United States Patent [19]

Glasser

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[54] **TREATMENT OF ARTHRITIS WITH COMBINATIONS OF ANTIHISTAMINIC COMPOUNDS AND DIURETICS**

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[21] Appl. No.: **714,413**

[52] **U.S. Cl.** **424/246,** 424/263, 424/330

[51] **Int. Cl.** **A61k 27/00**

[58] **Field of Search**.....424/240, 263, 330

[56] **References Cited**

OTHER PUBLICATIONS

Grollman, Pharmacology and Therapeutics, 6th Ed., (1965), pp. 444–445.

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Attorney—Hubbell, Cohen & Stiefel

[57] **ABSTRACT**

Therapeutic treatment of arthritis. Involves internally administering specified antihistaminic compounds in conjunction with specified diuretic compounds.

8 Claims, No Drawings

TREATMENT OF ARTHRITIS WITH COMBINATIONS OF ANTIHISTAMINIC COMPOUNDS AND DIURETICS

BACKGROUND OF THE INVENTION

1. Field of the Invention

This invention relates to a method of treating arthritis so as to substantially alleviate pain and suffering therefrom.

2. Description of the Prior Art

Heretofore a great number of different methods have been attempted in an effort to provide effective therapeutic treatment for arthritis. By way of example, the prior art has employed for such treatment indocin, butozolidine, salicylates, gold therapy, steroids, ACTH, quinine derivatives, etc., all without achieving a very satisfactory therapeutic effect.

SUMMARY OF THE INVENTION

I have found that by administering average therapeuitc doses of the antihistamine compounds and diuretic compounds listed hereinafter, in combination with one another, to individuals afflicted with arthritis, a marked improvement may be achieved. In distinct contrast, when used alone neither component is capable of eliciting such a response. The components apparently act synergistically with one another so as to become a potent anti-inflammatory agent.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

Satisfactory classification of the arthritides and related conditions is still considered unsatisfactory. The reason for this is that the etiological and basic pathological factors are not clearly understood. Be that as it may, wherever there is joint stiffness of the arthritic or related type accompanied by pain, swelling, or deformity, the method of my invention, involving administering the antihistaminic compound and diuretic compound in physiological doses, either intramuscularly or orally, has proven effective. Stiffness of the affected joint and its surrounding structures subsides, pain diminishes, and function improves. This generally is achieved within ten days after therapy is begun. If the sedimentation rate of the blood is elevated, it gradually returns to normal.

In gouty arthritis, patients may experience a substantial improvement within 48 hours with a corresponding drop in blood uric acid. For this reason, the combination of an antihistaminic compound and a diuretic compound employed in my method is also an excellent uricosuric agent.

Thus, by administering standard dosages (e.g. U.S.P. dosages) of the antihistamine and the diuretic at the same time, I have found that both compounds are capable of exerting a unique anti-arthritic effect when used in combination, although the use of either compound by itself has no apparent effect on the course of the disease. When a composition containing both the antihistaminic compound and the diuretic compound is administered to an arthritic patient either by injection (intramuscularly) or orally, the stiffness of the affected joint and its surrounding structures will subside, pain will be reduced, and function of the joint will improve.

The dosage of antihistaminic compound and diuretic compound should be such as to cause a physiological reaction. The composition, comprising an antihistamine and a diuretic, may be prepared in the form of an injectable solution for administration intramuscularly, or it may be compounded into a tablet for oral administration, the dosage in each case depending upon the particular antihistamine and diuretic employed.

The specific antihistamine compounds that I have found to be suitable in the method of my invention are: chlorpheniramine, brompheniramine, diphenhydramine, tripelennamine, and promethazine.

When employed in conjunction with one of the diuretics hereinafter specified, the dosage of these antihistaminic compounds is generally that recommended by the United States Pharmacopoeia as being the average adult dosage. In some instances several times the normal dosage may be employed. The minimum dosage need only be an amount sufficient to cause a physiological reaction. This may vary among different individuals.

The specific diuretic compounds that I have found to be suitable in the method of my invention are:

1. the following Mercurials:

Meralluride, Mercurophylline, Mersalyl, Merithoxylline, Mercumatilin, and Mercaptomerin;

2. the following Benzothiadiazides:

Chlorothiazide, Hydrochlorthiazide, Polythiazide, Flumethazide, Hydroflumethazide, Methylchlorthiazide, Trichlormethiazide, and Benzthiazide;

3. Chlorthalidone;

4. Ethacrynic acid; and

5. Furosemide

As in the case of the antihistamines, the minimum dosage of these diuretic compounds is that amount sufficient to cause a physiological reaction, although the normal dosage will be that recommended for the particular diuretic compound in the United States Pharmacopoeia.

Both the antihistamine compound and the diuretic compound may be prepared in the form of an injectable solution using water or any other pharmacologically accepted solvent. They may also be compounded into a tablet for oral ingestion, depending upon the manner chosen by the physician.

I have found that any of theforegoing enumerated antihistamine compounds may be combined with any of the foregoing diuretic compounds and the combination administered internally to a person suffering from arthritis, whereupon the remarkable therapeutic effects of my invention are realized.

