



A randomized comparison of intra-articular triamcinolone acetonide and oral meloxicam in management of knee osteoarthritis

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Abstract

Knee osteoarthritis is a common cause of knee pain in middle aged and elderly patients presenting in Orthopaedic Out- patient clinics in Nigeria. This study compared the pain control using the visual analog scores (VAS), improvement in function using the Western Ontario and McMaster Universities Osteoarthritis index (WOMAC) scores. Patients over 40 years with radiographically and clinically confirmed osteoarthritis of the knee (Kellegren and Lawrence Grade 1 and 2) who met study criteria were recruited with informed consent taken. The patients were randomized into 2 groups. Group A had a single intra-articular injection of 20mg triamcinolone acetonide (Kenalog) and Group B had oral Meloxicam (Melocap) 7.5 mg for 12 weeks. They had functional and pain scoring at intervals of 0, 1, 6, and 12 weeks using a (WOMAC) and the VAS respectively. Both study groups showed statistical difference in pain control (VAS) over the study period in the 6th and 12th week. There was however a statistically significant change in functional scores (WOMAC) in both study groups at Week 1, 6, and 12 ($p<0.05$).

Keywords: Triamcinolone Acetonide, meloxicam, knee osteoarthritis

Introduction

Osteoarthritis of the knee is a common cause of knee pain in the middle-aged and elderly presenting at the Orthopedic Out-patient clinic. In the United States, it is the most frequent cause of disability in adults affecting about 27million people ^[1]. In Nigeria, many hospital-based reviews have shown that osteoarthritis is quite common, the knee is the most affected joint and there is a female preponderance ^[2, 3, 4]. It is characterized by joint pain and dysfunction and in the advanced stages by limb deformity, muscle atrophy and contractures ^[5]. Osteoarthritis is the commonest cause of disability in older adults, the fourth commonest cause of hospitalization and leading indication for joint replacement surgeries with a total cost of \$42.3 billion in 2009 for hip and knee replacements in the United States of America alone ^[1].

The primary changes occur within the articular cartilage which is later followed by changes in the subchondral bone ^[6, 7]. Articular cartilage is rich in extracellular matrix, relatively avascular, lacking lymphatics and nerve supply and chondrocytes make up about 1% of its mass. There is little or no cell death or cell division in normal adult articular cartilage. The chondrocytes are responsible for the synthesis and breakdown of the cartilaginous matrix ^[7, 8, 9]. Osteoarthritis results from failure of the chondrocytes to maintain homeostasis between synthesis and degradation of extracellular matrix components. This leads to increased water component and decreased proteoglycan content of the extracellular matrix. There is also weakening of the collagen network due to reduced synthesis of type II collagen and breakdown of existing collagen. These changes are associated with contributions of intrinsic and extrinsic factors which further worsen the mechanical, metabolic and oxidative stress suffered by the articular cartilage ^[5]. Knee pain remains the commonest and most disturbing complaint in these patients and treatment is mainly symptomatic excluding joint replacement.

The goals of therapy are mainly pain relief and improvement in function. These include lifestyle modification such as weight loss, exercise, oral or topical non-steroidal anti-inflammatories, intra-articular injections, knee braces, osteotomies.

Intra-articular injections over the decades have become a popular modality of treatment to help in reducing the inflammatory component of disease, reduce frictional forces or supply growth factors to aid repair. Some common agents that have been used in the local treatment of knee osteoarthritis include steroids, visco-elastics, platelet-rich plasma. In the past intra-articular steroid injections were reserved for rheumatoid arthritis of large joints, however, recent studies show that there is an inflammatory component to the disease which is contrary to the older, more popular belief that osteoarthritis was just a disease of 'wear and tear'. Since the first injection of hydrocortisone in 1951, the use of steroids has steadily gained more acceptance [10]. These are however not without their attendant problems which include needle prick discomfort, allergic reactions and joint sepsis [11]. Problems with the use of oral non-steroidal anti-inflammatories (NSAIDs) include the discomfort of frequent pill swallowing, dyspepsia, gastritis, upper gastro-intestinal hemorrhage [12]. This study aims to compare in the short term, the early efficacy of intra-articular injections with a steroid (Triamcinolone) versus the use of an oral NSAID (Meloxicam) in improving pain and function in mild to moderate knee osteoarthritis.

