Palliative Treatment of Benign Prostatic Hypertrophy

Reprinted from the March 1958 issue of The Journal of The Maine Medical Association

Henry M. Feinblatt, M.D. and Julian C. Gant, M.D.

In a controlled clinical investigation of benign prostatic hypertrophy, a course of medication containing a mixture of amino acids (Glycine, Alanine and Glutamic Acid) was found to be effective in reducing the size of the prostate and relieving the associated symptoms of discomfort, nocturia, delayed micturition, frequent urination and urgency. As compared with the controls, the results are statistically significant. The value of the Glycine-Alanine-Glutamic Acid mixture for relief of symptoms of benign prostatic hypertrophy was suggested by a chance observation made by one of us (J.C.G.)(1) and an associate. A group of allergic patients were being given an amino acid mixture and during the course of treatment one of the patients volunteered the information that all of his urinary symptoms had disappeared. This led to a trial of that particular amino acid mixture in non-allergic patients with urinary symptoms. Patients with enlarged prostates and associated urinary symptoms experienced prompt and rather spectacular relief of their symptoms. A number of these patients have been observed over a prolonged period of time. They remain symptom free while taking the medication, but soon after discontinuing it the symptoms of urgency, nocturia, etc., returned. This has been the experience of several physicians who have tried the amino acid treatment at our suggestion.

These original findings have been confirmed by an independent controlled clinical test.

CONTROLLED CLINICAL TEST

To determine the value of the medication, a series of 40 cases of benign prostatic hypertrophy were treated with glycine-alanine-glutamic acid capsules for a period of three months. As controls, the same patients were given a placebo for a comparable period of two months. Our conclusions were drawn from this comparison.

The series included 40 men with diagnosed benign prostatic hypertrophy. Enlargement of the prostate was determined by rectal palpation. Patients having an indurated nodule located in one prostatic lobe were excluded because of possible malignancy (Jewett (2)). In addition, all subjects were given roentgenographic examination as an additional diagnostic precaution.

All patients were referred or checked by a urologist before assignment to this research program. Our consultations with urologists resulted in a decision in favor of conservative treatment. The conditions were diagnosed as benign and had not progressed at any significant rate of speed. If relief could be secured by non-surgical treatment, no advantage could be obtained by more radical procedures.

The age range was from 37 to 75, average 60. Weight ranged from 101 to 192 lb., average 163 lb. Height ranged from 65 to 73 in., average 68 in. The duration of the complaint ranged from one to six years, average four years.

The condition of the prostate on palpation was a swelling in nine cases, soft swelling in 23 cases, and prominent enlargement (easily felt) in eight cases.

The symptoms were discomfort in 35 cases, nocturia in 39, delayed micturition in 23, excessive frequency of urination in 29, and urgency of urination in 27 cases.

All patients with contributory diseases, as disclosed by the history and physical examination, were excluded from this group. In the even numbered cases, as they presented themselves, the placebo capsules were substituted for glycine-alanine-glutamic acid capsules. They were given according to the same dosage schedule and the patients were not aware of the fact that they were taking a placebo. This regimen was continued for a period of two months.

The odd numbered cases, as they presented themselves, were given glycine-alanine-glutamic acid, two capsules three times daily after meals for two weeks, thereafter one capsule three times daily. This regimen was continued for a period of three months. Later the placebo cases were switched to glycine-alanine-glutamic acid medication and vice versa. The results form a basis of comparison which gives a reliable indication of the therapeutic value of the medication. All signs and symptoms were re-evaluated periodically in both groups. Routine chemical and microscopical examination of the urine was performed. Individuals with positive urinary findings were excluded from the group.

RESULTS OF THERAPY

As shown in the table, the treatment was followed by reduction of prostatic enlargement and relief of the attending symptoms in significant percentages of cases. The size of the prostate was reduced in 92%, to normal size in 33%. Nocturia was relieved in 95% of cases (completely in 72%), urgent urination in 81%, frequency in 73%, discomfort in 71%, and delayed micturition in 70%. No comparable improvement was observed in the controls.

TABLE COMPARISON OF THERAPEUTIC RESULTS

Glycine-Alanine-Glutamic Acid Capsules vs. Placebo Capsules

	Glycine-Alanine-Glutamic Acid	*Placebo*
Enlargement Reduced	92%	5%
Restored to Normal Size	33%	0
Nocturia Relieved	95%	15%
Nocturia Relieved Completely	72%	5%
Urgent Urination Relieved	81%	11%
Frequency Urination Relieved	73%	15%
Discomfort Relieved	71%	9%
Delayed Micturition Relieved	70%	4%

There were no adverse reactions in any case.

