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THE EVALUATION OF EFFICACY AND SAFETY OF COLLAGEN PEPTIDE IN THE MANAGEMENT OF PATIENTS WITH KNEE JOINT OSTEOARTHRITIS

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ABSTRACT

AIM: To compare the efficacy and tolerability of collagen peptide as an Add on therapy to standard treatment compared to standard treatment alone in the management of patients with knee joint osteoarthritis. **METHODOLOGY:** This was an open label, comparative, randomized, prospective study. This study included 60 patients with osteoarthritis, who were randomized into two groups of 30 each. Control group received standard therapy (T.Diclofenac 100mg/day, T.Ranitidine 150mg twice daily and physiotherapy) and Study group received collagen peptide (10g/day) in addition to standard therapy for a period of 12 weeks. They were followed-up once in 2weeks for 12weeks. Pain, stiffness and functional disability were assessed using visual analogue pain scale (VAS) and WOMAC index at baseline and at the end of the study. **RESULTS:** 126 patients were screened and 60 patients were included in the study. All patients completed the study and were included in Analysis. On comparing the groups at the end of 12 weeks there was a statistically significant reduction in VAS and WOMAC INDEX score in Study group. No significant difference in the incidence of adverse events noted between the two groups. **CONCLUSION:** Collagen peptide along with standard therapy is highly effective in reducing Pain, Stiffness and Functional disability in patients with Knee joint Osteoarthritis.

1.0 INTRODUCTION

Osteoarthritis is the most common form of arthritis affecting millions of people around the world. It is characterized by progressive softening and disintegration of articular cartilage which leads to functional disability[1]. It is a dynamic phenomenon and shows features of both destruction and repair. The final outcome is determined by the relative vigour of these opposing processes.[2] The etiology of Osteoarthritis is multifactorial.[3] In most cases the precipitating cause of Osteoarthritis is increased mechanical stress in some part of the articular surface.[4] The prevalence of clinically diagnosed Knee Osteoarthritis in India ranges from 22-39%.[5] The most common joints affected in Osteoarthritis are hip, knee, spine and hands. The main symptom in Osteoarthritis is joint pain, which become worse with weight bearing and activity. . Other symptoms include stiffness of the joint, crepitus, joint swelling, limitation of movement and deformity.[6]

Management of osteoarthritis includes muscle strenghthening exercises and weight reduction. Paracetamol is the analgesic of choice for early cases with mild pain. Patients with severe pain require other Non steroidal anti-inflammatory drugs (NSAIDs).[7] Intra articular injection of steroids and hyaluronic acid is useful in very severe cases. Other drugs used in the management of osteoarthritis include glucosamine sulphate, chondroitin sulphate, collagen peptide, antioxidants etc.

Collagen peptides have gained huge public attention as nutraceuticals used for prophylaxis and management of osteoarthritis.[8] It contains different aminoacids, predominantly glycine, proline and hydroxyproline, which together represent 50% of the total aminoacid content. Beneficial action is likely due to collagen peptide accumulation in the cartilage and stimulated production of collagen and proteoglycans by the chondrocytes, the cells of cartilage.[9] With this novel mechanism of action, collagen peptide can slow the disease progression and can improve the symptoms in patients with Osteoarthritis. Hence this study has been undertaken to evaluate the efficacy and safety of collagen peptide in the reduction of symptoms in patients with knee joint osteoarthritis in our population.

2.0 METHODOLOGY

2.1OBJECTIVE

To evaluate the efficacy and safety of collagen peptide as add on therapy to standard treatment in the management of patients with knee joint osteoarthritis compared to standard treatment alone.

2.2 STUDY DESIGN

The study was a randomized, open label, prospective, parallel group two arm comparative study and conducted in patients with knee joint Osteoarthritis, diagnosed within one year and attending outpatient department of Orthopaedics, in our tertiary care hospital, Chennai.

The study was carried out from August 2013 to April 2014 for 16 weeks (12 weeks study period and 4 weeks follow up period) for each patient. Total number of patients was 60 and in each group (control and study groups), there was 30 patients.