Materials and Methods

This was a hospital-based prospective and comparative study of symptomatic relief in patients with clinically and radiographically confirmed mild to moderate osteoarthritis (K&L) (as shown in table 1) stage 1 and 2 after treatment with intra-articular injections of steroid or oral NSAIDs. This study was conducted in the Out-patient clinic of the Department of Orthopaedics Surgery and Traumatology, Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC) in South-Western Nigeria for a period of 1 year. The study population was comprised of adults of 40 years of age and above. They were assessed for eligibility for the study based on the study criteria. Those found eligible had an informed consent taken from them. Samples for full blood count, erythrocyte sedimentation rate, fasting and 2 hour post prandial blood sugar were taken. The population was randomized into two groups. Group A had a single intralesional triamcinolone 40mg injection and Group B had Oral Meloxicam 7.5mg daily for three months. At each visit assessment was made for the general well-being of the patient, assessment of symptomatology was done using the VAS and WOMAC scores.

Sample Size Estimation

Sample size was computed using WINPEPI statistical software accepting a 95% confidence interval, level of statistical significance of 0.05, and a power of 80% using the formula

$N = 2z^2pq/d^2$ (Where N is the desired sample size, z is the standard normal deviation (95% i.e. 1.96), p is the proportion of the total population that possess the study characteristic (i.e. knee osteoarthritis) 60% i.e. 0.6², q is 1-p = 0.4, d is the degree of accuracy required (85% i.e. 0.15) Thus:

$N = 2 \times 1.96 \times 1.96 \times 0.6 \times 0.4 / 0.0225 = 81.954$ (approximated to 82 subjects and rounded off to 90 to allow

for attrition.

These 90 patients were divided into 2 groups of equal halves each having 45 patients each.

Statistical analysis

Study data was collected using a proforma at each visit entered into a datasheet and analyzed using SPSS version 22 (IBM SPSS Incorporated, Chicago, Illinois). Frequency distributions were presented using tables and charts. Descriptive statistics were analyzed using mean, standard deviation and range. Independent T- tests were used to analyze the pain, functional scores and ESR in both study groups and correlational studies using a Pearson's coefficient were used to assess the relationship between pain scores and radiographic grading.

Ethical clearance and consent

Approval was obtained from the OAUTHC Ethical and Research Committee and informed consent was taken from the patients or their caregivers before recruitment into this study, explaining the nature of the research to the patients and that they would suffer no penalty if they do not wish to participate in the study. The cost of the intra-articular injections, oral medications, baseline investigations and radiographs were borne by me aided by a research grant given by the Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife.

Results

Ninety patients who met the inclusion criteria were recruited into the study and were randomized into 2 groups of 45 patients each. Group A had a single intra-articular triamcinolone Acetonide injection in the affected knee administered while Group B had oral Meloxicam. There was a female predominance in the sex distribution with 58 females (64.4%) and 32 males (35.6%) with a male to female ratio of 1: 1.8. The ages of the patient's ranged between 41-80 years with a mean age of 58.72±11.611 years. The ages were further sub-classified into groups, 30 (33.3%) patients ranged between the ages of 40 to 50 years, 18 patients (20%) fell between 51 to 60 years, 23 (25.6%) patients fell between the ages of 61 to 70 years, 19 subjects (21.1%) were older than 70 years.

The Body mass index of both study groups was analyzed and was found to range between 17.2 and 38.2kg/m² respectively with a mean of 25.119±4.637 kg/m². 18 (20%) respondents were found to be underweight, 27 (30%) were of normal weight, 31 (34.4%) were overweight, while 12 (13.3%) were Obese, 2 (2.2%) were morbidly obese. Thus 45 patients (50%) were either overweight or obese. The Body Mass Index was analyzed between both sexes, comparison between both sexes was statistically significant with a p value of 0.005 ($p < 0.05$) with a mean of 26.12 kg/m² for females and 23.30kg/m² for males. The distribution of the laterality of knees assessed showed that the left knee was involved in 26 patients (28.9%), right knee in 30 patients (33.3%) and bilateral in 34 (37.8%) patients. In patients with bilateral disease, the more painful knee was assessed for the study. The distribution of the Kellegren & Lawrence grades of knee osteoarthritis grades amongst the patients was assessed and 56 patients (62.2%) had grade 1 while 34 patients (37.8%) had grade 2.

