Ayurveda interventions for Gout: A systematic review

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Systematic Review

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Abstract

Background

Patients with Gout frequently use Complementary and Alternative Medicines (CAM therapies), which include Ayurveda medications and treatment procedures, and hence it is essential to determine their safety and efficacy/effectiveness.

Objectives

A systematic review of the published clinical data in view of the safety and efficacy/effectiveness of Ayurvedic treatment protocols in Gout viz-a-viz Vatarakta.

Methods

We searched the PubMed, Cochrane Library (Cochrane Central Register of Controlled Trials: Issue 6 of 12, June 2018), Google Scholar, AYUSH Research Portal (Govt. of India), DHARA, Ancient Science of Life, Shodhganga@INFLIBNET, Online clinical trial registers, and grey literature available from Government Ayurveda College, Trivandrum (Manual search) IPGT & RA, Gujrat Ayurveda University. We excluded abstract-only publications. We could not do a meta-analysis due to the unavailability of relevant studies. **Study eligibility criteria:** Cases diagnosed as Gout by laboratory findings and/or clinical symptoms, who underwent Ayurvedic treatment/Cases clinically diagnosed as Vatarakta, who underwent Ayurvedic treatment. **Participants and interventions and controls:** We included participants of either sex satisfying the inclusion criteria who underwent Ayurvedic treatment either Randomized controlled trials (RCTs), Quasi-Experimental Trials, Single group clinical trials, Comparative Clinical Trials (CCTs), and Pragmatic trials.

Results

A total of 398 potentially relevant studies were found, and 21studies met the inclusion criteria, among which ten studies were pre-post studies, seven studies were included among Randomized Comparative Clinical Trials, and four were among Comparative clinical trials.

Conclusions and implications of key findings

Even though Ayurveda physicians are pragmatically treating/rehabilitating *Vatarakta*/Gout cases and reported satisfactory results in terms of both safety and efficacy/effectiveness, this review is unable to produce strong valid evidence to prove the efficacy/effectiveness and safety of Ayurveda over Non-Ayurveda interventions or Placebo due to lack of quality and unavailability of published works. So the authors propose well-organized and methodologically sound quality research works in this regard.

Systematic review registration number- PROSPERO (CRD42019131198)

Introduction

Ayurveda, the science of life, gives a holistic approach to an individual's physical, mental, and social health. It is the Indian traditional system of medicine, which gives utmost importance to the preventive and curative aspects of healthcare. *Vatashonita*(VS) or *Vatarakta (V*R)in Ayurvedic parlance closely resembles Gout. Etiology, Pathology, and clinical features are common under both these headings (1).

Gout is a metabolic disorder that causes inflammation of the joints. Due to the excessive buildup of uric acid crystals in the body, tiny needle-shaped crystals of uric acid accumulate over joints which, in turn, trigger inflammation(2). According to available data, the worldwide prevalence of Gout ranges from 0.1% to approximately 10%, and the incidence ranges from 0.3 to 6 cases per 1,000 persons. Genetic and environmental factors play a significant role in contributing to the disease. Other major risk factors for Gout include hyperuricemia, dietary factors, medications, co-morbidities, and exposure to lead (3). Mortality is higher in individuals with cardiovascular co-morbidity. Tophi, joint deformity, osteoarthritis, bone loss, and ocular complications like conjunctivitis, uveitis, or scleritis are very common in Gout patients. Major complications like urate nephropathy and nephrolithiasis are not uncommon. Increased prevalence of Gout among individuals with chronic diseases such as hypertension, chronic kidney disease, diabetes, obesity, congestive heart failure, myocardial infarction, etc., increases the disease burden and risk of death (4) (5) (6) (7).

Patients usually present with acute joint pain. The pain is usually of sudden onset waking the patient from sleep, or it may have developed gradually over hours,reaching the maximum intensity in 24 hours (8). The pain will be excruciating. Gout flare-ups are often presented as local inflammation, which is erythematous, swollen, and a warm joint. Systemic features of the joint inflammation may include fever,

fatigue, and general malaise (9).Even though conventional treatment for Gout is suitable for managing symptoms, long-term adverse effects on vital organs are of great concern (10).

