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Homoeopathic management of hyperuricemia in primary gout: A randomized single blind placebo controlled study

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Abstract
Gout is a disorder of purine metabolism. Hyperuricemia alone is one of the most common risk factor for development of gout. Clinically gout is characterized by pain and swelling of joints, especially 1st metatarsal joint. Due to adverse drug reactions of modern medicines, there was a need to explore the role of homoeopathic medicines in management of hyperuricemia in primary gout. So, a prospective, randomized, single- blind placebo controlled study was conducted with an objective to evaluate improvement in the serum uric acid (SUA) level and visual analogous scale (VAS) score of pain. The experimental group received the indicated homoeopathic medicine while control group received identical placebo. Patients of both groups were assessed for SUA and VAS score from baseline to end of every three months. Ninety one patients were analyzed at the end of study. In medicinal group, serum uric acid was reduced to 4.96 ±1.99 from 8.61±.69 with mean reduction of 3.66 ± 2.10 and reduction of VAS score was 1.65± 1.87 from 7.1±.83, with mean reduction of 5.46 ± 2. 00. In placebo group serum uric acid was reduced to 7.60 ±.86 from 8.1± 69 with mean reduction of .51±.81 with VAS score reduction to 5.47±1.44 from 6.60 ±.98 with mean reduction of 1.14 ± 1.49. As per result, mean score reduction in medicinal group was higher than placebo, and the difference was also statistically significant. ($p<.0001$). The result of this study justifies the effectiveness of homoeopathic medicines in management of hyperuricemia in primary gout.

Keywords: Homoeopathy, hyperuricemia, primary gout, serum uric acid, VAS score

1. Introduction

Gout is a common disorder of purine metabolism [1]. It is a disease caused by deposition of monosodium urate (MSU) crystals in tissue such as cartilage, synovial membrane, bone and tissue. [2] This deposition occurs when serum uric acid levels exceed the saturation point of MSU crystal formation, a condition called Hyperuricemia [3].

Hyperuricemia has been defined as a serum or plasma urate concentration greater than 7.0 mg/dl in males and 6.0mg/dl in females [4].

The incidence of gout varies in population from 0.2 to 3.5 per 1000, with an overall prevalence of 2 to 26 per 1,000. [5-6] Many epidemiological studies have shown that hyperuricemia and gout are associated with the development of hypertension, cardiovascular disease, stroke, chronic kidney disease and diabetes, potentially through crystal-independent modes of action [7-11].

The primary aim of treatment for gout is to lower sUA. Several organizations have published guidelines for the diagnosis and management of gouty arthritis, including. The European League against Rheumatism (EULAR), The American College of Rheumatology (ACR), The American College of Physicians (ACP) and The British Society for Rheumatology (BSR) [12-15].

The overall management of gouty arthritis has three phases: controlling acute flares, controlling hyperuricemia, and prophylaxis to prevent painful recurrences.

Though a number of drug regimens have been advised for the management of gout in the modern medicine like Non-steroid anti-inflammatory drugs (NSAIDs), corticosteroids, anti-hyperuricemic drugs and uricosuric agents. These drugs are having many side effects like vomiting, hepato-renal toxicity, gastro-intestinal bleeding etc. [16]

Therefore, there is a definite need to explore more efficacious and radical cure to this ailment. Homoeopathy considers health as a state indicating harmonious functioning of life force. Disease is a deviation from health, which develops when vital force is unable to overcome obstruction to its smooth functioning. Miasms are the fundamental cause of every disease so as in case of hyperuricemia and gout.

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Miasms dispose the body towards a certain diathesis. Patient develops hyperuricemia due to their uric acid or lithic diathesis. Patient develops tendency to accumulation of uric acid crystals in his body due to his constitutional dyscrasia. It is the soil where disease grows. So in order to cure a patient we must treat his constitutional dyscrasia. So in the field of homeopathy this is the 1st ever single blind placebo controlled study over hyperuricemia and gout.

