(International Print/Online Journal)

SJIF IMPACT FACTOR: 5.565
PUBMED-National Library of Medicine ID-101739732

ISSN (Print): 2209-2870
ISSN (Online): 2209-2862

International Journal of Medical Science and Current Research (IJMSCR)
Available online at: www.ijmscr.com
Volume 5, Issue 3, Page No: 492-505
May-June 2022

IJMSCR

Homeopathic Management Of Pain And Stiffness Of Arthritic Knee Joint: Clinical Data Analysis Of Palliation Criteria In An Observational Study

[1] Suvojit Dutta, [2#] Saptarshi Choudhury, [3] Dibyendu Biswas, [4] Anisur Rahman Khuda-Bukhsh

[1,2]D.N. De Homeopathic Medical College & Hospital, 12, Gobinda Kathick Road, Kolkata-700046.

[2#]Presently at: Department of Practice of Medicine, MB Homeopathic Medical College & Hospital, Dr. BNC Sarani, Dumoorjala, Howrah-711104, WB.

[3]Department of Physics, Santipur College, Santipur- 741404, West Bengal, India.

[4]Department of Zoology, University of Kalyani, Kalyani-741235, W.B., India.

[1]Suvojitdutta000@gmail.com,[2] drcsaptarshi@gmail.com, [3] dbbesu@gmail.com

[4] prof_arkb@yahoo.co.in

.

***Corresponding Author:**

Anisur Rahman Khuda-Bukhsh

Formerly at: Department of Zoology, University of Kalyani, Kalyani-741235, W.B., India.

Phone: +913325828768; Mob: +919331040032.

Present Address: B-2/325, Kalyani, Husn Ara Manzil, Kalyani-741235, W.B., India.

Type of Publication: Original Research Paper

Conflicts of Interest: Nil

Abstract

Knee joint osteoarthritis (OA) is a progressive degenerative disease of the knee joint resulting in severe joint pain with stiffness and inflammation causing considerable impairment in daily activities of patients. Management of pain with routine non-steroidal anti-inflammatory drugs in such cases may give some patients temporary relief, but use of these drugs often causes unwanted side-effects. Limited clinical data available so far on homeopathic management of arthritic pain and stiffness are still inadequate and inconclusive for claiming efficacy of homeopathic drugs. Therefore, we undertook this pilot study with seventy patients of the "outpatient department" (OPD) to evaluate relative efficacy of certain commonly used homeopathic medicines selected strictly on the basis of *similia principle*. We objectively analyzed the data through certain accepted protocols of pain measurements as recommended by "American College of Rheumatology Criteria", like "Western Ontario and McMaster Universities Arthritis Index" (WOMAC) and also crosschecked by "Intermittent and Constant Osteoarthritis Pain Scale" (ICOAP) protocols, utilizing relevant statistical analyses. Most patients responded favorably to homeopathic drugs, showing amelioration of their joint pain, inflammation and joint stiffness; post-medication data were compared with pre-medication state after five to six consecutive visits at OPD wherein consecutive visits were separated by two weeks' interval between them. Statistical interpretation indicated a significant increase in index of daily performance in patients along with the decrease in pain measurement data ($P<0.001$).There is ample scope for effective management of arthritic muscle pain and stiffness of knee joint through administration of homeopathic drugs, which have no significant side-effects and relatively much cost-effective as compared to conventional treatment with modern medicines.

Keywords: Osteoarthritis; Knee joint pain and stiffness; Rheumatology, Homeopathy, Ultra diluted medicine, WOMAC Scale, ICOAP scale.

Introduction:

Osteoarthritis (OA) is one of the commonest forms of arthritis and is a leading cause of physical disability, increased health care usage and impaired quality of life. Osteoarthritis is the fourth leading cause of "year lived with disability" (YLDs), accounting for 3.0% of

total global YLDs [1]. It is also responsible for the decrease in "activities of daily living" (ADL) in elderly dependent population in the community [2].

Though OA may develop in any joint, most commonly it affects the knees, hips, hands, facet joints and feet. In them the most prevalent cause of disability amongst elderly patients suffering from OA is because of disease involvement of knee joints [3,4].

Although both sexes may suffer equally, peri- and post-menopausal aged females tend to suffer more than male. the reason for which may be attributed to the loss of estrogen at this age, while in contrast to that, generally younger males are affected more with this disease [5-9].

Besides age and sex, other varieties of both modifiable and non-modifiable factors among adult population responsible for increasing the risk of formation of knee OA and impaired quality of life exponentially are genetic predispositions, obesity, lack of exercise, bone density, faulty diet routine, trauma and work environment conditions among adult population [10].

The modern civilization and expanding industrialization have reduced the necessity of physical activity to a great extent but they have reciprocally helped to increase musculo-skeletal disorders. As per the global burden of disease recorded in 2010, the knee and hip joints OA have ranked to be the 11th highest contributors of global disability [11].

In 2005, it was estimated in a study that over 26 million people in the USA had some form of OA [12]. Other studies have observed that geographic variation modulates the disease outcome significantly. A cohort study on a Chinese population showed a higher affection for bilateral knee joint OA than their European or American counterpart [13]. The communityoriented program for control of rheumatic disorders (COPCORD) studies conducted in India showed that clinically diagnosed knee OA was higher in the urban (5.5%) than rural populations (3.3%) as per the crude data, while when this was adjusted in reference to age and sex distribution, the prevalence appeared to be a little higher in rural population [14]. Reasons for such variation may perhaps be due to occupational trauma, lack of knowledge leading to casual approach towards early symptoms of OA and lack of financial solvency preventing early medical consultation and therapy.

