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Clinical Evaluation of Siddha Drug *Gowri Chinthamani Chendooram* in the Management of Osteoarthritis

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ABSTRACT*: The present study was carried out to investigate the efficacy and safety of Siddha drug Gowri Chinthamani Chendooram (GCC) in the treatment of osteoarthritis (Keel Vayu). The raw drugs for the preparation of GCC were obtained and authenticated by the Gunapadam experts. The drugs were purified according to the specification given in the Siddha classical literature "Agasthiar Vaidhya Kaviyam – 1500". The purified raw drugs were then prepared under the capsule heating process. Fifty patients of either sex were selected for clinical trials and were given a dose of 100 – 200 mg thrice a day with Thirikadugu Choornam and sufficient honey after meals. The duration of the treatment depended on the severity from 30 – 60 days. The clinical efficacy with respect to symptoms and grade of movement restriction were assessed prior to and after the treatment. Majority of the patients showed a significant response in ways of remarkable reduction in various symptoms and joint swelling. None of the patients showed any adverse effects. The result of the present study suggested that the usefulness of GCC in patients with osteoarthritis.*

Keywords—*Osteoarthritis, Gowri Chinthamani Chendooram, Keel vayu, joint swelling, Siddha.*

I. INTRODUCTION

Osteoarthritis, strictly Osteoarthrosis, a chronic degenerative joint disease begins in all subjects by the end of fourth decade of life. In this modern era, due to the sedentary life style and less physical exercise, this incidence even gets reduced to the second decade of life [1]. Degeneration of joints in a normal response to ageing, so this disease is a major, common and universal to most of the old age group people which affects significantly the quality of geriatric life [2]. This disease is characterized by pain, tenderness, swelling of the major joints, difficulty in walking, crepitation of the joints and local inflammatory changes without systemic effect due to progressive softening and disintegration of articular cartilage which may lead to chronic disability.

The primary objective for osteoarthritis treatment is to control pain, inflammation and to improve the function of the joint. Even though many NSAIDs (Non steroidal anti-inflammatory drugs) and COX-2 selective inhibitor are available and administered in the treatment of osteoarthritis, they produce the so called adverse drug reactions (ADR) such as GI tract disturbances, renal impairment, increases the risk of myocardial infarction (MI) and stroke [3]. To overcome these problems, many safe, effective and challenging anti-inflammatory and analgesic drugs are available in the Siddha system of medicine, which are in a concealed state. To reveal the effective medicines, this is a single step from the treasure.

One of the best and potent compound drug for osteoarthritis mentioned in '*Agasthiar Vaidhya Kaviyam – 1500*' is '*Gowri Chinthamani Chendooram* (GCC) [4]. It has a long history in Siddha system of medicine for various ailments especially for the treatment of inflammation. It contains Mercury, Sulphur and Borax. Generally as per the Siddha and Tamil literature, the name '*Chinthamani*' is termed for the precious stone, which gives power, energy and vitality. Here the name refers for the character of alleviating diseased conditions thereby makes the individual to normal health. Under the title '*Chinthamani*', only very few preparations are explained in the literature which clearly denotes its supremacy. In the Siddha, the combination of Mercury and Sulphur is said to be very effective drug to treat all types of *Vatha* diseases including osteoarthritis. The trial drug has got the two mentioned drugs and hence, the author has selected GCC to evaluate the efficacy of the drug for the treatment of osteoarthritis.

II. MATERIALS AND METHODS

An open label non-comparative clinical study was designed to study the clinical efficacy and safety of GCC in patients with knee osteoarthritis from out-patient and in-patient department of Post Graduate

Gunapadam (Pharmacology) at Govt.Siddha Medical College Hospital, Chennai from June 2011 to August 2011. Total number of 50 Patients of either sex in the age group of 40 to 70 years with the symptoms of pain, swelling and stiffness in the joints and signs of tenderness and crepitus in the joints and radiologically confirmed patients for osteoarthritis which includes narrowing of the cartilage space, marginal osteophytes, subchondral sclerosis [5], visual analog scale (VAS) scored between 40 to 70 mm and Algofunctional index scored above 7 points were enrolled for the study [6].

Patients suffering from migrating polyarthritis, septic arthritis, tubercular arthritis, AFB, Mantoux positive, positive VDRL, psoriatic arthritis, gout, SLE, hemorrhagic conditions and other systemic diseases were excluded from the study.