As already mentioned,Gout closely resembles *Vatarakta* in Ayurvedic parlance, where the vitiation of *Vata* and *Rakta* causes the manifestation of the disease in joints. *Vatarakta* is characterized by *Ruk* (severe pain), *Swayathu* (swelling), *Daha* (burning sensation), *StabdhaSandhi* (joint stiffness), *Shyava Rakta Varnata* (blackish-red color), and *Sparsasahatwa* (severe tenderness and hyperesthesia) in the affected joint. The characteristic feature of this disease is that it begins at the *Hasta or PadaMoolam* (small joints of hands and foot) and spreads quickly like rat poison or *Akhuvisha*(11).

Research works on Ayurvedic treatment for Gout is not yet compiled and analyzed. A systemic review of Ayurveda interventions is of utmost importance to provide knowledge in detail regarding the safety and efficacy/effectiveness of Ayurveda interventions concerned in this regard. Asystematic review is defined as a comprehensive review of literaturethatdiffers from a traditional literature review in that it is conducted in a methodical (or systematic) manner, according to a pre-specified protocol to minimize bias, to synthesize the retrieved information (12). Assessments of the validity of the findings were carried out in detail to assess the safety and efficacy/effectiveness of Ayurveda interventions for the management of Gout. This study thoroughly reviewed published data and gray literature on Ayurveda management of Gout viz-à-vizVatarakta to establish its safety and clinical effectiveness. This study shall provide more precise estimates of various Ayurveda interventions' effects in the management of Gout either as stand-alone or as an add-on to conventional management.

Methods

The protocol for this review was published in a peer-reviewed journal **(**13**).**

2.1. Search strategy

For electronic searches, we used PubMed, Cochrane Library (Cochrane Central Register of Controlled Trials: Issue 6 of 12, June 2018), Google Scholar, AYUSH Research Portal (Govt. of India), DHARA, Ancient Science of Life, Shodhganga@INFLIBNET and Online clinical trial registries for identification of trials. We have done a manual search in the Central and departmental libraries of Govt. Ayurveda College, Trivandrum; IPGT & RA, GAU, Jamnagar with due permissions and Ayurveda Research Database from authorities. There were no language restrictions. Studies published to date (November 2020) were sought. We repeated the searches just before the final analyses, and further studies were retrieved for inclusion.

2.2 Inclusion criteria

Types of interventions

We included clinical trials with the following intervention and control groups.

1. Intervention - Ayurvedic treatment protocol (*Shamana* or/and *Shodhana*) with different dosage forms, types, schedules, drugs, treatment procedures, with or without *Pathayapathya* (Lifestyle modifications and or specific diet charts).
2. Control - Ayurvedic treatment protocol (*Shamana* or/and *Shodhana*) with different dosage forms, types, schedules, drugs, treatment procedures, with or without *Pathayapathya* (Lifestyle modifications and or specific diet charts) were the comparative group to intervention(s)/ exposure(s).Placebo and/or sham therapy and/or *Shamana* therapy were also considered.

2.3 Data extraction and quality assessment

1. Selection of studies: To determine the studies to be assessed further, three authors (APS, PPN, and SGN) independently scanned the abstracts andtitles.
2. The screening of the search results: Three investigators independently screened all citations and abstracts identified by a comprehensive primary search and sorted out potentially eligible trials. Full articles of potentially eligible trials were obtained and independently evaluated for inclusion in the review based on predefined inclusion criteria.
3. Data extraction and management: A data extraction and management form was prepared, which included 1) **Methods** used in the study (Randomization/ allocation concealment/blinding/ sampling and sample size calculation/length of follow up) 2) **Participant characteristics**of individual studies (along with disease characteristics/ Number of participants randomized/ Number of participants completing follow up/ reasons for withdrawal from the study) 3) **Interventions** (Treatment protocol administered/ Formulations used/

SOP's administered/) and 4) **Outcomes** (in terms of safety/efficacy/effectiveness/ Improvement in QoL). For each outcome measured from individual studies, efforts were taken to discuss the risk of bias, consistency, precision, and reporting bias. We fixed disagreements if any in data extraction by open communication and ensured the concluding remark was in accord. When needed, data was sought from the authors of the studies.(For details, see characteristics of studies and PRISMA flow chart (Table 1 & Fig 1) (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) (Liberati 2009)(14) (15).

4. Dealing with duplicate publications

In the case of identical publications and companion papers of a principal study, we tried to maximize the yield of information by simultaneous evaluation of all available data. In cases of doubt, the original publication (usually the oldest version) was given priority.