As per United Nations report, by 2050 people aged over 60 will account for more than 20% of the world's population [15]. Of that about 20% (a more conservative estimate of 15%) may have symptomatic OA, and one-third of these people would be severely disabled. This means that by 2050, 130 million people will suffer from OA worldwide, of whom 40 million will be severely disabled by the disease [15]. Therefore, this high prevalence of disease and its impact on the individual in particular and the society at large should be a major public health concern.

Osteoarthritis is currently diagnosed by clinical presentations, physical examination and wherever necessary for confirmation, with X-ray, MRI scan and arthroscopy. Typical radiographic features in knee OA include joint space narrowing, subchondral bone sclerosis, cyst formation and osteophytes which are a hallmark of OA. Loss of cartilage is an early and cardinal feature of OA leading to joint space narrowing shown in plain radiographs [16]. The thickness of articular cartilage varies between individuals and joint surfaces, therefore no reference values for thickness of joint space truly exist. Till now, there are no known specific biomarkers for OA that can be used in clinical practice.

As there is no known cure for OA till now, modern medicinal treatment primarily aims to control pain, and improving function and health-related qualities of life [17]. Acetaminophen, aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) are commonly prescribed in modern medicine as pain reliever for OA. However, most of these drugs also have unwanted side-effects. Excessive use of these drugs is reported occasionally to produce serious health hazards, like peptic ulcer syndrome, mood disorders, gastritis, gastric ulcers leading to hematemesis, melena, gastric perforation which also increase risk for hospitalization and can even cause death [18,19] Glucosamine sulfate and chondroitin sulfate are two well-known nutritional supplements which protect joint cartilages, and have been reported to be useful in cases of osteoarthritis, but hitherto it could not replace the necessity of NSAIDs for pain management. Visco-supplementation with intra

Volume 5, Issue 3; May-June 2022; Page No 492-505

articular hyaluronic acid is also in practice for long but it has only shown a limited benefit in treatment of knee OA [20] Lastly in cases of advanced OA with severe movement disability, a total knee joint replacement surgery (TKR) may provide help, however, many patients are not candidates for joint replacements because of their co-morbidities, besides that the surgery in itself is extremely expensive proposition leaving a little scope for general population in a country like India to opt for this.

With this background scenario, some studies have recently been carried out to ascertain if the complementary and alternative medicines (CAM), particularly the homeopathic medicines, which are generally used in ultra-high dilutions and in micro doses, and relatively more affordable to a larger section of the population because of lesser cost of homeopathic treatment, can be helpful in ameliorating the pain, stiffness and inflammation in arthritic knee joints, without producing any toxic side effects. However, the results of the limited studies done are rather inconclusive, some studies suggesting benefits while others reporting the benefits to be no more than placebo [24]. Therefore, we became interested to undertake an open label pilot clinical study with the primary objective to examine if some well selected homeopathic remedies can ameliorate the pain and sufferings of the patients. Since our major objective was set to remove the pain, stiffness and inflammation of knee joints, so that the patients could have a better quality of life, enabling them to increase their ALD, we adopted the most accepted protocols for measuring pain quantitatively and qualitatively by parameters like American College of Rheumatology Criteria (ACRC) and Western Ontario and McMaster Universities Arthritis Index (WOMAC) adopting Intermittent and Constant Osteoarthritis Pain Scale (ICOAP) and utilizing relevant statistical analyses [25,26].

Homeopathy as a therapeutic system may be studied to manage specifically the pain of knee joint OA beside minimizing joint stiffness to increase the ALD. Since homeopathy is relatively safe and without any known side effects, and easy to administer, we tried to extend the clinical data of efficacy of selected homeopathic remedies and analyzed the possible role of homeopathic remedies in pain and stiffness management of knee joints in patients of different ages in this study.

Therefore, the hypotheses to be tested in this study were: i) to find out relative efficacy of some suitable homeopathic drugs and potencies thereof, if possible, that can be confidently used in patients of different age groups and sex to reduce pain, stiffness and inflammation of arthritic knee joints without producing any toxic side- effects, and ii) to examine if there could be any one homeopathic drug that could give better results than others in a given patient with certain guiding symptoms.

Materials And Methods:

For the purpose of assessment of pre-and post-treatment outcomes particularly in relation to management of pain and stiffness in knee joint OA, two self-reported assessment questionnaires pertaining to pain index, namely i.) The Western Ontario and McMaster Universities Osteoarthritis index (WOMAC) and ii.) Intermittent and Constant Osteoarthritic Pain Score (ICOAP), were used as they are known to be most commonly used standard protocols to assess the outcome in such studies. Two different scales were chosen in order to cross check results to avoid any possible bias [25-28].

