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A DOUBLE BLIND TRIAL WITH CARTILAGE AND BONE MARROW EXTRACT* IN DEGENERATIVE GONARTHROSIS

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Summary: A double-blind trial with cartilage and bone-marrow extract (Rumalon A) and placebo (Rumalon B) was carried out on 106 patients with degenerative bilateral gonarthrosis. Favorable results were obtained in 64 % of the patients treated with Rumalon A and in only 29 % of the placebo group. This difference is statistically significant ($p < 0.05$). The slight influence of placebo can be related to the psychosomatic effect of injections and/or coincident spontaneous improvement of the gonarthrosis. Cartilage and bone marrow extract increases the therapeutic possibilities in degenerative joint disease. It is easy to administer and practically without side effects.

Degenerative osteoarthritis is a non-inflammatory disorder, characterized by degeneration of articular cartilage and formation of new bone at the joint surfaces.

An important role in the metabolism of the cartilage is played by chondroitin sulphate (2, 3, 4, 9) which is responsible for the physiological elasticity and solidity of the cartilage.

Osteoarthrotic cartilage lesions show a decrease in chondroitin sulphate concentration. This decrease is proportional to the severity of the osteoarthrotic lesions. Collagen concentration of cartilage virtually

* "Rumalon", Robapharm Ltd., Basel/Switzerland.

remains unchanged (2, 3). Collins and McElligott (7) demonstrated that human osteoarthrotic cartilage showed an increased uptake of radio sulphate, *in vitro*, when compared to normal cartilage from the same joints. This uptake is presumably a measure of the rate of chondroitin sulphate synthesis, suggesting greater synthesis in the areas which show decreased concentration of radiosulphate.

Diagnosis of degenerative joint diseases is relatively easy, but treatment is difficult. Many kinds of treatment are recommended, but their effect is mainly symptomatic and usually of very short duration.

"Rumalon" is a new cartilage and bone-marrow extract which activates the metabolism of chondroitin sulphate (1, 16, 17). In their experiments on rats, Weigel and Jasinski (17) proved that the uptake of radioactive sulphate in rat cartilage is significantly increased by Rumalon.

In a double blind test we compared the efficacy of Rumalon with a placebo, in degenerative gonarthrosis.

MATERIAL AND METHODS

106 patients (99 females and 7 males) with bilateral osteoarthrosis of the knee joints were treated in the out-patient clinic with one of two substances labelled Rumalon A and B, respectively. All of the patients were over 46 years of age.

55 patients received Rumalon A, while 51 received B. The dosage was the same as that recommended by the original investigators: an initial intramuscular injection of 0.1 ml. followed by 0.5 ml. and then 1.0 ml. three times a week until a total of 20 injections had been given.

Patients were examined before and during treatment, and for periods of 2 to 12 months afterwards. The gonarthrosis was confirmed by clinical, laboratory and x-ray findings. The patients had various stages of gonarthrosis (from moderate to mild), and were chosen at random when they visited our clinic.

The response to treatment was assessed subjectively and objectively: subjectively, by questioning the patient with regard to pain at rest and during movement, and to physical performance in general. Objective criteria were local findings in the joints, including swelling, crepitation, palpation of the periarticular tissue and especially measureable alterations in the degree of mobility of the knees.

After completing treatment, some of the patients returned spontaneously for a follow-up, while others were summoned by the physician. Only after the trial, which lasted about two years, had been completed and the results summarized did we learn that Rumalon B was the placebo.

All the results were statistically evaluated by the chi square (χ^2) test and by analysis of the variances and standard errors.

RESULTS

The patients were divided into two main groups:

1. 55, who received cartilage and bone marrow extract — Rumalon A.
2. 51, who received placebo — Rumalon B.

The results are presented in table I. Of the patients who received Rumalon A, 29 showed objective and subjective improvement, and 16 no improvement. Seven patients did not report for follow-up examination and could not be assessed, while in three cases treatment had to be discontinued — in two for technical reasons, and in one because of the development of urticaria. The latter was the only case in which the injections were not well tolerated. The injections were practically painless. Blood and urine examinations did not show any disturbance during and after administration of the extract. In the placebo group, 12 patients showed improvement and 29 no improvement. In two patients in this group treatment had to be discontinued for technical reasons, and eight failed to report for follow-up examination. These differences in the results obtained with Rumalon and placebo are statistically significant ($p < 0.05$). The patients were divided according to the severity of their arthrosis (Table II). The patients with "medium" or "average" severity were those with signs of inflammation, limitation of movements and pains in both knees, while those labelled as "mild" had joint pains and only crepitations on clinical examination. All patients had clear-cut changes of osteoarthritis on x-rays.

The patients who showed improvement could have been divided into three groups on the basis of their degree of response to therapy:

- (a) "excellent" — subjective and objective signs disappeared for a period of about one year.

- (b) "good" — considerable improvement for periods of up to five months, but without complete disappearance of symptoms.
- (c) "fair" — slight improvement during treatment, but further treatment needed immediately after termination of the series of injections.

The number of patients in each group was too small for separate analysis, but it is interesting to note that of the patients who received Rumalon A, 6 had "excellent", 19 "good" and 4 "fair" results. Of those who received the placebo, none showed "excellent" results, only three could be graded as "good" and the rest as "fair."

DISCUSSION

In this double-blind trial, 106 patients with different stages of gonarthrosis received cartilage and bone marrow extract (Rumalon A) or a placebo (Rumalon B).

64 % of the patients who received Rumalon A showed favorable results, whereas only 29 % who received placebo, Rumalon B, reported some kind of improvement. This difference is statistically significant ($p < 0.05$). Flemmich (8) also found satisfactory results, in about 80 % of 70 patients with osteoarthrosis. Large joints, in particular, responded well to this treatment. Wagenhäuser (14) in a series of 144 patients found that the cartilage and bone-marrow extract gave the best results in osteoarthrosis of the fingers (70 %) and the knees (62 %). In another trial with 151 patients (15) he obtained similar results, as did Ruffié (12) in 133 patients. Schiavetti and Bray (13) found favorable results in 71 of 371 patients with degenerative osteoarthrotic changes of the knees, hips and spine.

We had successful results with the placebo (Rumalon B), in 29 % of the patients. In none of them, however, could the response have been graded excellent. Most of the cases showed only slight improvement, and this can be explained by the fact that osteoarthrosis sometimes shows spontaneous remissions, and because injections sometimes have a psychosomatic influence on patients. It is of the utmost importance that this type of treatment can be administered to out-patients, and has only minimal side effects such as digestive or autonomic nervous system disturbances, sweating, tachycardia, headaches or, as in one of our cases, urticaria (5, 6, 10, 11, 15).

TABLE I

Results of Treatment.

Treatment	Improvement		No improvement		Total	
	No.	%	No.	%	No.	%*
Rumalon A	29	64	16	36	45	100
Rumalon B	12	29	29	71	41	100

* 20 patients are not included:
 15 because of lack of follow-up
 1 developed urticaria
 4 for technical reasons

TABLE II

Relationship between Results of Treatment and Severity of Gonarthrosis.

Severity of gonarthrosis	Treatment	Improvement		No improvement		Total	
		No.	%	No.	%	No.	%**
"Medium"	Rumalon A	4	67	2	33	6	100
	Rumalon B	3	23	10	77	13	100
"Mild"	Rumalon A	25	64	14	36	39	100
	Rumalon B	9	32	19	68	28	100

** 20 patients are not included (See footnote table I).

The results of our investigations indicate that the treatment with cartilage and bone-marrow extract increases the therapeutic possibilities, in degenerative joint disease.

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