Aim- This study was carried out with an aim to evaluate the role of individualized homoeopathic medicines in the management of hyperuricemia in primary gout.

Objective-The objective of this study was to evaluate the outcome in homoeopathic medicinal group and placebo group by analyzing the improvement in the serum uric acid (SUA) levels and visual analysis scale (VAS) score of pain.

2. Materials and Methods

This study was conducted at Solan Homoeopathic Medical College and Hospital, Solan, Himachal Pradesh, for a period of 18 months, from January 2018 to June 2019. It was a prospective, randomized, single- blind, placebo controlled clinical trial. The ethical clearance for the trial was obtained from Institutional ethical committee (IEC) of Homoeopathy University, Jaipur (Rajasthan) prior to conducting the study.

Out of 162 patients screened for this study, 110 patients were enrolled, following inclusion and exclusion criteria. The participants were equally allocated to experimental group (55 patients with individualized homoeopathic medicines) and Controlled placebo group (55 patients), using simple random sampling technique by using random number table.
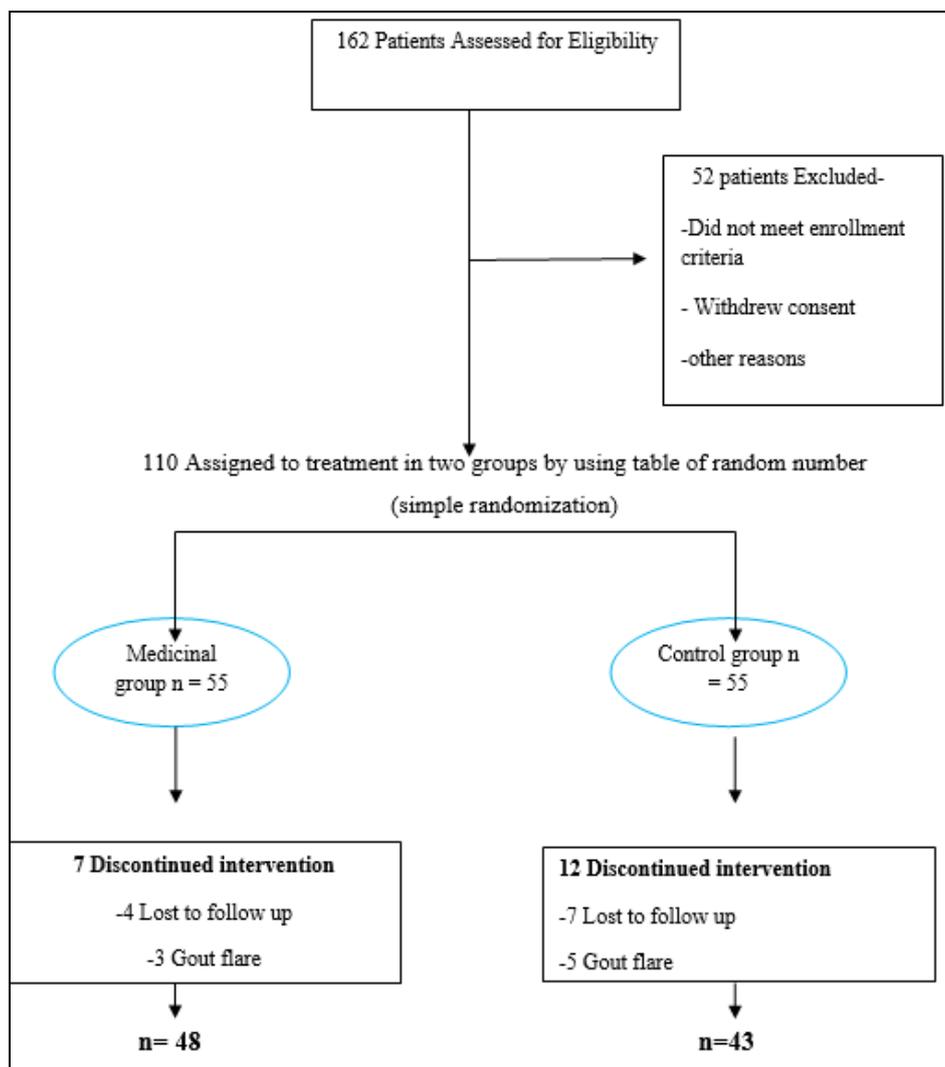
2.1 Sample size calculation