Study Design:

The study has been conducted at the D. N. De Homoeopathic Medical College & Hospital, 12, Gobinda Khatick Road, Kolkata- 700046, West Bengal, India. The study period was about five months (from 7.11.2017 to 13.04.2018) and it was conducted as an open label interventional study model as part of the STSH program under the Central Council for Research in Homoeopathy. Patients were randomly selected from Out Patient Department (OPD) of Practice of Medicine, D. N. De Homeopathic Medical College & Hospital, Kolkata. The necessary ethical clearance for the study was obtained from the institutional ethical committee. All patients were enrolled as volunteers to participate in the study and signed the “informed consent” after being given detailed information about the nature of the study before onset. The patients were systematically asked about details of their ailments and the data carefully recorded in structured and well-designed questionnaires (Fig. 1). A total of seventy willing patients randomly selected and

Volume 5, Issue 3; May-June 2022; Page No 492-505

diagnosed with knee joint osteoarthritis (as per ACRC Criteria) by clinical examinations and positive x-ray findings were included in the study. They were examined periodically and generally followed up for a period of ten weeks (minimum) to twelve weeks (maximum) during their treatment phases with an approximate interval of two weeks between their two consecutive visits at the OPD. Their treatment outcome was assessed through i.) WOMAC questionnaires having three subscales, pain, stiffness and difficulty performing daily activities and ii.) ICOAP questionnaires, having subscales – constant, intermittent and total pain scores. The condition-specific WOMAC questionnaire is a multidimensional measure of pain, stiffness, and physical functional disability consisting of 24 items graded in a numerical rating scale ranging from 0 ("no symptoms") to 10 ("extreme symptoms") and ICOAP is an 11 item tool which takes into account both intermittent and constant pains of knee joint OA sufferers, the scoring is from 0 (no pain at all) to 4 (extreme pain) for item no 1-11, except 7, for which the scoring stands as 0 (never/ I don't have) and 4 (very often)[22- 25]. Pre-and post-medication assessments chiefly of pain and stiffness of knee joint OA patients were done to understand the outcome.

Table-1. American College of Rheumatology criteria for classification of idiopathic osteoarthritis of knee joints

Clinical and laboratory	**Clinical & Radiographic**
Knee pain + at least 5 of 9	Knee pain + osteophytes on X-rays + at least 1 of 3 1. Age > 50 years 2. Stiffness < 30 min
1. Age > 50 years	1. Age > 50 years
2. Stiffness < 30 min	2. Stiffness < 30 min
3. Crepitus	3. Crepitus
4. Bony tenderness	
5. Bony enlargement	
6. No palpable warmth	
8. R F < 1: 40	
9. White blood cell count < 2000/mm^3	

Selection of Patients:

Patents were selected by adopting the following inclusion and exclusion criteria:

1. Inclusion criteria:

   Subjects suffering from pain and stiffness of knee joint osteoarthritis.

   Subjects of above 40 years in men

   Post-menopausal in female.

Volume 5, Issue 3; May-June 2022; Page No 492-505

Subject of both sexes.

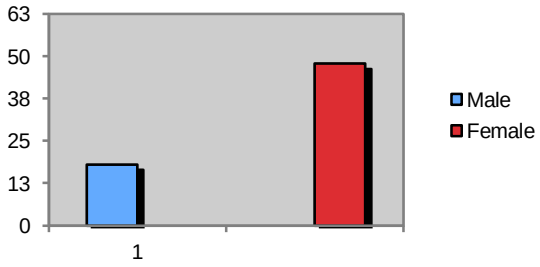
Subject of all religions.

2. Exclusion criteria:

1. Person's suffering from other associated severe illnesses requiring urgent medical intervention.
2. Patients taking any anti-inflammatory allopathic drugs.
3. Patients taking any type of pain reducing treatment.
4. Patient unwilling to participate in trial.

Results:

Out of 70 patients selected randomly for the study, 4 patients dropped out after first visit. Out of remaining 66 Patients 62 continued for the full tenure of 12 weeks while 4 patients continued for 10 weeks. Among these 66 patients, only 18 were male and 48 were female (see Bar Chart-1).

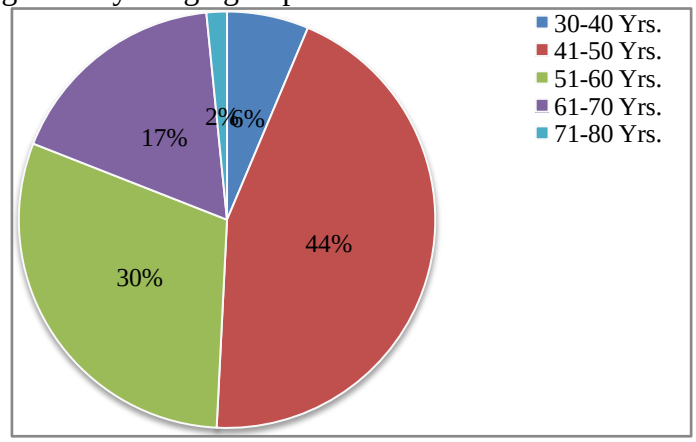


Bar Chart-1.

