves the method of therapeutic treatment of peptic ulcers with this composition.

Peptic ulcers are a distressing disease of man. A peptic ulcer is a circumscribed erosion of the mucous membrane of the lower end of the esophagus, in the stomach or duodenum, or on the jejunal side of a gastrojejunostomy. As the outstanding symptom of a peptic ulcer is pain, various modes of therapy have been attempted for its treatment. This pain may vary in degree from a mild discomfort to a sharp, severe, sometimes penetrating sensation. The discomfort may become so steady or gnawing that the patient is forced to seek relief from a physician. Moreover, uncontrolled bleeding from an ulcer occurs in some patients and the resulting loss of blood is of obvious serious consequence.

To relieve the symptoms of peptic ulcers and to bring about its healing, the physician resorts to several treatments. Primarily this may involve complete rest and frequent feedings of bland diets of a gruel-like consistency. Medication is aimed at minimizing the hyperacidity and intestinal spasms which are associated with peptic ulcers. This may include the administration of an alkali which will act as an antacid. Sedatives are frequently given to allay anxiety and reduce nervous tension, and antispasmodics may be given to control intestinal spasms.

More recent therapy has involved the administration of anticholinergic compounds which serve to reduce the secretion of acid into the stomach. The resulting reduced flow of hydrochloric acid relieves the pain symptoms and serves to produce a condition which is likely to induce healing. However, these anticholinergic drugs have the disadvantage that they are not specific in their action and the patient complains of a generally dry condition. The mouth and throat are dry as salivation is reduced. The skin feels dry as perspiration is reduced, and urinary output is greatly diminished. As a consequence many patients are reluctant to resort to treatment with these anticholinergic compounds.

In accordance with the present invention a composition is provided which is eminently suitable for the therapeutic treatment of peptic ulcers. Although its exact mode of action is not known, and although it does not appear to be anticholinergic in its activity, the preparation has been found to eliminate or greatly reduce the pain of peptic ulcers. Its administration also has been found to result in increased healing of the ulcer crater.

The principal ingredient of the preparation of the invention is glutamine. Although glutamine has been administered as a medicine for other purposes, the present invention involves the surprising discovery that it is particularly useful for the treatment of peptic ulcers.

The glutamine may be administered in daily amounts as low as 0.2 gram, and it may approach such large amounts that undesirable manifestations such as toxicity begin to occur, although this maximum amount has not been determined. As 27 grams have been administered

in a single dose without any obvious toxicity, it appears to be virtually non-toxic. A preferred dosage per day appears to be within the range of 0.2 to 10.0 grams, and the optimum is between 1 to 5 grams daily.

As glutamine is a powder it may be readily administered by its enclosure within capsules. Each capsule may contain as low as 100 milligrams of glutamine, or as high as 1 gram, or as large as may be easily swallowed. The powder may also be taken after suspending or dissolving in water by drinking the resulting preparation. Any other equivalent manner of orally taking the glutamine, such as compressing it in a tablet, will be as effective and such equivalent pharmaceutical preparations are contemplated by the invention.

In some instances the total daily dosage may be given at one time, but it is generally preferred to give the material four times daily, such as one hour after each meal and before retiring. Some cases have responded well by taking the glutamine 30 minutes before meals and also at bedtime. Greater or fewer subdivisions of the total daily desired dose may obviously be made to suit the particular conditions of the patient.

The invention will be further clarified by reference to the following examples:

EXAMPLE 1

Thirty grams of l-glutamine are evenly distributed into sixty capsules so that each contains 0.50 gram. Each capsule is regarded as a pharmaceutical composition constituting a single dosage and one or two of them are taken an hour after meals and at bedtime.

EXAMPLE 2

Thirty grams of l-glutamine are evenly distributed into one hundred twenty capsules so that each contains 250 mg. Each capsule is regarded as a pharmaceutical composition constituting a single dosage and as they are smaller than the capsules of Example 1 they are more acceptable to some patients. Two or three of them may be taken at a time a half hour before meals and at bedtime.

EXAMPLE 3

Sixty grams of l-glutamine are evenly distributed into sixty capsules so that each contains 1.0 gram. Each capsule is regarded as a pharmaceutical composition constituting a single dosage and one or two of them is taken an hour after meals and at bedtime.

EXAMPLE 4

Tablets containing l-glutamine are made by first combining the following ingredients:

	Grams
l-Glutamine	50.0
Lactose	14.0
Starch	11.8
Starch (10% paste)	2.0
Magnesium stearate	0.7
	78.5

These ingredients are thoroughly mixed and compressed into one hundred tablets, using known pharmaceutical techniques. Each tablet is regarded as a pharmaceutical composition constituting a single dosage and one or two of them is taken a half hour before meals and at bedtime.

EXAMPLE 5

Half a gram of l-glutamine is measured out and added to half a glass of water. It is vigorously stirred and drunk. This is regarded as a pharmaceutical composition constituting a single dosage and is taken a half hour before meals and at bedtime.

If satisfactory results are obtained with the dosage

schedule mentioned in the above examples, the total amount taken each day is reduced by omitting one or two of the usual medication intervals, or by taking a smaller amount each time. On the other hand, if satisfactory results are not obtained, the total amount taken each day is increased by adding one or several more times during the day at which medication is given or by taking an increased amount each time.