RATIONALE

During the course of medication we frequently observed disappearance of pitting edema in the legs and various parts of the body. Since the prostate and surrounding pelvic tissues are often congested and edematous in cases of benign prostatic hypertrophy, leading to pressure upon the base of the bladder in the region of the sensitive trigonum vesicae, the swelling leads to characteristic symptoms of bladder irritability which are associated with benign prostatic hypertrophy.

There is reason to believe that the anti-edemic action of glycine, alanine and glutamic acid reduces edematous swelling of the prostate and neighboring pelvic tissues and in this way provides the therapeutic benefits described in this paper. Edema is one of the most important symptoms of protein deficiency (Youmans (3)) and in such cases dietary protein and amino acids serve a useful function as a diuretic agent (Stare and Thorn (4)).

Glycine, alanine and glutamic acid are three of the dispensable amino acids (Elman (5)). As such they are unit components of food and tissue proteins. We must therefore consider the possibility of a definite metabolic effect in explanation of the results. Therapeutic properties have been established

definitely for certain individual amino acids. Thus methionine has proved to be useful in cases of cirrhosis of the liver (Beams and Endicott (6)), diaper rash (Goldstein (7)), and vitreous opacities (Eggers (8)). Administration of lysine to nutritionally substandard infants produces marked increases in body weight and appetite (Albanese et al. (9, 10)). Many other examples of therapeutic effects produced by individual amino acids could be cited.

Glycine has been used with reported benefit in the treatment of various myopathies and peripheral vascular insufficiency (United States Dispensatory (11)).

Favorable results with glutamic acid have been reported in the treatment of petit mal and psychomotor epilepsy (Price, Waelsch and Putnam (12)) and of mental deficiency (Zimmerman and Ross; (13) Albert, Hoch and Waelsch (14)). Numerous other therapeutic uses have been published (United States Dispensatory (15)).

We believe that ours is the first published report on the value of glycine, alanine and glutamic acid in the treatment of benign prostatic hypertrophy. It is hoped that other physicians will investigate this field of usefulness.

DISCUSSION

Prostatic hypertrophy is part of the normal aging process and is undoubtedly present to a certain extent in all elderly men. After forty-five, more than 50% of all men develop benign prostatic hypertrophy (Hinman (16)). Pathologically, the condition is a benign hyperplasia of the prostatic glandular tissue of an adeno-fibromatous nature.

Statistics supplied to the authors by the Metropolitan Life Insurance Company (17) report a death rate of 3.9 per 100,000 population from benign prostatic hypertrophy in 1953, 3.8 in 1954, and 3.7 in 1955.

As Chapman (18) has written, prostatic enlargement should be regarded, like arcus senilis and canities, as normal concomitants of old age which occur often enough to be regarded as a variety of the normal. Only when there is obstruction to the flow of urine does the condition become a disease. Usually the growth of the prostate slows down around the age of sixty. Non-progressive types of the disease should be treated expectantly. Chapman states, and we agree, that it is unjustifiable to remove the prostate merely because it is enlarged and has been associated with some urinary symptoms.

In the great majority of cases of benign prostatic hypertrophy, there is a large field for medical treatment including the use of glycine-alanine-glutamic acid mixture. Except in emergencies, conservative measures should be given a fair trial before resorting to prostatectomy.

CASE REPORTS

Case 1. J. B., age 57, weight 181 lb., height 72 in., complained of prostatic symptoms dating back five years. He suffered from a feeling of pressure in the perineal region, discomfort on urination, difficulty in starting micturition, nocturia (twice per night), excessive frequency and urgency.

On rectal palpation enlargement of the prostate took the form of a soft swelling. Otherwise there were no physical findings. Roentgenographic examination was negative.

The diagnosis was benign prostatic hypertrophy.

Placebo capsules were administered according to a definite schedule: two capsules three times daily after meals for two weeks, thereafter one capsule three times daily. This regimen was continued for two months. The patient was not told that he was taking a placebo.

At periodic examinations and also at the end of the two months, there was no change in the size or condition of the prostate gland. None of the symptoms were relieved, even partially.

The patient was then switched to glycine-alanine-glutamic acid capsules, two capsules three times daily after meals for two weeks, thereafter one capsule three times daily. This regimen was continued for three months.

With this treatment the symptoms of discomfort, nocturia, difficulty in starting micturition, excessive frequency and urgency were relieved completely. On rectal palpation the size of the prostate gland was

reduced to normal.

There were no untoward reactions and the urine was negative throughout both periods of observation. Case 2. P.W., age 66, weight 152 lb., height 67 in., complained of prostatic symptoms dating back six years. He suffered from difficulty in starting micturition, scanty flow after beginning, discomfort on urination, a feeling of pressure in the perineal region, and nocturia (twice per night).