The sample size calculation was based on the assumption that there will be a mean decrease of 2 mg/dL of serum uric acid from baseline to the end of treatment. With 80 % power (β) and at 5 % level of significance (α) sample size of 88 patients was sufficient to get the desirable result. Anticipating 20% drop out rates, 110 subjects were enrolled to get 88 evaluable cases at the end of the study.

2.2 Inclusion criteria

Clinically diagnosed case of primary gout confirmed by laboratory investigation of hyperuricemia, of either sex; age

group of 20-70 years; cases who were ready to give voluntary written consent to participate in this study.

2.3 Exclusion criteria

Patients suffering from severe gout, rheumatoid arthritis, osteoarthritis, other auto-immune disorders, pregnant and lactating mothers were excluded.

2.4 Intervention

Patients of experimental group were prescribed with Individualized medicine and controlled group received placebo. Diet and life style measures were advised in both

groups. Selection of potencies and repetitions were based on principles of Organon of medicine.

In certain cases where pain was severe and was not better with auxiliary measures, analgesics were also prescribed after consultation with general physician. To overcome selection bias patients were randomized by using table of random numbers.

Blood sample was taken for serum uric acid level at the baseline (1st visit) and medicine was prescribed, strictly on the basis of standard homoeopathic guidelines, by analysis of symptoms, evaluation of symptoms, by framing the totality of symptoms and after repertorization using complete repertory in Rapid aid to drug aimed research (RADAR) repertory software and final consultation with material medica. Medicines were prescribed in centesimal

potency. Un-medicated medicine as identical placebo, were prescribed in control group. Subsequent blood sample was taken for serum uric acid level after every three months, six months and nine months. Assessment of VAS score was also done from baseline to each subsequent visit and final assessment was done on the basis of baseline score and score after 9th month.

Statistical technique- Paired t-test was used for pre-test and post –test changes of uric acid and VAS score within the groups and independent t test is used to compare mean SUA level and VAS score in between both the groups before and after.

3. Results

Table 1: Demographic Profile of patients in medicinal and placebo group

Variable	Medicinal group n = 48	Placebo Group n = 43
Mean Age(years)	46.25 ± 11.4	45.86 ± 11.1
Sex		
Male	29 (60%)	27 (62.8%)
Female	19 (40%)	16 (37.2%)
Food habits		
Vegetarian	19 (39.5%)	16 (37.2%)
Non vegetarian	29 (60.5%)	27 (62.7%)
Socioeconomic status		
Lower	6 (12.5%)	8 (18.6%)
Middle	23 (47.9)	19 (44.1%)
Higher	19 (39.5)	16 (37.2%)
Occupation		
Employee	13 (27%)	13 (30.2%)
Own business	15 (31.2%)	11 (25.5%)
Farmer	6 (12.5%)	5 (11.6%)
Student	2 (4.1%)	1(2.3%)
At home	6 (12.5%)	7 (16.2%)
Others	4 (8.33%)	6 (13.9%)
Alcoholic status		
Alcoholic	17 (58.6%) (n=29)	15 (55.5%) (n =27)
Non alcoholic	12 (41.4%)	12 (44.4%)
Disease Presentation		
Monoarthritis	28 (58.3%)	27 (62.8%)
Polyarthritis	20 (41.7%)	16 (37.2%)
SUA	8.61±.68	8.10±.69
VAS score	7.1±.83	6.6±.97

Medicines were prescribed on the basis of totality of symptoms in 48 patients. *Lycopodium clavatum* was prescribed in most number of cases (n= 4), followed *by nux vomica* (n=3), sulphur (n=3), sepia (n=3), acid bezoic (n=3), and colchicum (n=3). *Lithium carbonicum* (n=2), *Pulsatilla Nigricans* (n=2), *dulacamar* (n=2), *Urtica urens* (n=2), and ledum palustre (n=2).