The female sex distribution in the triamcinolone and meloxicam groups was 30 (66.7%) and 28 (62.2%) while the

male sex distribution was 15 (33.3%) and 17 (37.8%) respectively. The age class interval distribution for the triamcinolone group was 14 (31.1%) for 40 to 50 years, 7 (15.6%) for 51-60 years, 11 (24.4%) for 61 to 70 years and 13 (28.9%) for those older than 70 years. The age class interval distribution for the Meloxicam group was 16 (35.6%) for the 40 to 50 years group, 11 (24.4%) for the 51-60 years group, 12 (26.7%) for the 61 to 70 years interval, and 6 (13.3%) for the greater than 70 years group as shown in Table 6.5. The mean age was 56.3 ± 10.5 years for the meloxicam and 61.11 ± 12.3 years for the triamcinolone group. There was no statistical difference between the means ($p > 0.05$). The body mass index distribution for the triamcinolone group was for the underweight group there were 3 (6.6%), normal weight there were 23 (51.1%), overweight were 11 (24.4%), obese were 7 (15.6%), morbidly obese was 1 (2.2%). For the meloxicam group the Body Mass index distribution was 1 (2.2%) for the underweight group, normal weight were 18 (40%), overweight were 20 (44.4%), obese were 5 (11.1%), morbidly obese 1.0 (2.2). The mean body mass index for the triamcinolone group was 24.6 ± 4.7 kg/m² and for the meloxicam group was 25.6 ± 4.7 kg/m². There was no statistical difference between the means ($p > 0.05$).

The laterality of the affected knee joints in the triamcinolone group was 15 (33.3%) on the left, 12 (26.7%) on the right and 18 (40%) were bilateral. In the meloxicam group, 11 (24.4%) were on the left, 18 (40%) were on the right, 16 (35.6%) were

bilateral. The Kellegren and Lawrence grading in the triamcinolone group was as follows: Grade 1 were 32 (71.1%), Grade 2 were 13 (28.9%) respectively. For the meloxicam group, 24 (53.3%) were Grade 1 and 21 (46.7%) were Grade 2. There was no statistically significant difference in age, sex and BMI distribution in both groups. The visual analog pain scores of patients in both treatment groups were analyzed on contact, at 1 week, 6 weeks and 12 weeks respectively. There was a statistically significant change in pain score for both groups at 6 and 12 weeks respectively with p values of 0.000 and 0.002 respectively ($p < 0.05$).

The functional scores (WOMAC) of both treatment groups were analyzed at contact, 1 week, 6 weeks and 12 weeks. There was a statistically significant change ($p < 0.05$) with p values of 0.004, 0.005, 0.019 in the WOMAC scores at 1, 6 and 12 weeks respectively as shown in Table 2. The changes in ESR over the study period in both groups was analysed and no statistically significant change in ESR was seen in both groups. Correlational analysis of the Kellegren and Lawrence grade of subjects and pain scores at contact showed no relationship where $r = -0.002$ and p is 0.984 ($p > 0.05$). 13 patients (14.4%) on oral meloxicam had epigastric discomfort which was treated with omeprazole, a proton pump inhibitor while 4 patients (4.4%) had post injection flares of knee pain following intra-articular injections of triamcinolone acetate. 73 (81.1%) respondents were free from side effects as shown in Table 4.

Table 1: Kellegren and Lawrence Radiographic Staging of Osteoarthritis

	Features
0	No radiographic features are present.
1	Doubtful joint space narrowing and possible osteophytic lipping.
2	Presence of definite osteophytes and joint space narrowing on anteroposterior weight bearing radiograph.
3	Multiple osteophytes, definite joint space narrowing, possible bony deformity.
4	Large osteophytes, marked joint space narrowing and definitely bony deformity

Table 2: Comparison of treatment options with functional scores

	RX	N	Mean	Std. Deviation	Std. Error Mean	t	P value
WOMAC0	meloxicam	45	44.93	10.654	1.588	.696	0.488
	triamcinolone	45	43.24	12.318	1.836		
WOMAC1	meloxicam	45	30.78	8.584	1.280	2.923	0.004
	triamcinolone	45	36.44	9.771	1.457		
WOMAC6	meloxicam	45	31.98	8.041	1.199	2.865	0.005
	triamcinolone	45	27.47	6.851	1.021		
WOMAC12	meloxicam	45	33.42	8.693	1.296	2.388	0.019
	triamcinolone	45	29.43	6.953	1.048		