As previously indicated, the dosage of antihistamine and diuretic is generally a standard dosage as described by the U.S.P., and is such as to cause a physiological reaction. Particularly suitable dosages are set out in Table I hereinafter.

TABLE I

Compound	Daily Dosage
Antihistamine	
1. Chlorpheniramine or brompheniramine	16 to 48 mg.
2. Diphenhydramine	50 to 400 mg.
3. Tripelennamine	50 to 400 mg.
4. Promethazine	12.5 mg. to 200 mg.
Diuretic	
1. Mercurials:	
Merraluride	0.5 to 2.0 ml.
Mercurophylline	0.2 to 2.0 ml.

Mersalyl	0.5 to 2.0 ml.
Merithozylline	0.5 to 2.0 ml.
Mercumatilin	0.5 to 2.0 ml.
Mercaptomerin	0.2 to 2.0 ml.
2. Benzothiadiazide	
Chlorothiazide	500 to 2000 mg.
Hydrochlorthiazide	25 to 100 mg.
Polythiazide	4 to 8 mg.
Flumethazide	500 to 2000 mg.
Hydroflumethazide	25 to 50 mg.
Methylchlorthiazide	4 to 10 mg.
Trichlormethiazide	4 to 8 mg.
Benzthiazide	25 to 50 mg.
3. Chlorthalidone	25 to 100 mg.
4. Ethacrynic acid	20 to 200 mg.
5. Furosemide	40 to 80 mg.

Both the antihistaminic compound and the diuretic compound may be prepared in the form of an injectable solution, using water or some other pharmacologically aceptable solvent, or they may be compounded into a tablet for oral ingestion, depending upon the mode of therapy selected by the physician.

In general where my therapeutic composition is to be administered orally, I prefer that standard U.S.P. dosages be given daily. Where the therapeutic composition is injected, however, I prefer that the dosages be given every other day. (Here too, the dosages are preferably standard U.S.P. dosages.)

Table II sets forth the results of a series of clinical tests in which a number of arthritic patients were parenterally treated with anti-arthritic compositions of the present invention. The type of arthritis and its relative severity are indicated in the table. The intramuscular injections were administered every other day, the number of injections being set out in the table. The percentage improvement in each case is also set forth, with complete subsidence of signs and symptoms corresponding to 100 percent.

In each of cases 1,5,9,10–12, and 32–40 the dosage for each injection consisted of 1 cc of meralluride plus 10 mg chlorpheniramine. In cases 1,5,9,11,12,33–37 .39 and 40 no maintenance therapy was given after the series of injections. In case 10 the maintenance therapy involved an oral dosage of 2 mg polythiazide and 8 mg chlorpheniramine q.i.d. In cases 32 and 38 the maintenance therapy involved a weekly dosage of 1 cc meralluride plus 20 mg chlorpheniramine injected parenterally.

In each of cases 2-4, 7 and 8 the dosage for each injection consisted of 1 cc mersalyl plus 10 mg chlorpheniramine. In cases 3,4, 7 and 8 there was no maintenance therapy. In case 2 the maintenance therapy consisted of one injection weekly for 2 months.

In case 6 the dosage for each injection consisted of 1 cc of mersalyl and 50 mg benadryl. Maintenance therapy involved orally administering 4 mg polythiazide daily and 8 mg chlorpheniramine q.i.d.

In each of cases 13–15, 17,18,22,23, and 26–31 the dosage for each injection consisted of 1 cc of meralluride plus 20 mg of chlorpheniramine. In cases 13–15, 17,18, and 26–30 there was no maintenance therapy. In cases 22 and 31 the maintenance therapy involved 1 dosage weekly of 1 cc of mersalyl plus 20 mg chlorpheneramine, injected parenterally; in case 23, 1 dosage weekly of 1 cc of mersalyl plus 50 mg tripelennamine, injected parenterally.

In case 16 the dosage for each injection consisted of 1 cc mersalyl plus 50 mg diphenhydramine. Maintenance therapy involved oral administration of a dosage of 50 mg chlorothiazide and 8 mg chlorpheniramine q.i.d.

In each of cases 19,20, 24 and 25 the dosage for each injection was 1 cc mersalyl plus 20 mg chlorpheniramine. No maintenance therapy was given in cases 19,20, and 25. In case 24 therapy was maintained with a weekly parenteral injection of 1 cc mersalyl plus 50 mg diphenhydramine.

In case 21 the dosage for each injection was 1 cc meralluride plus 50 mg diphenhydramine. Therapy was maintained with a weekly parenteral injection of the same dosage.

The data is fully set forth in Table II hereinafter.