2.3SELECTION CRITERIA

2.3.1 Inclusion criteria:

- Age – 40 years to 70 years
- Sex – both genders
- Patients with primary osteoarthritis of knee joint diagnosed less than 1 year
- Patients willing to give written informed consent.
- Subjects capable and willing to comply with all study procedures

2.3.2 Exclusion criteria:

- Patients with secondary osteoarthritis.
- Patients with genu varum, genu valgum, gouty arthritis, rheumatoid arthritis.
- Patients with known hypersensitivity to NSAIDs, collagen peptide.
- Patients on oral or parenteral corticosteroid therapy
- Patients with chronic systemic illness of liver, heart, kidney, gastrointestinal tract etc.
- Patients who had taken other osteoarthritis treatment (glucosamine sulphate, chondroitin sulphate, diacerin, hyaluronic acid) within past 1 month.
- Pregnant and lactating women

2.4 STUDY PROCEDURE

The study was started after obtaining approval and clearance from the Institutional Ethics Committee (No.04082013). Information sheet and informed consent forms written in the regional language were provided to each patient and patient willing to participate in the study signed the required forms. 126 patients were screened and 30 patients in each group (control and study groups) who fulfilled the inclusion and exclusion criteria were recruited and ramdomized by odd number patients assigned to study group and even number patients to control group.

2.5 TREATMENT PLAN:

30 patients in the **Control group** received Standard treatment with Tab.Diclofenac 50mg orally twice daily and Tab.Ranitidine 150mg orally twice daily along with Physiotherapy. Tab.Diclofenac and Tab.Ranitidine were given initially for a period of 2 weeks. Then depending on the pain assessment every 2 weeks, these drugs were continued during the study period. 30 patients in the **study group** received Standard treatment plus Collagen peptide 10g sachet orally per day for 12 weeks. Patients were asked to return the empty packets during every visit.

- **ASSESSMENT PARAMETERS:**

The parameters used for assessment of effectiveness of the study drug are (1) Joint tenderness and pain during Range of movement assessed by VISUAL ANALOGUE SCALE. (2) Pain, stiffness and functional disability assessed by WOMAC Osteoarthritis index score and (3) X-ray Knee joint – Anteroposterior & Lateral view

2.7 EVALUATION

The obtained data was analyzed statistically. Distribution of age was analyzed using one way ANOVA and Sex distribution was analyzed by Pearson chi- square test. The biochemical investigations were performed at baseline and at the end of 12 weeks. The differences within the groups in lab parameters before and after treatment were analyzed using student's paired t- test. The difference in pain assessment score and WOMAC Osteoarthritis index score within the groups was analyzed using students paired t-test. Similarly the difference between the control and test groups was analyzed using independent t-test. Statistical analysis was done by using SPSS software. p value <0.05 was considered to be statistically significant.

3.0 RESULTS

BASELINE CHARACTERISTICS	CONTROL	STUDY	p VALUE
Mean age distribution	54.36 (4.64)	54.43 (5.37)	0.43
Gender distribution Male Female	 12 18	 10 20	 0.61
No. knee joint involved Unilateral Bilateral	 21 9	 23 7	 0.57
Xray Grading Grade 1 Grade 2	 21 9	 19 11	 0.59

Table-1 shows the baseline characteristics of both the control and study group patients

	CONTROL GROUP		STUDY GROUP		INDEPENDENT T-TEST
	MEAN	SD	MEAN	SD	
BASELINE	7.63	0.54	7.7	0.45	p=0.62
WEEK 2	6.76	0.66	6.53	0.71	p=0.21
WEEK 4	6.36	0.79	6.13	0.88	p=0.29
WEEK 6	6.03	0.60	5.8	0.74	p=0.19
WEEK 8	5.76	0.76	5.33	0.74	p=0.03
WEEK 10	5.66	0.69	4.5	0.56	p<0.01
WEEK 12	5.53	0.56	3.8	0.65	p<0.01
WEEK 16	5.43	0.55	3.66	0.53	p<0.01
p-VALUE	p<0.01		p<0.01		

Table-2 shows mean pain score in both the groups by visual analogue pain scale from baseline to week 16.

	CONTROL GROUP		STUDY GROUP		INDEPENDENT T-TEST
	MEAN	SD	MEAN	SD	
BASELINE	64.99	5.43	66.15	5.36	p=0.25
WEEK 2	61.26	4.93	60.42	4.83	p=0.29
WEEK 4	55.63	4.33	54.62	4.26	p=0.29
WEEK 6	51.19	4.13	49.23	4.03	p=0.21
WEEK 8	49.52	4.03	42.86	3.63	p=0.02
WEEK 10	48.99	3.96	37.72	2.86	p<0.01
WEEK 12	47.49	3.76	32.69	2.33	p<0.01
WEEK 16	46.29	3.61	32.29	2.53	p<0.01

Table-3 shows mean osteoarthritis index score in both the groups by WOMAC score from baseline to week 16