4 of 66 patients were from age group of 30-40 yrs., 28 patients from the age group 41-50 yrs., 22 patients from the age group of 51-60 yrs., 11 patients were from the 61-70 yrs. age group and only 1 was from 71-80 yrs. age group category. (see Pie Chart-1)

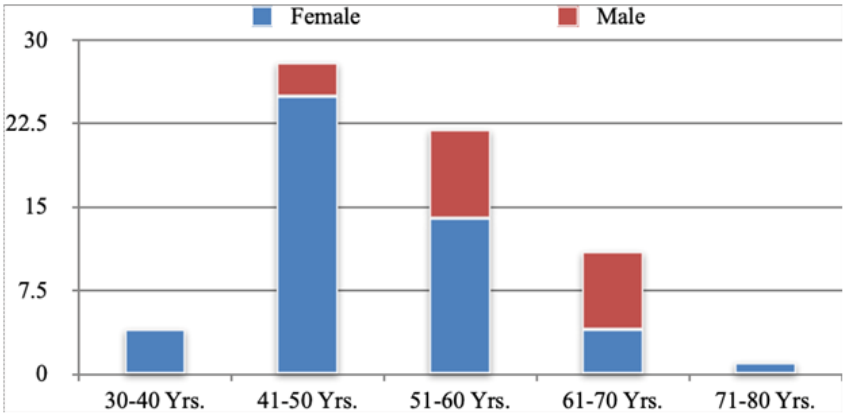
Pie Chart-1.

Of these, 4 patients belonging to 30-40 yrs. age group were all female. In 41-50 yrs. age group, 28 were female and 5 were male, among 51-60 yrs. age group 14 were female and 08 were male, among 61-70 yrs. age group



04 were female and 06 were male and there was only single female patient under the 71-80 yrs age group. (see

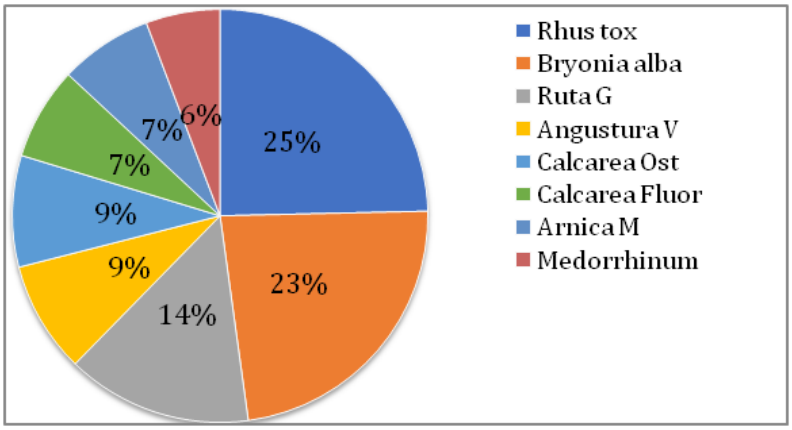
Volume 5, Issue 3; May-June 2022; Page No 492-505



2D Stacked column chart-1

2D Stacked column chart-1).

The pie chart 2 summarizes different drugs required to be administered in different patients like Rhus Tox, Bryonia Alba, Ruta Graveolens, Angustura V., Calcarea Ost, Calcarea fluor, Arnica Montana and Medorrhinum (4 patients). However, occasionally, a few patients had sometimes to be temporarily given intermittent remedies on symptomatic demand, although they were again returned to their respective selected remedy.



Pie chart- 2

Besides them other drugs which were prescribed and in less frequency are Calcarea iod, Causticum, Hypericum, Lachesis, Natrum Mur, Natrum sulph, Phytolacca, Pulsatilla nigricans, Sepia, Staphysargia and Thuja. Medorrhinum and Thuja came mostly as inter-current remedy with the other drug.

Potencies used were Decimal (X), Centesimal (C) and 50 millesimal (LM). Of them centesimal potencies were mostly used in OPD and of which the 200C potency has been prescribed in maximum numbers of time.(Pie

Volume 5, Issue 3; May-June 2022; Page No 492-505

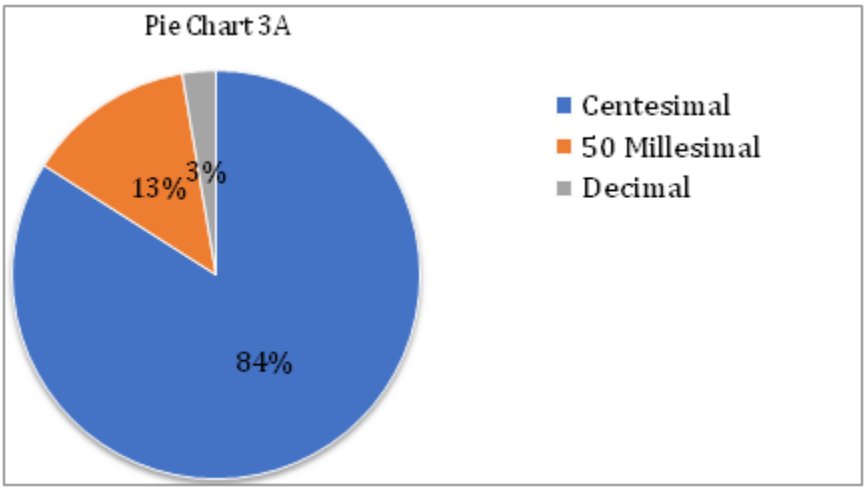
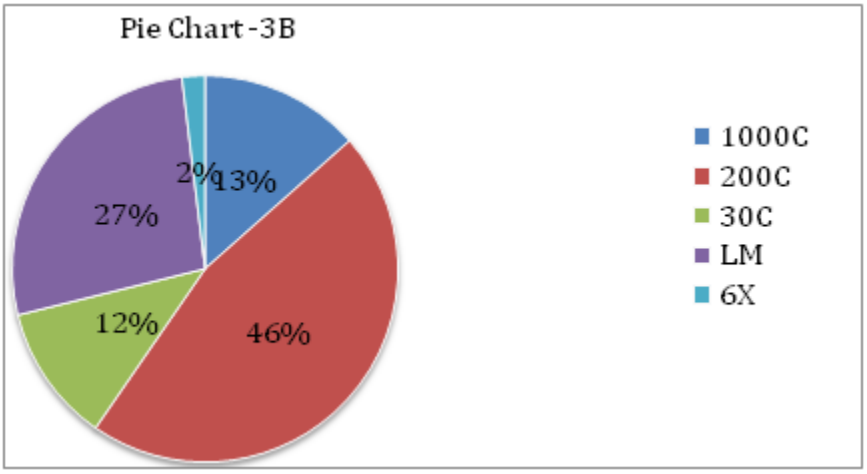