Calcarea cabonicum, Bryonia alba, Phosphorus, Arnica montana, Kali carbonicum, Natrum muraticum, Argentum metallicum, Berberis vulgaris, Apis mellifica, Lachesis, rhododenderon, Thuja occidantalis, chamomilla, Magnesium carbonicum, Calcarea muriaticum, Medorrhinum and *Thuja occidntalis* were prescribed singly.

3.1 Statistical analysis

Data was analyzed by using Graphpad prism 8.2.1software. To analyze the changes in the SUA level paired t test was applied in the both groups. In the study population the mean

of SUA level before treatment was 8.61 and after homoeopathic treatment it was 4.96 in medicinal group.

In control group mean of SUA before treatment was 8.10 and after treatment it was 7.6. The changes were relatively greater in medicinal group; however the changes were statistically significant in both groups.

In these results, the null hypothesis states that the mean difference level of SUA before and after the study is 0. Because the P value is.0001, which is less than the significance level of.05, the decision is to reject the null hypothesis and conclude that there is a statistically significant difference in the level of SUA before and after the study.

For medicinal group (Table 2) before and after treatment, t value is 12.09 and *P* value is < 0.0001; for control group (Table 3) before and after treatment t value is 4.13 and *P* value is < 0.0002. These results are significant at *P*<.05.

Table 2: Paired t test statistics of SUA levels in Medicinal Group

Paired samples statistics					
Particulars	**Group**	**Mean**	**N**	**Std. Deviation**	**Std. Error Mean**
SUA _ BT	Medicinal Group	8.61	48	.69	.10
SUA _AT		4.96	48	1.99	.29
Paired samples correlations					
Particulars	**Group**	**N**		**Correlation**	**Sig.**
Pair SUA _BT & SUA_ AT	Medicinal Group	48		.01	.947

Samples test									
		Paired Differences							
		Mean	**Std. Deviation**	**Std. Error Mean**	**95% Confidence Interval of the Difference**		**t**	**df**	**Sig. (2-tailed)**
					Lower	**Upper**			
SUA_BT SUA_AT	Group I	3.66	2.10	.30	3.05	4.26	12.09	47	.000

Table 3: Paired t test statistics of SUA levels in control Group

Paired samples statistics					
Particulars	**Group**	**Mean**	**N**	**Std. Deviation**	**Std. Error Mean**
SUA _ BT	Control Group	8.10	43	.70	.11
SUA _AT		7.60	43	.86	.13
Paired samples correlations					
Particulars	**Group**	**N**		**Correlation**	**Sig.**
Pair SUA _BT & SUA_ AT	Control Group	43		.48	.001

Samples test									
		Paired Differences							
		Mean	**Std. Deviation**	**Std. Error Mean**	**95% Confidence Interval of the Difference**		**t**	**df**	**Sig. (2-tailed)**
					Lower	**Upper**			
SUA_BT SUA_AT	Control	.51	.81	.12	.26	.76	4.13	42	.000

Further, the SUA level of medicinal and control groups were compared after treatment to assess the effects of treatment, by using independent t test.

Table 4: Independent t test for SUA level of Medicinal group and placebo group after treatment

Group	Average Score	Mean	Diff.	95%CI		t	df		sig.
	Control Group	Medicinal Group		upper	lower				
Control/ Medicinal	7.59	4.95	2.63	3.29	1.98	8	89		000

The results shows that the mean SUA level in medicinal group was lower than the mean SUA level of control group, and the difference was statically significant, as $p<.0001$.