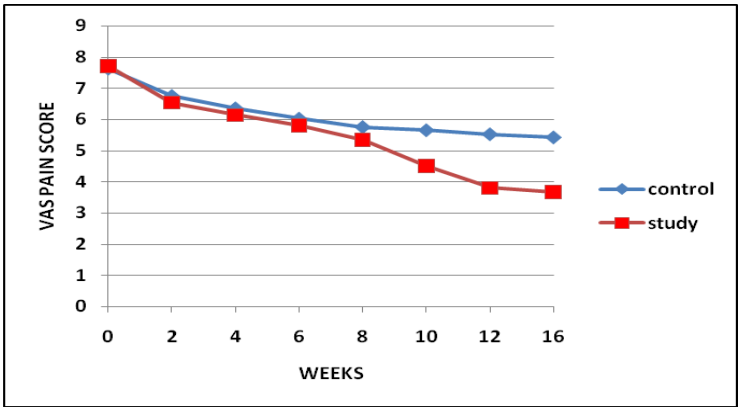

Figure-1 is the graphical representation of Table-2. Comparison between the groups showed statistically significant decrease in mean pain score in the study group from week 8 onwards. Post treatment follow up period at week 16 showed less pain score in study group than the control group.

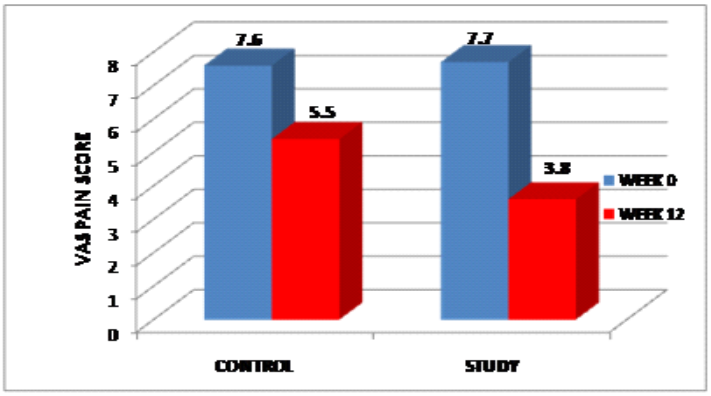

Figure-1A shows the comparison of VAS pain score in both the groups at baseline and 12 weeks

Figure-2 is the graphical representation of Table-3. Comparison between the groups showed statistically significant decrease in mean WOMAC score in the study group from week 8 onwards. Post treatment follow up period at week 16 showed less WOMAC index score in the study group than the control group.

Figure-2A shows the comparison of WOMAC score in both the groups at baseline and 12 weeks

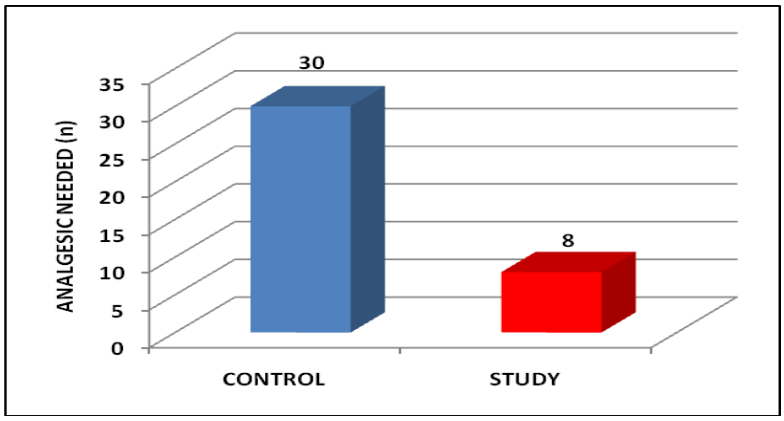

Figure-3 shows analgesic needed in number of patients (n) in both the groups during post treatment follow up period

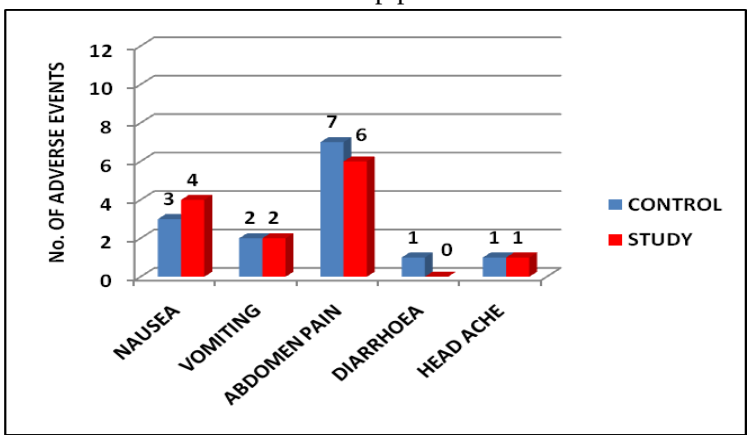

Figure-4 shows the adverse events noted during the study period in both groups.