Chart -3A & 3B



Statistical Interpretation of the study considering both ICOAP & WOMAC

Scoring correlation:

Paired samples T-test:

Out of seventy patients, sixtysix were considered here for statistical analysis because four patients were unavailable for reporting after their first visit. Among sixty six cases, four cases did not turn up after 5th visit, i.e, in their last visit.

Student's T-test has been performed using SPSS 17.0 to find statistical properties of the study. Paired samples – (i) Constant score and intermittent score, (ii) Constant score and Total ICOAP score, (iii) Intermittent score and Total ICOAP score, and (iv) WOMAC score and Total ICOAP score were chosen to execute the test. It helped us to check the consistency of different scores. The findings are given below in the form of tables.

Volume 5, Issue 3; May-June 2022; Page No 492-505

Table – I

Paired Samples Statistics

Pairs		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Constant score	32.3393	392	21.24894	1.07323
	Intermittent score	34.6392		20.32182	1.02641
Pair 2	Constant score	32.3393		21.24894	1.07323
	Total ICOAP score	33.7061		20.06149	1.01326
Pair 3	Intermittent score	34.6392		20.32182	1.02641
	Total ICOAP score	33.7061		20.06149	1.01326
Pair 4	WOMAC Score	0.0044		20.06149	1.01326
	Total ICOAP score	33.7061		0.00159	0.00008

Table – II

Paired Samples Correlations and test

Paired Samples	Paired Differences					t	df	Correlation
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
				Lower	Upper			
constant score – Intermittent score	-2.29990	11.63123	0.58747	-3.45488	-1.14491	-3.915	391	0.844
Constant score – Total ICOAP score	-1.36686	6.21270	0.31379	-1.98379	-.74994	-4.356		0.956

Volume 5, Issue 3; May-June 2022; Page No 492-505

Intermittent score - Total ICOAP score	0.93304	5.63462	.28459	.37352	1.49256	3.279		0.961
WOMAC Score – Total ICOAP Score	33.70170	20.06032	1.01320	31.70970	35.69370	33.263		0.732

Power law relation:

To measure the response of a patient undergoing treatment, a power law like relation was assumed between WOMAC score (or ICOAP score) and number of visits of concerned patients. Therefore, it was expressed as $x = a\, y^{\alpha}$; where x was WOMAC score (or ICOAP score) and y was number of visits of the patient to the doctor. To find the scaling coefficient, the software ORIGIN 7.0 was used to apply linear regression. The value of α for WOMAC score was -0.45041 ($P < 0.0001$) whereas it was -0.71923 in case of ICOAP score ($P < 0.0001$) for the entire study.

The statistical description for the dependence of WOMAC score on number of visits is given below:

Table – III

Model: Linear regression [Ln (WOMAC score) = Ln (a) + α × Ln (no. of visit)]

Parameter	***Value***	***Error***	***R***	***SD***	***N***	***P***
Ln (a)	-4.99474	0.02864	-0.70444	0.27496	392	<0.0001
α	-0.45041	0.02298				

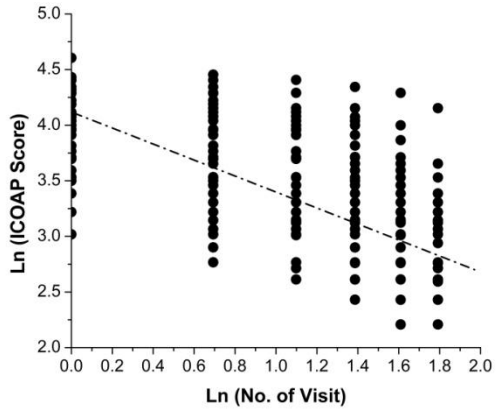
The statistical description for the dependence of ICOAP score on number of visits is given below:

Table – IV

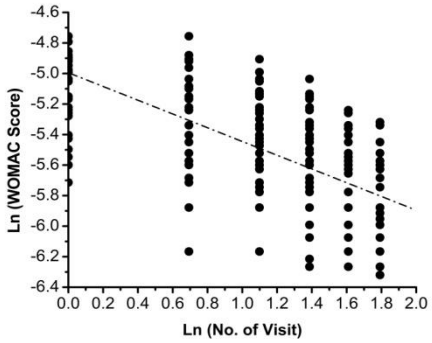
Model: Linear regression [Ln (ICOAP score) = Ln (a) + α × Ln (no. of visit)]

Parameter	***Value***	***Error***	***R***	***SD***	***N***	***P***
Ln (a)	4.11821	0.04852	-0.68311	0.46589	392	<0.0001
α	-0.71923	0.03894				

Volume 5, Issue 3; May-June 2022; Page No 492-505



(a)



(b)

Figure: (a) The plot of ICOAP score and the number of visits in log-log scale.
(b) The variation of WOMAC score with number of visits in log-log scale.