The following case histories show the effectiveness of the pharmaceutical compositions:

Case 1

W. A., a 34 year old white, married male when first seen had the complaint of stomach trouble for about six months. Pain was described as deep burning, worse when nervous. For several weeks he had noted relief for about one and a half hours after eating.

X-ray of the stomach revealed a crater in the midportion of the duodenum measuring 0.5 x 0.5 cm. There was a large area of inflammatory reaction about the crater. At this time the patient was placed on an ulcer regimen as follows: (1) Bland, low residue diet with milk every two hours when awake. (2) Antacids 1 hour P. C. and P. R. N. (3) Anticholinergic with phenobarbital 1 t. i. d. A. C. and 2 H. S. (4) Multivitamins.

Recheck X-ray about two weeks later revealed the previously described crater which was said to have increased slightly in size. Four days later he was started on glutamine, two 250 mg. capsules, t. i. d. for 10 days with meals, in addition to the above regimen. At this time he was having very little epigastric discomfort. Eleven days after glutamine therapy was started, X-ray studies revealed no evidence of duodenal ulcer.

Case 2

A chronic ulcer patient for about 35 years, D. M. had had two operations for this. She continued to experience pain despite fairly strict medical management.

When first seen upper GI series showed coarse gastric mucosa, marked deformity of the pyloric end of the stomach, the pylorus and the duodenal bulb with evidence of an ulcer crater in the duodenum, no significant obstruction, and a pseudodiverticulum at the pyloric end of the stomach from scarring. Two days later, when she was placed on glutamine therapy, two 200 mg. capsules, 4 times daily, she was having considerable pain and marked tenderness over the duodenum.

She experienced almost complete relief within about 4 days and when seen on the eighth day was free of pain. She felt definitely more relaxed and even slightly euphoric. On the tenth day upper GI tract studies showed a constant deformity of the duodenal bulb, and whether or not an ulcer crater was present was questionable, but at least an ulcer scar was visualized. The ulcer if present at all was almost completely healed.

Case 3

F. G., a 48 year old white male, was found to have an ulcer which was 8–10 mm. by 3–5 mm. in size. He was placed on hourly milk and cream regimen.

X-ray two weeks later indicated approximately the same measurements in size of the ulcer. Glutamine capsules (200 mg.) 2, four times daily were started in addition to his ulcer regimen of diet, Belladonna and Equanil. He was free of symptoms at this time.

He was again X-rayed after completion of eleven days of glutamine therapy. At this time, the presence of an ulcer crater was doubtful and difficult to determine because of scarring. Routine continued without glutamine, and X-ray a month later showed scarring only. Patient is being continued on modified ulcer regimen.

Case 4

M. G., white female, age 38, complained of abdominal pain of three weeks duration. The pain was located in the epigastrium and left upper quadrant and similar to pain noted a year earlier, when a diagnosis of duodenal ulcer was made following X-ray studies. At that time the patient was placed on a bland diet, antacid (gelucil), and antispasmodic (centrine). She responded to this regimen but noted that she had recurrences of epigastric distress when she became nervous and tense. She would obtain relief by going on a soft diet during these periods.

Four days before she was seen, the abdominal pain became more severe in spite of the intensified antacid and antispasmodic therapy as well as the soft bland diet.

Physical examination: Temperature—98.6; pulse—80; respiration—20; blood pressure—116/60. The patient did not appear ill. Tenderness midway between the zyphoid process and the umbilical area was noted as was tenderness in the left upper quadrant. Routine laboratory work-up including urinalysis, sedimentation rate, hemoglobin, and differential count, were within normal limits.

Upper G. I. X-rays revealed a peptic ulcer 10 x 5 mm. on the lesser curvature. The patient was continued on the same treatment that she had placed herself on, and glutamine was added in dose of 1.6 grams per day. The pain cleared on the third day following the institution of glutamine therapy which was continued for ten days.

Follow-up X-rays eleven days later revealed faintly visualized base of the crater at the lesser curvature. These findings were considered to indicate approximately 80% healing of the ulcer.

Three weeks after the start of glutamine therapy, X-ray visualization of the upper G. I. tract revealed complete healing of the ulcer on the lesser curvature.

There was no recurrence of ulcer symptoms when last seen one month later.

Case 5

A. H., female, 51 years old, reported that she had intermittent pains in her stomach since 1943. Five years ago the pains became more or less constant which the patient described as continuous pain. The pain was more intense on eating certain foods. Two years ago, she had her gall bladder removed, but no stones were found and her pain was not relieved. Recently, radiological examination revealed a gastric ulcer 28 mm. wide and 20 mm. in depth. The patient was given two 200 mg. capsules of glutamine four times daily, one hour after meals and before retiring, and was placed on a bland diet. The patient was free of pain after 7 days of therapy, and radiological examination two weeks later showed that 94 percent of the area was healed. Subsequent radiological examination at one month showed complete healing of the ulcer crater.

What is claimed is:

1. The method of treating peptic ulcers in humans which comprises introducing into the stomach of the person suffering from said ulcers at least 0.20 grams of glutamine per day, and less than the amount which incites toxicity manifestations.

2. The method of treating peptic ulcers in humans which comprises introducing into the stomach of the person suffering from said ulcers from 0.2 to 10.0 grams of glutamine per day.

References Cited in the file of this patent

UNITED STATES PATENTS

2,283,817 Martin ..... May 19, 1942

OTHER REFERENCES

Archibald: Chem. Rev., vol. 37, 1945, p. 162.