The protocol for carrying out the clinical study was approved by the Institutional Ethical Committee (IEC). This study has been conducted according to the principles of good clinical practice [7], i.e. a written informed consent (both English and Tamil) was obtained from all the patients before enrollment and proper history and clinical examination were recorded at base line and on each follow up.

2.1. Pre-study screening and baseline evaluation

The full details of history and physical examination of the patients were recorded. All the patients were scored for pain and physical functions as per Visual analog scale (VAS) and Algofunctional index which was done initially, at the end of 14 days, 28 days, 40 days and 60 days. Follow-ups were done for one month after completion of the study. The laboratory investigation and x-ray findings were recorded initially and at the end of trial period. The key radiographic features of osteoarthritis include joint space narrowing, osteophytes formation, subchondral sclerosis and cysts [8].

2.2. Study Assessment

The improvement of the clinical conditions were assessed on the basis of the improvement in pain, swelling, physical function of the joints, comparison of VAS pain score, Algofunctional index and radiological findings between the pre and post treatment.

2.3. Scoring of the signs and symptoms

Scoring of signs and symptoms of osteoarthritis was based on the severity (no sign or symptom = 0, mild = 1, moderate = 2 and severe =3).

2.4. Pain Visual Analog Score (VAS)

Lack of attention paid to pain leads to reduced mobilization of the patient. Because of its importance, the pain has been called 'fifth vital sign' along with heart rate, pressure, temperature and respiratory rate [9].

The Visual Analogue Scale (VAS) is one of the commonly used tool as the outcome measure for pain. This scale is based on patient own report, behavioral observation and physiological data. Active pain VAS scale is usually constituted as 0 to 100 mm score on a horizontal line and the pain intensity is analyzed by the numbers (0 indicates no pain and 100 indicates severe pain). [10]

2.5. Algofunctional index

The Lequesne algofunctional index of severity for osteoarthritis of the knee was developed by Lequesne, [11] which was designed for the assessment of the efficacy of trial drug for osteoarthritis. The index was modified in 1997 with some minor changes and termed as 'Algofunctional index' [12].

The total index score is in the range 0 - 24, but disease is considered extremely severe if the score is 13. The indices contain elements that tap into pain, stiffness, maximum distance walked and activities of daily living.

2.6. X-ray findings

The key radiographic findings of OA include the formation of marginal osteophytes, the narrowing of the joint cartilage space, subchondral bone sclerosis and altered shape of bone end. Radiological findings and improvement were assessed based on Kellgren Lawrence Grading score [13-14]. These criteria were accepted by the World Health Organization in 1961[15].

2.7. Kellgren Lawrence Grading scores

Grade 0: normal
Grade 1: Doubtful joint space narrowing and possible osteophytic lipping
Grade 2: Definite osteophytes and possible joint space narrowing
Grade 3: Moderate multiple osteophytes, definite joint space narrowing, and some sclerosis and possible deformity of bone ends
Grade 4: Large osteophytes marked joint space narrowing, severe sclerosis and definite deformity of bone ends.
Based on the above grading, entry level findings and improvement results of all the patients were statistically analyzed.

2.8. Gradation of result

Overall results were graded based on the improvement in signs and symptoms.

Marked improvement: >75 % improvement in the clinical signs and symptoms

Moderate improvement: > 51–74 % improvement in the clinical signs and symptoms
Mild improvement: >26 — 50 % improvement in the clinical signs and symptoms
Poor improvement: < 25 % improvement in the clinical signs and symptoms

2.9. Formulation of trial drug GCC

2.9.1. Materials for the trial drug

The raw drugs required for the preparation of *Gowri Chinthamani Chendooram* as mentioned in "*Agasthiar Vaidhya Kaviyam -1500*" are Mercury, Sulphur and Borax [4].

2.9.2. Purification

The raw drugs Mercury, Sulphur and Borax were obtained from a country drug shop at Chennai, Tamilnadu, authenticated by the experts of department of *Gunapadam* (Pharmacology), Government Siddha Medical College, Chennai and voucher specimen has been preserved in the department for future reference. Before preparation of the trial drug GCC, the above raw drugs were subjected to undergo '*Suddhi'* (purification process) as per Siddha Classical text [16].

Mercury (70 gm) was purified by mixing separately with brick powder and turmeric powder and grounded for 1 hour respectively. Then it was washed in clean water. This purified mercury was then placed in an earthen pot over the flame and 2.6 litres of the juice of *Acalypha indica* was gradually added until the juice was completely evaporated. Then mercury was taken away from the earthen pot and again cleaned with water and stored. Sulphur was purified by adding butter in an iron ladle and both were melted over fire. During this process, milk was added to the mixture and the same procedure was repeated for the 30 times. Borax was purified by heated up to be totally devoid of water.