Table 3: Relationship between treatment options & financial costs

	RX	n	Mean	Std. Deviation	Std. Error Mean	t	P value
COST	meloxicam	45	5530.00	694.449	103.522	15.759	0.001
	triamcinolone	45	3433.56	560.508	83.556		

Table 4: Complications of treatment

Treatment	n	Complication	f	%
triamcinolone	45	post injection flare	4	4.40%
meloxicam	45	epigastric discomfort	13	14.44
		free	73	81.11
Total	90		90	100

Discussion

There was a female predominance in the study population with a male to female ratio of 1:1.8. This finding agrees with

studies done by Akinpelu *et al.* and Odole *et al.* which showed a male to female ratio of 1: 1.2 and 1: 2.9 respectively and mean ages of 54 ± 11.7 and 55.7 ± 13.4 years respectively [2, 16]. However the mean age of the disease in local studies is lower than what obtains in Caucasian populations as seen in the study by Creamer *et al.* and which gave a mean age of 65.8 ± 10.4 years. This might be due to poor life expectancy indices, racial differences, paucity of transportation options, poverty and obesity in Negroid population [17]. Fifty percent of the study population were either overweight

or obese. This underscores the importance of increased body mass index in individuals as a risk factor for the development of knee osteoarthritis due to mechanical factors such as increased joint loading. The analysis of the Body Mass Index between the male and female respondents showed a statistically significant difference with more females having increased BMI when compared to males with a mean of 26.12 kg/m² for females and 23.30 kg/m² for males. This may explain why both study groups have a female preponderance. This is in tandem with previous studies which have shown the black race, female, sex and increased BMI as risk factors for the development of knee osteoarthritis ^[18].

A third of the patients (33.3%) had symptomatic bilateral knee disease, 43.3% had on the right and 34.4% on the left. Laterality may be dependent on a host of factors including the alignment of joint axes, prior trauma or inflammatory process, occupations with increased knee bending stress and sports ^[17]. Fifty-six patients (62.2%) had Kellgren and Lawrence radiographic grade 1 disease while 34 (37.8%) had grade 2 disease. Attempt to assess the relationship between radiographic grades and pain scores at first contact showed was done using correlational analysis which showed no relationship. This is similar to findings by Hannan and co-workers which showed that symptomatology is not a useful predictor of the radiographic grade of the disease ^[19].

The visual analog pain scores of patients in both the triamcinolone and meloxicam groups showed statistically significant differences in pain scores at the 6th week and 12 weeks, a cursory glance indicates the triamcinolone group having better improvement in pain scores. They however showed no statistical difference at the end of the first week. The inference drawn from this is that both treatments are comparable at the first week, however intra-articular triamcinolone gives better relief between 6 to 12 weeks. This consolidates the evidence of the meta-analysis by Bruce Aroll and co-workers which showed that the effects of intra-articular steroid injections were beneficial up to 12-16 weeks post administration.

The changes in functional (WOMAC) scores from that at first contact to scores obtained in Week 1, 6, 12 were statistically significant for both triamcinolone and meloxicam groups. This infers that patients with mild to moderate pain would in the long run benefit from treatment as it improves their quality of life and helps them to better cope with their activities of daily living. This corroborates the findings in studies by Gaffney *et al.* who compared the benefits of intra-articular triamcinolone and placebo and that of Roth SH and co-workers which compared oral and topical administration of diclofenac in knee osteoarthritis with placebo with significant changes in pain and function scores in treatment groups over placebo groups ^[15, 19]. There was no statistical difference in the changes in erythrocyte sedimentation rates in both study groups showing that they had outcomes that were not statistically different in controlling the inflammatory component of knee osteoarthritis.

Conclusion

The Body Mass Index was either overweight or obese in 50% of subjects. Female subjects showed higher BMI scores than their male counterparts. There was no relationship between radiologic grade and pain scores at first contact. Both study groups showed no statistical difference in pain control in the first week but showed marked improvement in the 6th and 12th week when the triamcinolone group had more significant

reductions in pain scores. There was however a statistically significant change in functional (WOMAC) in both study groups at Week 1, 6, and 12.

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Declaration of interest statement

The authors declare no conflicts of interest during the course of the study.

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