The prostate was palpated via the rectum and outlined as a soft swelling. Physical and roentgenographic examinations were otherwise negative.

The diagnosis was benign prostatic hypertrophy.

Placebo capsules were administered according to a definite schedule: two capsules three times daily after meals for two weeks, thereafter one capsule three times daily. This regimen was continued for two months. The patient was not informed that he was taking a placebo.

At each regular examination and also at the end of the observation period, no change was found in the size or condition of the prostate gland. None of the symptoms were relieved, even partially.

The patient was then switched to glycine-alanine-glutamic acid capsules, two capsules three times daily after meals for two weeks, thereafter one capsule three times daily. This regimen was continued for three months.

Under the glycine-alanine-glutamic acid treatment, the size of the prostate gland was reduced to normal. All of the symptoms of delayed micturition, scanty flow after starting, discomfort, perineal pressure and nocturia were relieved completely.

No untoward reactions were observed at any time and the urine remained constantly normal.

CONCLUSIONS

1. In a series of 40 cases of diagnosed benign prostatic hypertrophy, the use of glycine-alanine-glutamic acid capsules reduced the size of the enlarged prostate in 93% cases, including 33% in which the gland was restored to normal size. With the placebo only 5% showed partial reduction of prostatic enlargement, in no case to normal size.
2. The treatment relieved nocturia in 95% (complete relief in 72%), urgency in 81%, frequency in 73%, discomfort in 71%, and delayed micturition in 70%. With the placebo nocturia was relieved in 15% (complete relief in 5%), urgency in 11%, frequency in 15%, discomfort in 9%, and delayed micturition in 4%.
3. No untoward effects were observed in any case.
4. The modus operandi appears to be an anti-edemic (diuretic) action whereby edematous swelling affecting the prostate gland and surrounding perineal tissues is reduced. A special metabolic activity may be a factor.
5. The great majority of cases of benign prostatic hypertrophy should be treated conservatively and the glycine-alanine-glutamic acid mixture is recommended as an effective palliative.

REFERENCES

1. *Gant J.C., jt. auth.*
2. *Jewett, H. J., Significance of the palpable prostatic nodule, J.A.M.A. 160:838, 1956.*
3. *Youmans, J. B., The clinical detection of protein deficiency, J.A.M.A. 128:439, 1945.*
4. *Stare, F. J., and Thorn, G. W., Protein nutrition in problems of medical interest, J.A.M.A. 127:1120, 1945.*
5. *Elman, R., The practical use of amino acids in protein nutrition, J.A.M.A. 128:659, 1945.*
6. *Beams, A. J., and Endicott, E. T., Histologic changes in livers of patients with cirrhosis treated with methionine, Gastroenterology 9:718, 1947.*
7. *Goldstein, L. S., Napkin dermatitis caused by ammoniacal urine; treatment with methionine, Arch. Pediat. 66:553, 1949.*
8. *Eggers, H., Lipotropic substances for absorption of vitreous opacities, New York J. Med. 51:2255, 1951.*
9. *Albanese, A. A. et al., Biochemical and nutritional effects of Lysine-reinforced diets, Am. J. Clin. Nutrition 3:121, 1955.*

10. *Albanese, A. A. et al., Lysine supplementation in infant feeding; dosage considerations, New York State J. Med. 55:3453, 1955.*
11. *U.S. Dispensatory, ed. 25, Philadelphia, J. B. Lippincott Co., 1955, pp. 63-64.*
12. *Price, J. C., Waelsch, H., and Putnam, T. J., dl-Glutamic acid hydrochloride in treatment of petit mal and psycho-motor seizures, J.A.M.A. 122:1153, 1943.*
13. *Zimmerman, F. T., and Ross, S., Effect of glutamic acid and other amino acid on maze learning in white rat, Arch. Neurol. & Psychiat. 51:446, 1944.*
14. *Albert, K., Hoch, P., and Waelsch, H., Preliminary report on effect of glutamic acid administration in mentally retarded subjects, J. Nerv. & Ment Dis. 104:263, 1946.*
15. *Ibid. ref. No. 10, p. 610.*
16. *Hinman, F., The obstructive prostate, J.A.M.A. 135:136, 1947.*
17. *Metropolitan Life Insurance Company, National Office of Vital Statistics, Special Reports Volume 46, No. 1.*
18. *Chapman, T. L., Expectant treatment of benign prostatic enlargement, Lancet 2:684, 1949.*

Dr. Feinblatt, 154 Woodruff Avenue, Brooklyn 26, New York

Dr. Gant, Madison Sanitarium and Hospital, Madison College, Tennessee