2.9.3. Preparation of the trial drug

After purification, these processed drugs were used for GCC preparation. The procedure for the preparation of formulation as described in the original text was strictly adhered and was standardized. GCC was prepared by special calcination process called '*Manal Maraivu Pudam'* (capsule heating process) as follows.

Mercury and sulphur were added in *Kalvam* (Stone mortar with pestle) and grounded till black fine powder was obtained (Mercury and Sulphur are ground together forms a black coloured compound called '*Kajjali*'). In Ayurveda, it is experimentally proved that it has only very low toxicity [17-18]. Then borax was added and triturated well and obtained homogenous mixture. This mixture was placed in a small cloth bundles called '*Kizhi'*. Then a big pot half filled with sand was taken and the mixture was placed in a big pot and then remaining part of the pot was also filled with sand which was sealed by appropriate lid and covered by *'Seelai*' (layer of thin moist clay coated cloth). This sealed capsule was kept under sunlight until it completely dried.

A small pit having a measurement of 3x3x3 feet was made. The sealed capsule was inverted and placed in the pit. Around the capsule 100 numbers of *Varatties* (cow dung cake) were placed and fired then. After 24 hours, the cloth bundles were taken and allowed for cooling, and grounded well for 24 hours and made it to a fine powder and was labeled as GCC.

2.9.4. Recommended dose

The recommended dosage of *Gowri Chinthamani Chendooram* according to Siddha classical text was 100 mg to 200 mg along with sufficient honey, thrice a day after meals for a period of 30 to 60 days depending on the severity of the symptoms.

2.9.5. Diet restriction

Drug with appropriate diet and restrictions during drug treatment are the key advantage of Siddha system of medicine. Because proper diet will enhance the ability of the drugs to cure diseases effectively. And sometimes foods can also alleviating the symptoms. So the patients were advised to take fresh fruits, green vegetables, low salt diet, fiber rich food and advised to avoid aggravating foods like potatoes, capsicum, tomatoes, dairy products, oily food, acid forming foods, alcohol and smoking. Patients who are obese were instructed to do mild and comfortable exercise like isometric knee exercise, quadriceps strengthening exercise and walking to attain the right weight to prevent further complication of osteoarthritis.

2.9.6. Adverse reaction or side effects

At each visit, patients were asked for occurrence of any undesirable effect based on the tools and classifications developed by the UMC [19] and WHO-ART [20] and improvement in the signs and symptoms observed and recorded.

2.10. Clinical information sheet (CIS)

The clinical information sheet has been generated for osteoarthritis patients which contains the records of diagnostic studies, diagnosis, signs and symptoms, medications, ongoing management, adverse drug reactions if any, summary and evaluation of individual cases.

III. STATISTICAL ANALYSIS

The results of all patients enrolled in this clinical trial were analyzed by Student's paired t-test. The changes in the various clinical parameters, pain assessment score (VAS) and Algofuncitonal index between the pre and post treatment were analyzed and summarized in the result column. Statistical significance was considered at the 95% confidence interval level. P values ≤0.05 were considered statistically significant and were expressed as Mean ± standard deviation (Mean±SD).

IV. RESULTS AND DISCUSSION

In this present study, a total number of 50 patients were participated and completed the trial. Out of this, 8 were male and 32 were female. Baseline demographic features were noted which was summarized in TABLE NO.1. The age group of patients ranged from 31 to 65 years with mean of age was 332.3. Socio-economic status of the patients of present trial showed that 30% of the patients were poor, 33 % were from lower middle class, 33% were from upper middle class and 33% were rich. Occupational status of the patients of the present study showed that 33% were regular employee, 33% were worked in the unorganized sectors and 44% were home maker and only 33% were unemployed. Majority of the patients were Non-vegetarians (45%) and the rest of the patients (45%) were vegetarians. 44% had a positive family history of osteoarthritis and 33% only had a negative family history. 34% had clinical obesity, 33% were average weight and 33% were thin with mean weight of 67.4. the onset of OA in 33% patients were more than a year and only 44% affected less than a year.

The main aim of this present trial is to evaluate the efficacy of the trial drug GCC based on the degree of relief of pain, swelling, stiffness and tenderness. After one month study, all the patients taking the GCC orally, three times per day with honey reported improved range of motion in their joints and decreased pain, swelling and tenderness in knees.