Table 5: Comparison of VAS score of Medicinal group and placebo group after treatment

Group	Average Score	Mean	Diff.	95%CI		t	df		sig.
	Control Group	Medicinal Group		upper	lower				
Control/ Medicinal	5.46	1.64	3.81	4.52	3.11	10	89	89	000

Above results shows that the mean VAS score in medicinal group was lower than the mean VAS score of control group, and the difference was statically significant, as $p<.0001$.

Thus, from above analysis it is clear that there is a difference between homoeopathic group and control placebo group in management of hyperuricemia.

Thus, from above analysis it is clear that there is a difference between reduction of VAS score in homoeopathic group and controlled placebo group.
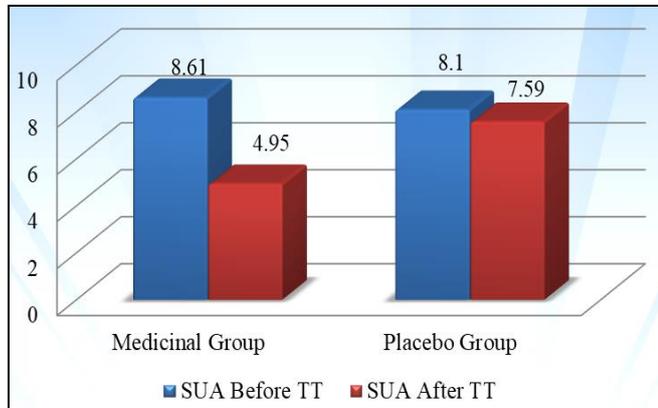
Graph 1: Improvement in SUA levels in medicinal and placebo group before and after treatment
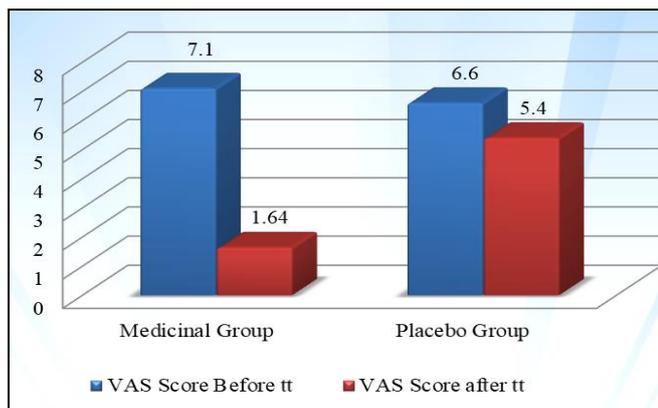
Graph 2: Improvement in VAS score in medicinal and placebo group before & after treatment

4. Discussion and Conclusion

Hyperuricemia have a definitive role in the development of gout and principle management of gout is reduction in serum uric acid level less than 6 mg/dL. This study was a single blind randomized placebo controlled study with an aim to evaluate the role of individualized homoeopathic medicine in management of hyperuricemia in patients of primary gout. This study was carried out with an objective to access the role of individualized homoeopathic medicines in reduction of serum uric acid and visual analogous scale score.

It was observed that there was significant reduction of SUA and VAS score in the medicinal group in contrast to placebo group. Homoeopathic medicines were prescribed on the basis of totality of symptoms. Life style medications were also advised in both groups.

In medicinal group, serum uric acid was reduced to 4.96 ±1.99 from 8.61±.69 with mean reduction of 3.66 ± 2.10. Similarly VAS score was also reduced to 1.65± 1.87 from 7.1±.83, with mean reduction of 5.46 ± 2. 00.

In placebo group serum uric acid was reduced to 7.60 ±.86 from 8.1± 69 with means reduction of.51±.81. VAS score also reduced to 5.47±1.44 from 6.60 ±.98 with mean reduction of 1.14 ± 1.49.

The result shows that mean score reduction in medicinal group were higher than the mean score reduction in placebo group, and the difference was also statistically significant $p<.0001$.

From this study we can conclude that homoeopathic medicines can play significant role in management of hyperuricemia in patients of primary gout.

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