The clinical courses of improvements were scored by two independent reviewers as per modified Naranjo algorithm and their agreed scores were as follows

Modified Naranjo Algorithm

Serial No.	Questions	Reviewer 1	Reviewer 2	Agreed Score
1	Was there an improvement in the main symptom or condition for which the homeopathic medicine was prescribed?	(+)2	(+)2	(+)2
2	Did the clinical improvement occur within a plausible time frame relative to the drug intake?	(+)1	(+)1	(+)1
3	Was there an initial aggravation of symptoms?	0	0	0
4	Did the effect encompass more than the main symptom or condition, i.e. were other symptoms ultimately improved or changed?	(+)1	(+)1	(+)1
5	Did overall wellbeing improve? (to suggest using validated scale)	(+)1	(+)1	(+)1

Volume 5, Issue 3; May-June 2022; Page No 492-505

6	Did the course of improvement follow Hering's Rule?	(+)2	(+)2	(+)2
7	Did "old symptoms" (non-seasonal and non-cyclical symptoms that were previously thought to have resolved) reappear temporarily during the course of improvement?	0	0	0
8	Are there alternate causes (other than the medicine) that solely could have caused the improvement? (to consider known course of disease, other forms of treatment, and other clinically relevant interventions)	(+)1	(+)1	(+)1
9	Was the effect confirmed by objective evidence as measured by external observation(s)?	(+)2	(+)2	(+)2
10	Did repeat dosing, if conducted, create similar clinical improvement?	(+)1	(+)1	(+)1
	Total	(+)11	(+)11	(+)11

According to the interpretation of total Naranjo score predicting drug action, score more than or equals to +9 is considered as definite attribution of homoeopathic medicinal treatment.

Discussion And Conclusion:

The results of the present study reveal that several homeopathic medicines could effectively reduce knee joint osteoarthritic pain and stiffness to improve performance of daily activities. In this study, the homeopathic remedies had been prescribed on the basis of totality of symptoms or on similia principle. In the recent study, Rajgurav and Aphale [29] published data on some 30 patients treated only with Rhus Tox by following the criteria recommended in WOMAC and Kelgren and Lawrence system and found Rhus Tox to give amelioration to patients with knee joint pain and stiffness. In another placebo-controlled study, Koley et al [24] reported some ameliorative effects of several homeopathic remedies like Bryonia Alba, Rhus Tox, Calcarea carb, Arnica Montana and Natrum Mur, but unfortunately, they could not find the efficacy of the drugs any more than placebo. However, in the present study, we used a few drugs common to both the studies, like Bryonia Alba, Rhus Tox and Arnica Montana apart from five other drugs not used so far by other workers, but we got favorable ameliorating effects of these drugs when we compared the data in terms of parameters used before and after drug administration. In fine, the following points were noted:

1. The drugs which are mentioned in the textbook of homoeopathic Materia Medica were as effective to manage knee joint osteoarthritis pain and stiffness as they were found previously while their proving and repeated clinical verifications [30]. They were found to be useful at least for patients residing on the Gangetic planes of west Bengal (Kolkata & surroundings) on whom the trial was conducted.
2. The centesimal potency scale was effective in treating knee joint OA patients for managing their pain and specifically 200C potency was found to act more prominently in this case.
3. Since these drugs are ultra-highly diluted and not known to cause any secondary adverse effect to the system therefore hostile/adverse effects of using NSAIDs can be well avoided under this treatment.
4. Since cost of homeopathy medicine is relatively much less in comparison to modern medicine, therefore effective patient care in knee joint OA with less financial involvement on the part of the

Volume 5, Issue 3; May-June 2022; Page No 492-505

patient/hospital can be quite possible and recommended for getting treatment outside.

5. Admittedly, the five and half months-time period is too short a time to come up with any concrete conclusion, but the results of the present study would definitely stimulate further extensive studies to arrive at a more conclusive and dependable conclusion.

Finally, in this study, we found significantly better way of life of the patients who took the homeopathic drugs as per similia principle, with their measurement criteria much improved during and after the period of treatment. Mostly ultra-highly dituted potentized drugs were used in low intermittent doses. However, how the ultra-highly diluted homeopathic drugs could bring in such spectacular ameliorative effects to reduce significantly the sufferings of the patients could not be clearly understood and it would probably continue to be a subject of in-depth quest for future researchers; however, there have been some advancement in understanding the possible mechanism through which these drugs possibly act. These ultra- highly diluted drugs have now been known to contain nanoparticles of original drug substance(s) [31-32] which are capable of acting at the molecular level, possibly triggering their action through impacting on DNA and triggering a cascade of some relevant target gene expressions in a favourable manner [33-38], presumably via their regulatory action through epigenetic modifications [39-42]; that could in turn initiate and manage the recovery process in such a way that it would not only give relief to their joint pain, stiffness of muscle and favorably modify inflammatory changes, but would increase thereby their day to day activities yielding greater output of their daily productivity and thus give them a better way of life.