The signs and symptoms of osteoarthritis in all patients were noted and recorded at the initial period, during every visit and at the end of the clinical trial. Initially all the patients had pain, 42 patients had swelling, 47 had stiffness, 29 had tenderness, 47 patients had crepitus on movements and 32 had restriction on movements. After one month of GCC treatment, maximum reduction of pain was observed in all the patients. Before treatment the pain score was 2.76±0.59 (Mean±SD) and after treatment it was 0.96±0.35 (Mean±SD) which is statistically extremely significant (P<0.0001). Before treatment the swelling score was 1.69±0.47 (Mean±SD) and after treatment it was 0.76±0.43 (Mean±SD) which is statistically extremely significant (P<0.0001). Before treatment the stiffness score was 2.55±0.50 (Mean±SD) and after treatment it was 1.26±0.44 (Mean±SD) which is statistically extremely significant (P<0.0001). Before treatment the tenderness score was 1.66±0.48 (Mean±SD) and after treatment it was 0.79±0.41 (Mean±SD) which is statistically extremely significant (P<0.0001). Before treatment the crepitus score was 1.62±0.49 (Mean±SD) and after treatment it was 1.19±0.40 (Mean±SD) which is statistically extremely significant (P<0.0001). Before treatment the restriction on movements score was 2.10±0.60 (Mean±SD) and after treatment it was 1.29±0.46 (Mean±SD) which is statistically extremely significant (P<0.0001).There was a gradual and marked improvement in other signs and symptoms were observed in all the patients and were recorded. The effects are shown in TABLE NO.2. In general, the level of clinical improvement represented by statistical analysis which were extremely significant in all the signs and symptoms. P<0.0001.

4.1. Pain Visual Analog Score (VAS)

Baseline Vas – pain assessment score was 59.08±5.21 (Mean±SD). After the trial drug GCC treatment for one month, the mean ± SD change in the VAS score was 16.82±4.75 (Mean±SD) which indicated that there was extremely significant (p <0.0001) improvement from baseline over the period of one month drug treatment (TABLE NO.3 and Fig No.1).

Baseline Algofunctional index was 8.54±1.42 (Mean±SD). After the trial drug GCC treatment for one month, the (Mean±SD) change in the Algofuncitonal index was 2.94±0.84. From this result it was noted that the Algofuncitonal index was extremely significant (p <0.0001) improved after the trial period of one month. (TABLE NO.3 and Fig No.2)

Before treatment, mean score of arthritic changes in X-ray (joint space, subarticular sclerosis and synovial effusion) was 2.04±0.49 (Mean±SD) and after treatment the mean score was reduced to 1.36±0.48 (Mean±SD) which was statistically extremely significant (*P*<0.0001). All are summarized in TABLE NO.3 and Fig No.3.

At the end of the study period, marked improvement was seen in 64% of the patients, while moderate improvement was seen in 24%, whereas mild improvement was found in 10% and only 02% of the patients had poor improvement. (TABLE NO.4)

4.2. Safety of the trial drug

All the patients were carefully monitored for any incidence of adverse drug reactions or side effects during the trial period and follow up and no such an effects were noted in any of the patients.

Table No.1. Statistic information and baseline features of the patient with Knee Osteoarthritis

Baseline Characters	**No. of Patients (n=50)**		**(%)**
	Male	**Female**	
Age Mean±SD 51.26±9.44			
31-40	5	4	18
41-50	8	7	30
51-60	7	9	32
> 60	4	6	20
Socio-economic status			
Poor	8	7	30
Lower middle	6	8	28
Higher middle	7	8	30
Rich	3	3	12
Occupational status			
Regular Employee	7	5	24
Unorganized sectors	12	7	38
Home maker	0	11	22
Unemployee	7	3	20
Diet			
Vegetarian	08	14	44
Non-vegetarian	16	12	56
Family History			
Present	08	07	30
Absent	16	19	70
Body weight Mean±SD 67.56±7.36			
Average	12	11	46
Thin	7	6	26
Obese	5	9	28
BMI (Kg/m^2) Mean±SD 23.03±3.26			
Duration of illness			
< one year	7	6	26
> one year	17	20	74

Table No.2. Comparison of signs and symptoms between Pre and Post evaluation of drug treatment.