INVESTIGATIONS	CONTROL GROUP			STUDY GROUP		
	BASELINE	12 WEEKS	p-VALUE	BASELINE	12 WEEKS	p-VALUE
HEMOGLOBIN (g%)	11.3	11.8	0.42	11.8	12.1	0.71
TOTAL WBC COUNT (cells/mm3)	9642	9234	0.34	8953	9178	0.81
BLOOD SUGAR (mg/dl)	104	110	0.88	109	105	0.84
BLOOD UREA (mg/dl)	23.2	24.6	0.41	24.1	23.4	0.62
SERUM CREATININE (mg/dl)	0.88	0.91	0.78	0.82	0.86	0.46
SGOT (IU/L)	32	35	0.46	36	35	0.72
SGPT (IU/L)	38	36	0.84	40	37	0.54

Table 4 shows the laboratory investigations mean values done in both the groups at baseline and 12 weeks.

4.0 DISCUSSION

The efficacy and safety of collagen peptide in the management of patients with knee joint osteoarthritis was assessed in this study. There was no significant difference in the mean age and sex distribution in both the control and the study groups. The mean age distribution in both the groups was 54. More number of female patients were in both the groups. The number of knee joint involvement was also equally distributed in both the groups. There was no significant difference in Xray grading in both the groups. Grade 1 Xray changes were present in more number of patients in both groups (Table-1). Repeat x ray grading at the end of the study period of 12 weeks in both the groups also showed same results.

In this study**, pain assessment with visual analogue scale** and **WOMAC osteoarthritis index score** showed a statistically significant decrease in mean pain score ($p<0.01$) at the end of 12 weeks in both the control and study groups (Table-2, Table-3, Figure-1A, Figure-2A). **Comparison between the groups showed a statistically significant ($p<0.01$) improvement in the study group than the control group from week 8 onwards** (Figure-1, Figure-2).

Since pain was very much reduced in the study group patients (mean pain score of 3.8) at the end of 12 weeks, Tab.Diclofenac was stopped in all the patients in the study group. But in the control group patients (mean pain score of 5.5), Tab.Diclofenac was continued. The patients in both the groups were then assessed after the post treatment follow up period of 4 weeks.

During the **post treatment follow up period**, the need for analgesics was drastically reduced in the study group patients. Only 8 patients needed analgesics as and when required (less than 5 days). But in the control group, the need for analgesics was there and continued in all the 30 patients (Figure-3).

Assessment of post treatment follow up period at week 16 showed that the statistically significant reduction in mean pain score was maintained in the study group even without

analgesics (Table-2, Table-3). **This shows that collagen peptide when used for a period of 12 weeks acts as a disease modifying agent and retards the disease progression and decreases the requirement of analgesics.** This is similar to the placebo controlled study done by Jian-Xin Jiang et al (2012),[10] O.Bruyere et al (2012)[11] and Kumar S et al (2014)[12]

This study showed that collagen peptide does not affect the haematological and biochemical lab parameters and has no significant adverse effect on hepatic and renal functions (Table-4). No serious adverse events were reported in our study. Abdomen pain and Nausea were the common adverse events reported during the study period in both the groups (Figure-4). Abdomen pain, when reported was treated with Tab.Pantoprazole 40mg once daily. Tab.Diclofenac was stopped temporarily for 3 days and patient was advised to apply topical Diclofenac ointment locally. Then after 3 days as pain subsided, Tab.Diclofenac was continued with Tab.Pantoprazole with careful monitoring. Other adverse events noted were vomiting, diarrhea, and headache and were managed symptomatically with standard care. These findings regarding the safety of collagen peptide are consistent with studies[13, 14, 15].

CONCLUSION

In this study, it has been proved that Collagen peptide when added to standard treatment of analgesics along with physiotherapy, is more effective in symptomatic improvement in patients with knee joint osteoarthritis. Collagen peptide is well tolerated and is not associated with serious adverse events. Treatment with Collagen peptide acts as disease modifying agent and decreases the requirement of analgesics and increases the quality of life in these patients.

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