5. Assessment of risk of bias in included studies

Two authors (APS and PPN) independently assessed each trial. We resolved any disagreements by consensus or consultation with a third author (SGN). We evaluated the risk of bias by using the Cochrane RoB tool (Fig 2 and 3) (Sterne JAC 2019). We used the Measures of treatment effect: The treatment effect was measured by using data available in the individual studies.

6. Unit of analysis issues: The levels at which randomization was done and the effect of interventions in the included studies.

Dealing with missing data, we obtained relevant missing data if needed from the authors themselves. We cautiously assessed such as screened patients, randomized patients, and ITT (Intention to treat) and PP (Treated and per-protocol) population. We investigated dropouts, losses to follow-up, and ADR/AE (Adverse Drug Reaction or Adverse Events).

2.4 **Data presentation**

We presented the characteristics of each study with the type of study, sample size, outcome measures, findings, and adverse events so that the readers can easily access the risk and benefits of each study (Table 1).

Results

As shown in fig.1, we found 398 potentially relevant studies after searching electronic databases and grey literature. After analysis of the titles and abstracts, we excluded 377 trials because they didn't meet the inclusion criteria. 21 studies were included in this review, among which ten studies were pre-post studies, seven studies were included among Randomized Comparative Clinical Trials, and four among Comparative clinical trials– (Figure 1) (Table 1) (16-36)

Risk of bias in included studies

Out of seven RCTs selected for the review, only two studies had blinding (single blinding) in the procedure (2 studies conducted by Kuvettu H et al., 2016). All remaining others were open trials. Two of them were three-arm trials (AfshanBegam et al., 2019; VishwajeetManjhi et al., 2015), and the remaining studies had only two arms (Aditya Acharya K et al., 2013; Deepika Gupta et al., 2019; Sharma Praveshet al., 2019; Kuvettu H et al., 2016 (2)).The risk of bias assessments is summarized in Figures2 3. The bias assessment of Non-randomized-comparative parallel design is outlined in figure 4.

Effect of Ayurvedic herbal preparations/ Ayurvedic procedures

No study was reported or designed to investigate complications, hospitalizations, death from any cause, and economic data.

Adverse Effects-Adverse effects were not reported in any of the studies.

Discussion

This review included trials on *Vatrakta* or Gout. While searching electronic databases and grey literature, there are discrepancies in diagnosing cases such as gouty arthritis to Vatarakta by some authors. Some authors considered RA, ischemic conditions, psoriatic arthritis, SLE, peripheral ischemia, etc. as *Vatarakta*. The nonuniformdiagnosis was the major problem faced while screening and selecting trials. We included cases diagnosed as *Vatarkta*/Gout based on signs and symptoms of *Vatarakta* and serum uric acid levels and excluded patients diagnosed as RA, SLE, psoriatic arthritis, etc. Few studies used only pure Ayurveda diagnostic criteria which were also included in this review.

Out of sevenRCTs selected for the review, only two studies had blinding (single blinding) in the procedure, and all remaining others were open trials.Two of them were three-arm trials, and the remaining studies had only two arms. Subgroup analyses were performed in one study, but only for participant variables such as Prakruti and Agni, not for assessment parameters. One thousand seventy-three participants from these seven studies diagnosed with Gout were randomly allocated into study and comparison groups. The sample size varies from 462 to 30 in RCTs. The method of sampling was mentioned only in one study. Six studies used classical symptoms of *Vatarakta* as per Ayurveda and elevated serum uric levels as the diagnostic parameter for Gout, whereas one study used only the classical symptoms of *Vatarakta* as the diagnostic feature.Out of the seven RCTs, the interventions in 3 studies were only internal medications. In the remaining four studies, three had procedures such as *Basti* treatment in one group, while the fourth one had *Pradeha* (local applicants). A similar comparator was found in only one study.

Four non-randomized comparative parallel design studies were included in the review; three studies clearly described the interventions, while one study had not mentioned this vividly. The assessment criteria were purely based on signs and symptoms of *Vatarakta* in one study;Ayurvedic parameters like *Sandhishula (musculoskeletal pain)*, *Sandhishotha*, (joint swelling), *Raga (redness secondary to inflammation)*, *Tvakavaivarnya (skin discoloration)*, *Sparsashyata (tenderness)*, *Vidaha (burning sensation), Stabdhata (stiffness)*, *Shithilata (instability/loosening of joints)* along with modern parameters in another study.The third study used the American College of Rheumatology 1980 classification criteria. There was no clarity in the assessment parameter, age specificity, and procedure adopted in the fourth study.