TABLE II.—TREATMENT OF ARTHRITIS

		Age	Sex	Type of arthritis	Joints involved	Duration of disease prior to my treatment	Number of injections	Percent improvement
1	HK	51	M	Osteo	Left 2-4 fingers, both knees	8 months	3	100
2	RK	35	M	Rheumatoid	Hands, wrists, knees, etc	4 years	3	100
3	JH	57	F	do	do	Since age 20	6	100
4	HK	61	M	Osteo	Both knees	1 year	6	90
5	NL	59	M	do	Cervical to lumbar spine and fingers	3 years	3	60
6	JG	57	M	Gouty	Both great toes	25 years	6	80
7	MC	54	F	Osteo	Right wrist, hands and knee	7 years	2	90
8	HI	60	F	do	Knees, feet, and back	1 year	3	100
9	EB	70	M	do	Right knee	10 years	3	80
10	RB	28	M	Gouty	Great toes	14 months	6	90
11	HB	52	F	Osteo	Hands, wrists, knees	7 years	6	90
12	SC	50	F	do	Ankles and feet	6 months	4	100
13	MC	47	F	do	Cervical to lumbar spine	10 years	6	90
14	MD	62	M	do	Cervical	12 years	3	90
15	MA	42	M	do	All fingers, knees	15 years	12	60
16	JG	56	F	do	Lumbar, spine, knees	4 years	4	80
17	KH	60	F	do	Hands, fingers, wrists	3 years	3	90
18	GY	60	F	do	Right wrist	2 months	3	100
19	AO	56	F	do	Wrists, hands, fingers	2 years	10	90
20	RM	58	F	do	Both knees	do	6	80
21	FT	83	F	do	Back, knees, ankles	12 years	12	90
22	LS	60	M	do	Knees (hospitalized)	5 years	6	80
23	HS	53	F	Rheumatoid	Back, knees (hospitalized)	do	5	100
24	MO	61	F	Osteo	Both knees	8 months	3	80
25	MS	61	F	do	Left knee	6 years	9	100
26	JM	70	M	do	Both knees	5 months	6	80
27	ML	72	F	do	do	2 years	3	80
28	WJ	57	M	do	do	8 months	6	100
29	JI	56	F	do	do	1 year	6	70
30	MH	50	F	Left knee infection	Left knee	4 months	6	80
31	HG	68	F	Osteo	Both knees	10 years	16	80
32	AC	51	M	Gouty	Elbows, wrists, fingers, great toes (hospitalized)	do	6	90
33	JC	41	M	do	Great toes, right knee	4 years	16	100
34	JC	70	M	Osteo	Knees and ankles	2 years	3	60
35	AC	59	M	Rheumatoid	Elbows, wrists, hands	8 years	12	50
36	JB	65	F	Osteo	Both knees	3 years	3	90
37	HS	23	F	Psoriatic	Cervical Spine	2 years	6	100
38	JA	32	M	Rheumatoid	Knees and ankles	8 years	5	70
39	LH	59	M	Osteo	Right hip	4 years	6	100
40	AE	37	M	do	Dorse lumbar spine	3 years	12	70

It will be understood that while the foregoing clinical tests have demonstrated the results obtained when an arthritic patient undergoes parenteral treatment using my anti-arthritic compositions, comparable results may be obtained by administering such compositions orally.

Variations can, of course, be made without departing from the spirit of my invention.

Having thus described my invention, what I desire to secure and claim by Letters Patent is:

1. A method of alleviating arthritis comprising internally administering to an arthritic person a therapeutic composition comprising an antihistiminic compound selected from the group consisting of chlorpheniramine, brompheniramine, diphenhydramine, tripelennamine, and promethazine and a diruetic compound selected from the group consisting of meralluride, mercurophylline, mersalyl, merithozylline, mercumatilin, mercaptomerin, chlorothiazide, hydrochlorthiazide, polythiazide, flumethazide, hydroflumethazide, methylchlorthiazide, benzthiazide, chlorthalidone, ethacrynic acid, and furosemide in standard U. S. P. dosages until the arthritic condition diminishes.

2. The method of claim 1 wherein the antihistaminic compound is shlorpheniramine.

3. The method of claim 1 wherein the antihistaminic compound is diphenhydramine.

4. The method of claim 1 wherein the antihistaminic compound is tripelennamine.

5. The method of claim 1 wherein the diuretic compound is meralluride.

6. The method of claim 1 wherein the diuretic compound is mersalyl.

7. The method of claim 1 wherein the diuretic compound is chlorothiazide.

8. The method of claim 1 wherein the diuretic compound is polythiazide.

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UNITED STATES PATENT OFFICE
CERTIFICATE OF CORRECTION

Patent No. 3,726,976 Dated April 10, 1973

Inventor(s) JOSEPH GLASSER

It is certified that error appears in the above-identified patent and that said Letters Patent are hereby corrected as shown below:

Column 2, line 47: "theforegoing" should read --the foregoing--. Column 2, Table 1: "Merraluride" should read --Meralluride--. Column 3, lines 37-38: "33-37 .39" should read --33-37, 39--. Column 4, line 21: "chlorpheneramine" should read --chlorpheniramine--. Column 6, line 6: "shlorpheniramine" should read --chlorpheniramine--.

Signed and sealed this 8th day of January 1974.

(SEAL)
Attest:

EDWARD M.FLETCHER,JR.
Attesting Officer

RENE D. TEGTMEYER
Acting Commissioner of Patents

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