Signs and Symptoms	**No. of Patients (n=50)**	**B.T (Mean±SD)**	**A.T (Mean±SD)**	**P value**
Pain	**50**	**2.76±0.59**	**0.96±0.35**	**<0.0001**
Swelling	**42**	**1.69±0.47**	**0.76±0.43**	**<0.0001**
Stiffness	**47**	**2.55±0.50**	**1.26±0.44**	**<0.0001**
Tenderness	**29**	**1.66±0.48**	**0.79±0.41**	**<0.0001**
Crepitus on movement	**47**	**1.62±0.49**	**1.19±0.40**	**<0.0001**
Restriction of movement	**32**	**2.10±0.60**	**1.29±0.46**	**<0.0001**

Values are expressed in Mean ± SD (n= 50) Student's t test for paired values. Where P **** represents extremely statistically significant at P<0.0001.

Table No.3: Improvement in pain VAS, Algofunctional index and X-ray findings score of OA patients from baseline to 4weeks trial drug treatment.

Outcome measures	No. of Patients (n=50)	B.T (Mean±SD)	A.T (Mean±SD)	P value
VAS	50	59.08 ± 5.21	16.82 ± 4.75	<0.0001
Algofunctional index	50	8.54 ± 1.42	2.94 ± 0.84	<0.0001
X-ray findings	50	2.04 ± 0.49	1.36 ± 0.48	<0.0001

Values are expressed in Mean ± SD (n= 50) Student's t test for paired values. Where P **** represents extremely statistically significant at P<0.0001.

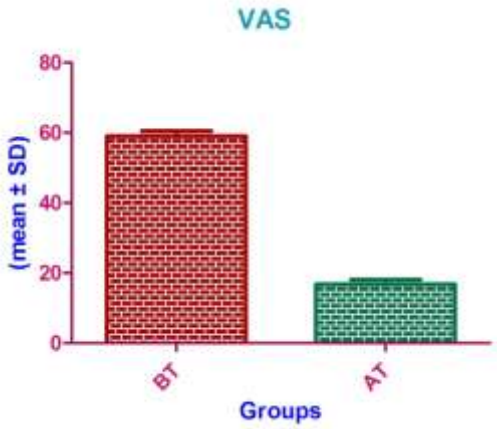

Fig No.1. Visual analog score

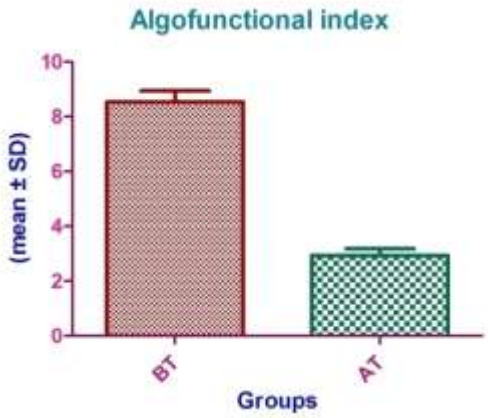

Fig No.2. Algofunctional index score

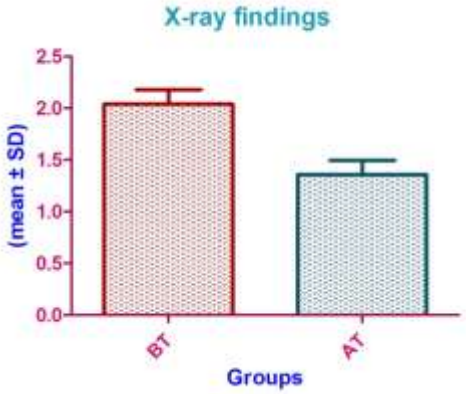

Fig No.3. Radiological improvement score

Table No.4 Gradation of result

Sl.no.	Level of improvement	No. of patients	Percentage (%)
1	Marked	32	64
2	Moderate	12	24
3	Mild	5	10
4	Poor	1	02
TOTAL		50	100

V. CONCLUSION

So for chronic ailments, Siddha system seems to be superior because of long term treatment with available anti-inflammatory analgesic and steroid drugs often causes major disastrous and toxic effects. As there

is no cure for osteoarthritis, the main goal of this present study is to relieve pain, inflammation, improve the range of motion and increase the quality of life with less or no toxic effects. Gowri Chinthamani Chendooram is one of the potential drug which is proved by the highly significant improvement in pain, inflammation and joint movements. There was remarkable relief of signs, symptoms and global assessment of arthritis in 64% patients and moderate relief in 24% patients which showed its potent analgesic and anti inflammatory effect. Majority of the patients responded well within the treatment period of one month. Gowri Chinthamani Chendooram was well tolerated and no incidence of untoward effects was noted during the trial period and one month follows up. Hence, the authors concluded that Gowri Chinthamani Chendooram provided good relief of signs and symptoms and improvement in joint movements in osteoarthritic patients.

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