Out of ten non-comparative before-after trials, five trials were about the effect of simple formulations or single drugs. Four trials comprised interventions with internal medication along with some procedures and one trial was about the impact of leech therapy.

The significant change in efficacy/effectiveness between groups of each study was slight as there was a little difference in interventions adopted in the study and comparators groups. Understandably, the chances of confounders could not be excluded as there was no proper randomization in most of the studies. Only the effect of the individual intervention/Panchakarma procedure as part of a treatment protocol can be assessed in single-group, before-after trials. The rational value of such interventions can't be understood unless an RCT is conducted.

Thus the following drawbacks exist while the systematic review of all these studies.

- The method of randomization was not proper in most of the trials. Hence, studies with the correct methods of randomization and blinding will give more unbiased results.
- Few trials are a combination of procedures and medications. Hence, the protocol for a black box or Pragmatic trials will be more suitable than strict RCTs.
- Replications of the same or similar studies, i.e. in terms of population, intervention, and assessment criteria, are needed to establish the effectiveness of protocols.
- Proper follow-ups were not mentioned in any of the studies to discuss the effect of sustenance.
- These studies did not state quality control measures to get a consistent and replicable result.
- Most studies did not mention proper statistical measures with valid significance levels in most.

Hence it will be challenging to give a conclusive remark on the cumulative efficacies or effects of Ayurvedic treatment or protocols in *Vatarkta*/gout with these published documents. However, the effectiveness of such protocols is clinically evident in real settings.

Conclusion

Even though Ayurveda physicians are pragmatically treating/rehabilitating *Vatarakta*/gout cases and reported satisfactory results in terms of both safety and efficacy/effectiveness, this review is unable to produce strong valid evidence to prove the efficacy/effectiveness and safety of Ayurveda over Non-Ayurveda interventions or Placebo due to lack of quality and unavailability of such trials. So the authors propose well-organized and methodologically sound quality research works in this regard.

Declarations

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Disclosure

Any authors of this study declared no conflict of interest.

