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Original Article

Intra-articular Treatment with Hyaluronic Acid. Comparative Study of Hyalgan and Adant

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Abstract: Forty-nine patients diagnosed as having gonarthrosis were given intra-articular treatment with hyaluronic acid (Adant or Hyalgan) in a blind randomised study. We concluded that the efficacy with Adant at 3 months after treatment was greater than with Hyalgan (50% versus 21.1%). The maximum improvement with hyaluronic acid was seen at 5 weeks in 75.4% and the adverse effects consisted of pain in the infiltration side which was almost twice as great with Adant (16.3%).

Keywords: Hyaluronic acid; Intra-articular; Osteoarthritis

Introduction

Different studies [1–3] confirm that hyaluronic acid (HA) therapy relieves pain, reduces the consumption of non-steroidal anti-inflamatory drugs (NSAIDs) and delays surgery; however, results vary according to the product used, and to our knowledge no studies comparing the efficacy and safety of different HAs have been reported. The aim of this study was to assess the efficacy and safety of intra-articular therapy in patients suffering from gonarthrosis as a whole and to identify the variables resulting from the type of HA (Hyalgan versus Adant).

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Materials and Methods

Forty-nine patients diagnosed as having gonarthrosis following clinical and radiological criteria (states II and III according to Kellgren and Lawrence) were included in a blind randomised study. All were given intra-articular treatment with HA (five injections into the knee at weekly intervals) by the same doctor using the routine technique.

Two groups were established depending on the type of the HA used. Age and gender were evaluated between the groups and no differences were found. No drop-outs occurred and all patients were evaluated.

- Adant: 5 injections of 25 mg (2.5 ml). This is a 1% sodic hyaluronate solution with a mean molecular weight of 900 000 D biotechnically obtained.
- Hyalgan: 5 injections of 20 mg (2 ml). This is a 1% sodic hyaluronate solution with a mean molecular weight of 800 000 D from an animal source (cock's crest).

A total of 49 intra-articular treatments (245 infiltrations) were carried out on 49 patients, of whom 30 were given Adant and 19 Hyalgan.

The clinical evaluation criteria were according to the subjective assessment of each patient. The results were divided into four groups according to clinical improvement criteria: excellent ($>75\%$), good (50%–75%), fair (25%–50%) and no clinical response ($<25\%$).The assessment took place the week following the fifth infiltration, at 3 months and at 6 months. All patients were also questioned on their consumption of analgesic and/or anti-inflammatory drugs at the beginning and end of treatment.

The sample of patients was described according to age (mean and standard deviation) and gender (frequencies),

comparing those treated with each drug. A prospective study assessing the evolution in time (5 weeks, 3 months and 6 months) of the clinical improvement due to Adant and Hyalgan using a comparison of proportions (χ^2 of 95% of three sections of the study) was carried out. Secondly, the difference in the therapeutic results was assessed according to the patient's response between drugs, comparing the proportions (χ^2 of 95% confidence). Thirdly, adverse reactions (painful articular punctures) were studied (χ^2 of 95% confidence) and the relative risk from this adverse reaction in both drugs was assessed.

Results

Of the 49 patients, 8 were male and 41 were female; their ages ranged from 41 to 86 years (mean 65.14, SD 9.77 years).

The results according to the efficacy assessment were good or excellent at 5 weeks in 40.8% of cases, in 38.8% at 3 months and in 26.5% at 6 months. The maximum improvement obtained in each patient was at 5 weeks in 75.4% (37 intra-articular treatments), at 3 months in 22.4% (11 intra-articular treatments) and at 6 months in only one case (2%) ($p < 0.0001$); 73.5% of cases showed fair or no clinical response at 6 months ($p < 0.01$). To summarise, when the result was excellent or good the improvement was immediate and maintained in time; however, when the result was fair or with no clinical response at 5 weeks no improvement could be expected.

In the comparative study (Table 1) excellent and good results were obtained at 3 months in 50% of cases with Adant and in 21.1% with Hyalgan ($p < 0.05$).

Eight patients had some painful infiltrations (20%), six with Adant (16.3%) and two with Hyalgan (10.5%) ($p < 0.001$). The relative risk of suffering a painful injection was almost twice as great with Adant (RR = 1.9).

We asked patients whether their analgesic or anti-inflammatory drug consumption requirements after treatment with HA had changed at 6 months and no modifications were found.

Discussion

Our overall results are consistent with other series [1,2,4,5], being good and excellent in 40.8% of cases. The efficacy of the viscosupplementation decreased according to the time elapsed since the end of the treatment. In our study 73.5% of cases were fair or with no clinical response at 6 months, and so we recommend repeat treatment at 6 months if it has been effective. Most patients obtained maximum effect at 5 weeks and a few at 3 months: thus if no clinical improvement has occurred a different therapy should be suggested.

We used the recommended dose of HA. No more benefits have been found when a larger dose is injected in each administration, and the best interval between two consecutive injections is 1 week [5]. It seems that the joint eliminates the HA excess, but on the other hand the presence of HA in the joint is needed for a number of weeks to re-establish the capacity of the synovial membrane to produce normal synovial fluid. This could explain the better results obtained with Adant, as well as more adverse effects, as the viscosity and volume are greater than with Hyalgan. We do not know whether the improvement is due to the larger dose or to the viscosity. A review of the literature identified no comparative study between the two products.

The incidence of adverse effects with intra-articular injections of HA has been comparable to that described in the literature [1,4,5,6]. Although it varies considerably between authors, probably because of the different subjective assessment of pain, it is usually located in the injection site and consists of a painful transitory reaction which at times is accompanied by a rise in temperature, which lasts 1 or 2 days and resolves spontaneously.

Conclusions

The efficacy with Adant at 3 months (50%) after treatment was greater than with Hyalgan (21.1%), probably because its greater viscosity increases its half-life in the joint.

Table 1. Results according to the assessment of the efficacy of Adant and Hyalgan

		5 weeks	3 months	6 months	χ^2
Excellent	Adant	2 (6.7%)	1 (3.3%)	1 (3.3%)	n.s.
	Hyalgan	2 (10.5%)	1 (5.3%)	1 (5.3%)	n.s.
	χ^2	n.s.	n.s.	n.s.	
Good	Adant	11 (36.7%)	14 (46.7%)	9 (30%)	n.s.
	Hyalgan	5 (26.3%)	3 (15.8%)	2 (10.5%)	n.s.
	χ^2	n.s.	$p = 0.026$	n.s.	
Fair	Adant	8 (26.7%)	3 (10%)	3 (10%)	n.s.
	Hyalgan	9 (47.4%)	2 (10.5%)	1 (5.3%)	
	χ^2	$p = 0.13$	n.s.	n.s.	
No response	Adant	9 (30%)	12 (40%)	17 (56.7%)	$p < 0.05$
	Hyalgan	3 (15.8%)	13 (68.4%)	15 (78.9%)	$p < 0.0001$
	χ^2	n.s.	$p < 0.05$	n.s.	
		49	49	49	

The maximum improvement was seen at 5 weeks in 75.4% and decreased gradually with time. Thus, if the treatment is effective it is necessary to consider restarting the treatment at 6 months. If, during the first 3 months no improvement occurs, another therapy must be used.

The adverse effects (20%) consisted of pain in the infiltration site, mainly related to the greater viscosity of Adant (almost twice as often as with Hyalgan).

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