Acknowledgements:

We convey our sincere thanks to the Principal, Dr. Shyamal Kumar Mukherjee, D. N. De H M C & H, Kolkata- 700046 for his encouragements. Sincere thanks are also due to Dr. Samit Dey, Asst. Prof. & Head, Dept. of Repertory for his kind help in verification of computerized repartorial process. We convey our appreciation to Dr.Smriti Das, Deptt. of Repertory, MBHM College and Hospital, Howrah, for her help in collecting some data of this work.

References:

[1].World Health Organization. World Health Report 2002. Reducing Risks, Promoting Healthy Life. Geneva: WHO; 2002.

[2]. Felson DT. The epidemiology of knee osteoarthritis: results from the Framingham Osteoarthritis Study. Semin Arthritis Rheum 1990;20:42-50.

[3]. Urwin M, Symmons D, Allison T, Brammah T, Busby H, Roxby M, etal. Estimating the burden of musculoskeletal disorders in the community: the comparative prevalence of symptoms at different anatomical sites, and the relation to social deprivation. Ann Rheum Dis 1998; 57: 649e55.

[4] Silverstein FE, Graham D Y, Senior JR, Davies H W, Stuthers B J, Bittman R M, et al. Misoprostol reduces serious gastrointestinal complications in patients with rheumatoid arthritis receiving NSAIDS. Ann Intern Med 1995;3:241-9.

[5]. Spector TD, Campion GD. Generalized

osteoarthritis is a hormonally mediated disease. Ann Rheum Dis 1989;48:2566.

[6].Likivainio T, Bragge T, Hakkarainen M, Karjalainen PA, Arokoski J. Gait and muscle activation changes in men with knee osteoarthritis. Knee. 2010;17:69–76. [PubMed: 19556137]

[7]. Childs JD, Sparto PJ, Fitzgerald GK, Bizzini M, Irrgang JJ. Alterations in lower extremity movement and muscle activation patterns in individuals with knee osteoarthritis. Clin Biomech (Bristol, Avon) 2004;19:44–9.

[8]. Likivainio T, Arokoski J. Physical function and properties of quadriceps femoris muscle in men with knee osteoarthritis. Arch Phys Med Rehabil. 2008;89:2185–93. [PubMed: 18996249]

[9]. Hinman RS, Bennel K, Metcalf B, Crossley K.

Delayed onset of quadriceps activity and altered knee joint kinematics during stair stepping in individuals with knee osteoarthritis. *Arch Phys Med Rehabil*. 2002;**83**:1080–6. [PubMed: 12161828]

[10]. Esser S, Bailey A. Effects of exercise and physical activity on knee OA. *Curr Pain Headache Rep*. 2011;15:423–30. [PubMed: 21956792]

[11]. Cross M, Smith E, Hoy D, Nolte S, Ackerman I, Fransen M, et al. The global burden of hip and knee osteoarthritis: estimates from the global burden of disease 2010 studyAnn Rheum Dis

. 2014 Jul;73(7):1323-30.doi: 10.1136/annrheumdis-2013-204763. Epub 2014 Feb 19.

[12]. Lawrence RC, Felson DT, Helmick CG et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. *Part II. Arthritis Rheum* 2008;**58**:26–35.

[13]. Fransen M, Bridgett L, March L et al. The epidemiology of osteoarthritis in Asia. *Int J Rheum Dis* 2011;**4**:113–21.

[14]. Haq SA. Osteoarthritis of the knees in the COPCORD world. *Int J Rheum Dis*

2011;**14**:122 – 9.

[15]. United Nations. World Population to 2300. Available at:

http://www.un.org/esa/population/publications/.../WorldPop2300final.pdf

[16]. Textbook of RADIOLOGY AND IMAGING.7e, Volume- 2, set by Devid

Sutton.Elsevier Limited,First printed in India 2009, p1225

[17]. Smink AJ, van den Ende CH, Vliet Vlieland TP. Beating osteoarthritis: Development of a stepped care strategy to optimize utilization and timing of non-surgical treatment modalities for patients with hip or knee osteoarthritis. *Clin Rheumatol*. 2011;30:1623–9. [PubMed: 21887488].

[18]. Kon E, Filardo G, Drobnic M, Madry H, Jelic M, Dijk N, et al. Non-surgical management of early knee osteoarthritis. Knee Surg Sports Traumatol Arthrosc. 2012;20:436–9. [PubMed: 22037809]

[19]. Pinals RS. Pharmacologic treatment of osteoarthritis. Clin Ther. 1992;14:336–46. [PubMed: 1386287]

[20]. Lo GH, LaValley M, McAlindon T, Felson D. Intra-articular hyaluronic acid in treatment of knee osteoarthritis. JAMA. 2003;290:3115–21. [PubMed: 14679274]

[21]. Knuesel O, Weber M, Suter A. Arnica montana gel in osteoarthritis of the knee: an open, multicenter clinical trial. Advances in Therapy. Sep-Oct 2002;19(5):209-18. doi: 10.1007/BF02850361.PMID: 12539881 DOI: 10.1007/BF02850361.