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References

1. Badugu, srivani; rao, k.v.ramsubba. Management of vatarakta (gouty arthritis) in Ayurveda- a review. **Journal of Ayurveda and Integrated Medical Sciences (ISSN 2456-3110)**, http://www.jaims.in/index.php/jaims/pages/view/Citation, v. 4, n. 5, p. 323 - 336, Nov. 2019. ISSN 2456-3110. Available at: <https://www.jaims.in/index.php/jaims/article/view/919>. Date accessed: 26 Nov. 2020.
2. InformedHealth.org [Internet]. Cologne, Germany: Institute for Quality and Efficiency in Health Care (IQWiG); 2006-. Gout: Overview. 2015 Mar 11 [Updated 2018 May 17]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK284934/
3. Kuo, CF, Grainge, M., Zhang, W. *et al.* Global epidemiology of gout: prevalence, incidence and risk factors. *Nat Rev Rheumatol***11,** 649–662 (2015). https://doi.org/10.1038/nrrheum.2015.91
4. Berman EL. Clues in the eye: ocular signs of metabolic and nutritional disorders. Geriatrics. 1995 Jul;50(7):34-6, 43-4. PMID: 7601360.
5. Fenando A, Widrich J. Gout. [Updated 2020 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK546606/
6. Singh JA. Gout and co-morbidity: a nominal group study of people with gout. Arthritis Res Ther. 2017 Sep 15;19(1):204.
7. Singh JA. Challenges faced by patients in gout treatment: a qualitative study. *J Clin Rheumatol*. 2014;20(3):172-174. doi:10.1097/RHU.0000000000000091
8. Choi HK, Niu J, Neogi T, Chen CA, Chaisson C, Hunter D, Zhang Y. Nocturnal risk of gout attacks. Arthritis Rheumatol. 2015 Feb;67(2):555-62.
9. Neogi T. Gout. Ann Intern Med. 2016 Jul 05;165(1):ITC1-ITC16.
10. Kushwaha, Singh HS, ed. CharakaSamhita of Agnivesha, ChikitsaSthana, Ch. 29, Ver. 10-11, Reprint ed. Varanasi: ChaukhambhaOrientalia; 2012. p. 773.
11. Kushwaha, Singh HS, ed. Charaka Samhita of Agnivesha, Chikitsa Sthana, Ch. 29, Ver. 20-21, Reprinted. Varanasi: ChaukhambhaOrientalia; 2012. p. 776.
12. Petticrew, M. & Roberts, H. (2006). Systematic reviews in social sciences. A practical guide. Oxford:Blackwell Publishing.
13. Aswani PS, Nair PP, Deepthi GN, Swamy GK. A Systematic Review Protocol to Assess the Effectiveness of Ayurveda Interventions in Gout. J Res Ayurvedic Sci 2019; 3 (1):22-26.
14. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, Clarke M, Devereaux PJ, Kleijnen J, Moher D. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ. 2009 DOI21;339:b2700. DOI: 10.1136/BMJ.b2700. PMID: 19622552; PMCID: PMC2714672.
15. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, Cates CJ, Cheng H-Y, Corbett MS, Eldridge SM, Hernán MA, Hopewell S, Hróbjartsson A, Junqueira DR, Jüni P, Kirkham JJ, Lasserson T, Li T, McAleenan A, Reeves BC, Shepperd S, Shrier I, Stewart LA, Tilling K, White IR, Whiting PF, Higgins JPT. RoB 2: a revised tool for assessing risk of bias in randomized trials. *BMJ* 2019; **366**: l4898.
16. AfshanBegam, Ram Adhar Sing, Amarndra Kumar : A pharmaco-therapeutic study on Guduchi kwath and guduchi w. s. r. to vatarakta (gout)" Ayurline: International Journal of Research In Indian Medicine 2019; 3(1): 1-8
17. Adithya Acharya K,Ahalya Sharma : Evaluation of the efficacy of Siravyadha and Guduchi Siddha Yoga Basti in the management of Vatarakta with special reference to Gout. IJRAP_International Journal of Research in Ayurveda and Pharmacy May-June 2013.
18. VishwajeetManjhiet.:A Clinical Study Of AmritadiKashayaandArdhamatrikaBasti In The Management Ofvata-Raktaw.S.R. Gout.International Journal Of Medical Science And Clinical Inventions Volume 2 issue 06 2015 page no. 994-1009
19. Dr. Deepika Gupta, Dr. Kamal Sachdev, Dr.RichaGarg : A clinical study to evaluate the efficacy of PatoladiKwath (SU. CH.) with or without RasnadiPradeh (CH. SU.) in cases of Vatarakta (W.S.R. to Gouty Arthritis). Journal of Drug Delivery and Therapeutics

20. Dr. Sharma Parvesh : A Comparative Study of BodhitawakChuran in The Management of Vata-Raktaw.s.rAnupanaMadhu and Jala. World Journal of Pharmaceutical and Life Sciences
21. H Kuvettu, S Acharya, AN Nagappa: Clinical Evaluation of AmrithaGuggulu in the Management of Gout: Open Archive. DOI: https://doi.org/10.1016/j.jval.2016.08.116
22. H Kuvettu1, AJyothy, S Acharya, AN Nagappa: Clinical Evaluation of GuduchiSadhitaSneha in the Management of Gout: Open Archive. DOI: https://doi.org/10.1016/j.jval.2016.03.1169
23. Mehta Chetan1, Bhardwaj Anil,Bhatia Yogesh, Tripathy B. P: A Comparative Study of Siravyadha and KokilakshadiKshayama in Vaatarakta W.S.R to GOUT Research and Reviews: A Journal of Ayurvedic Science, Yoga and Naturopathy ISSN: 2395-6682 (Online) Volume 4, Issue 3 www.stmjournals.com
24. Dr. VikasRana, Dr.Anjana Mishra, Prof. B. L. Mehra : Effect of punarnavamritaguggulu with amritadikvath in the management of vataraktaw.s.r. to gout – a clinical trial. World Journal of Pharmaceutical Research Vol 6, Issue 8, 2017
25. Ashok Kumar Panda et. Al: Effectiveness of Leech Therapy in GambhiraVata-Rakta (Acute Gout): A Pilot Study. J HomeopAyurv Med 2012, 1:2 http://dx.doi.org/10.4172/2167-1206.10.00108
26. Dr V Balendu Krishnan, Dr. Prashanth A S, Dr. S G Chavan: Pre test and post test design study to evaluate the efficacy of vasti and virechana in gouty arthritis. Pparveshana international journal of ayurvedic research pijar [July-august-2018/volume-2/issue-6
27. Harbans Singh et al:An Open-Label Efficacy Study of Amrita Guggulu and PindaTaila in the Management of Hyperuricemia in Gout (Vatarakta) Patients. Journal of Research in Ayurvedic Sciences, January-March 2017;1(1):25-3325JRASJRAS10.5005/jp-journals-10064-
28. ShashankJha, 2.Londhe PD ROLE OF LEECH APPLICATION IN VATARAKTA: A PILOT STUDY International Journal of Ayurvedic Medicine | Year: 2014 | Volume: 5 | Issue: 1 | Page: 129-132
29. Dr. G.P.Upadhyay, Dr.AnuragGirdharVatrakt- A Clinical Study.Journal of Ayurveda Vo\.2 No.2 Apr-Jun 2008
30. L.Prasanna KumarRole Of GudoochyadiKsheeraVasti in VataRakta: International Journal of Research in Ayurveda and Pharmacy | Year: 2011 | Volume: 2 | Issue: 1 | Pag : 44-46
31. Dr. Harsh Sehgal*1, Dr. Bhavna Singh2 and Dr. Sanandan Thapliyal3Role of Kalmegha (Andrographispaniculata (Burm.F.) Wall. Ex Nees) in treating Vatarakta (Gout) Available online on 15.11.2018 at http://jddtonline.info Journal of Drug Delivery and Therapeutics Open Access to Pharmaceutical and Medical Research
32. Alok Kumar et al. Role of Amrita Gugguluin the management of Vata-rakta -A Clinical Trial International Journal of Pharmaceutical & Biological Archives 2014; 5(4): 45 -51
33. Usha Sharma, Krishna Kumar Sharma, Maksudan Singh, Alok Kumar Srivastava, Gyanendra Datta Shukla Mohita Bohra : ROLE OF PUNARNAVA AMRITA GUGGULU IN THE MANAGEMENT OF VATARAKTA – A CLINICAL TRIAL AyurpharmInt J AyurAlli Sci., Vol. 4, No. 1 (2015) Pages 1 – 9
34. Yogita Deepak Khore, SubodhPatil : Efficacy of drakshakashayaerand tail virachana in vatrakta (w.s.r. gout) international ayurvedic medical journal IAMJ: Volume 8, Issue 1, January - 2020 (www.iamj.in)
35. ShivaprasadHuded, 2. Sonia V Gummadi, 3. KuberSankh, 2. H.N. Asha, 2. H.S. Ashwini, 2. K. Lingadore : Evaluation ofguduchiyoga in the management of vatarakta (gouty arthritis): a clinical study International Journal of Research in Ayurveda and Pharmacy | Year : 2013 | Volume : 4 | Issue : 5 | Page : 688-692
36. PundpalAmitkumar B A clinical study to evaluate the therapeutic effect of vataraktantak rasa and lekhanabasti in vataraktaInternational Ayurvedic Medical Journal ISSN:2320 5091 IAMJ: Volume 4; Issue 04; March- 2016.

Tables

CHARACTERISTICS OF STUDIES							
Reference	**Study design**	**N; mean age (years)**	**Disease**	**Intervention (name; dosage or frequency; duration)**	**Outcome measures**	**Findings and comments**	**Side Effects**
Afshan Begam et al.	Comparative Clinical Trial	68 11 to 70 years	Signs and symptoms of Vatarakta	**Group 1**-Aswath Kasaya Dosage-40 ml bd Duration-90 days **Group 2**-Guduchi Kashaya Dosage-40 ml bd Duration-90 days **Group 3**-Combined group –Aswath Guduchi Kashaya Dosage-40 ml bd Duration-90 days	Subjective Criteria-Pain index Objective criteria-Serum uric acid	Group 3 is more effective	Not reported
Adithya Acharya K et al.	Comparative Clinical Trial	40 20-65 years	Hyperuricemia, less than 10 year's chronicity, without manifestation of tophi and joint destruction.	**Group A**-Siravyadha/ bloodletting twice with an interval of 11 days. Follow up on 24 th day **Group B**-Guduchi siddha yogabasti in 8 days Follow up on 24 th day	Subjective parameters-Pricking pain (Sandhi toda), Tenderness (Sparshasahyata), Redness (Raga), Swelling (Sandhishotha), Sandhi Supti (Numbness of joints), Objective parameters Serum Uric acid	Subjective parameters- In Group A Pricking pain (Sandhi toda) relieved rapidly, but in group B gradual relieved . Tenderness (Sparshasahyata)-highly significant result in group B, Redness (Raga)-Early relief observed in Group A than group B, Swelling (Sandhishotha) Early relief observed in Group A than group B, Sandhi Supti (Numbness of joints) Early relief observed in Group A than group B, Overall response was marked in Group A (35%) than Group B (0 %) Objective parameters Serum Uric acid Group B (21 %) showed more reduction in serum uric acid compared to group A (13.33%).	Not reported
Vishwajeet Manjhi et al.	Randomised open comparative clinical trial	45 20-60 years	Elevated serum uric acid level > 6.8 mg/dl, Vatarakta	**Group A** – Amritadi Kashaya 80 ml bd in empty stomach with 10 ml castor oil for 16 days. **Group B**-Ardhamatrika basti as per Kalabasti schedule (16 days) Group C-combined group for 16 days.	Subjective criteria-Signs and symptoms of Vatarakta with scoring pattern. Objective parameter-Serum Uric acid	Group A- 26.75 % were moderately improved, 46.75 % got mild improvement and 26.75 % showed no improvement. Group B-46.75 % got moderate improvement, 53.33 % showed mild improvement and 0 % was in unimproved category.	Not reported