[22]. Hielm-Bjo¨rkman A, Tulamo RM, Salonen H, et. al. Evaluating Complementary Therapies for Canine Osteoarthritis—Part II: A Homeopathic Combination Preparation (Zeel). eCAM 2009;6(4)465–471 doi:10.1093/ecam/nem143. PMID: 18955260 PMCID: PMC2781775

[23]. Lennihan B. Homeopathy for pain management. Alt and Comp Ther, Mary Ann Liebert Inc., 2017, 23 (5): 2017, DOI: 10.1089/act.2017.29129.ble

[24]. Koley M, Saha S, Ghosh S. A double-blind randomized placebo-controlled feasibility study evaluating individualized omeopathy in managing pain of knee osteoarthritis. Journal of Evidence-Based Complementary & Alternative Medicine 2015, Vol. 20(3) 186-191. PMID: 25636410

[25]. Wolfe F, Pincus T . Listening to the patient: a practical guide to self-report questionnaires in clinical care. Arthritis Rheum. 1999; 42. 1797-1808.

[26]. Bellamy N. WOMAC Osteoarthritis Index: a user's guide. London, Ontario, Canada: University of Western Ontario; 2004.

[27]. Kellgren JH, Lawrence JS. Radiological assessment of osteoarthrosis.

Ann Rheum Dis. 1957;16:494–502.

[28]. Mark D. Kohn BA, Adam A. Sassoon MD, Navin D. Fernando MD. Classifications in Brief: Kellgren-Lawrence Classification of Osteoarthritis.Clin Orthop Relat Res. 2016; 474:1886–1893. DOI 10.1007/s11999-016-4732-4

[29]. Atul B. Rajgurav A B and , Aphale P. To study the efficacy of Rhus tox in management of cases of

Volume 5, Issue 3; May-June 2022; Page No 492-505

osteoarthritis of knee joint Int J Res Orthop. 2017 Jan;3(1):54-60

[30]. Boericke's new manual of homoeopathic materia medica with repertory 3rd

revised. Kuldeep Jain New Delhi, Jain publisher;2016.

[31]. Chikramane PS, Suresh AK, Kane SG, Bellare JR. Metal nanoparticle induced hormetic activation: a novel mechanism of homeopathic medicines. Homeopathy. 2017;106(3):135-144. doi:10.1016/j.homp.2017.06.002

[32]. Bell IR, Schwartz GE. Adaptive network nanomedicine: an integrated model for homeopathic medicine. Front Biosci (Schol Ed). 2013 Jan 1;5(2):685-708. doi: 10.2741/s400.

PMID: 23277079

[33]. Khuda-Bukhsh A R. Potentized homeopathic drugs act through regulation of gene-expression: a hypothesis to explain their mechanism and pathways of action in vitro. Complementary Therapies in Medicine, 1997; Volume 5 (1): 43-46.

[34]. Khuda-Bukhsh AR. Towards understanding molecular mechanisms of action of homeopathic drugs: an overview. Mol Cell Biochem. Review. 2003 Nov;253(1-2):339-45. doi: 10.1023/a:1026048907739.PMID: 14619985.

[35]. Khuda-Bukhsh AR, Pathak S. Homeopathic drug discovery: theory update and methodological aspect. Expert Opin Drug Discov. 2008 Aug;3(8):979-90. doi: 10.1517/17460441.3.8.979. PMID: 23484971

[36]. Khuda-Bukhsh AR. Laboratory research in homeopathy: pro.

Integr Cancer Ther. 2006 Dec;5(4):320-32. doi: 10.1177/1534735406294794.

PMID: 17101761. Review.

[37]. Khuda-Bukhsh A R. Current trends in high dilution research with particular reference to gene regulatory hypothesis. The Nucleus, March 2014, DOI 10.1007/s13237-014-0105-0 Review.

[38]. Khuda-Bukhsh AR. An overview of research at University of Kalyani in exploring some basic issues of homoeopathy. Indian J Res Homeopathy 2017;11:147-57. DOI: 10.4103/ijrh.ijrh_25_17

[39]. Mallick P, Mallick JC, Guha B, Khuda-Bukhsh AR. Ameliorating effect of microdoses of a potentized homeopathic drug, Arsenicum album, on arsenic-induced toxicity in mice. BMC Complement Altern Med 2003;3:7.

[40]. Khuda-Bukhsh AR, Sikdar S. Condurango 30C Induces epigenetic modification of lung cancer-specific tumour suppressor genes via demethylation. Forsch Komplementmed. 2015;22(3):172-9. doi: 10.1159/000433485. Epub 2015 Jun 18. PMID: 26088552

[41]. Bishayee K, Sikdar S, Khuda-Bukhsh AR. Evidence of an epigenetic modification in cell-cycle arrest uaused by the use of ultra-highly-diluted *Gonolobus condurango* extract. J Pharmacopuncture. 2013,Dec;16(4):7-13. doi: 10.3831/KPI.2013.16.024.PMID: 25780677

[42]. Saha SK, Roy S, Khuda-Bukhsh AR. Ultra-highly diluted plant extracts of *Hydrastis canadensis* and *Marsdenia condurango* induce epigenetic modifications and alter gene expression profiles in HeLa cells in vitro. J Integr Med. 2015 Nov;13(6):400-11. doi: 10.1016/S2095-4964(15)60201-1. PMID: 26559365

Volume 5, Issue 3; May-June 2022; Page No 492-505