						Group C- 73.33 % showed moderate improvement, 26.75 % showed mild improvwmt. No patient showed complete cure in any groups. Objective criteria-Group A showed significant improvement in serum uric acid level, Group B and C showed highly significant improvement.	
Deeika Gupta et al.	Phase-2 rational randomized (sequential pattern) parallel group study.	56 21-60 years	Vatarkata (Gouty arthritis) Having Seum uric acid > 7 mg/dl in males and >5.7 mg/dl in females	**Group A**-Patoladi kwath 40 ml bd after food for 90 days **Group B**-Patoladi kwath 40 ml bd & Rasnadi pradeha (local application) During evening for 90 days.	Subjective criteria-Sandhishu ruk-pain in affected joint, Sandhishu Raga - Redness , Sandhishu swayathu-Swelling, Sparshasahyata – Tenderness, sandhishu kathinya-decreased / restricted movements, , skin discoloration of affected area, itching on affected part, burning sensation Objective parameter-Serum uric acid, ESR, Hb, TLC, DLC, KFT, LFT, FBS, PPBSassessment done on every fortnight after administration of trial drugs.	Group A-48% got complete relief, 28% moderately relieved and 20 % got mild improvement and 4 % not responded to treatment. In Group B-76 % got complete relief, 16 % got moderate improvement, 8 % showed mild improvement and no case recorded as unchanged.	Not reported
Dr Sharma Parvesh et al.	30 20-60 years	Randomised open clinical trial.	Vatarakta, serum uric acid level 5.5-10 mg/dl.	**Group A-** Bodhivriksha twak churn with madhu 3 gm bd **Group B-** Bodhivriksha twak churn with jala 3 gm bd Duration-45 days	Pain, tenderness, swelling, stiffness, burning sensation in joints, Hb, serum Uric acid, Serum creatinine, X-Ray, Urine RE and Microscopic examination.	The study was highly significant (P<0.001) for all subjective parameters, serum uric acid and was insignificant(P>0.05) for Haemoglobin and serum creatinine in group A. In group B, swelling, stiffness, joint pain and serum uric acid showed highly significant results. For tenderness and burning sensation the p value was <0.05 and for haemoglobin and serum creatinine the result was	Not reported

						insignificant (P>0.005) in group B.	
H Kuvettu et.al	A randomized single blind clinical study with pretest and posttest design	378 20-60 years	Gouty arthritis	**Group A** - 190 patients were administered *Amritaguggulu* 500 mg 2 tablets thrice daily for 30 days. **Group B** - 188 patients were administered *Kaisoraguggulu* 500 mg 2 tablets thrice daily for 30 days. During the study, special diet was followed	Subjective parameter-The signs and symptoms of gout-burning sensation, pain, swelling, stiffness, mobility, deformity of joints. were assessed. Objective parameters - haemoglobin percentage, ESR and serum uric acid.	Marked improvement was found for 68% of patients in group A, whereas in group B it was only 42%. The study showed statistically highly significant results for all subjective and objective parameters in both the groups. The study concluded that Amritaguggulu was more effective than Kaisoragugguluin the management of gouty arthritis.	Not reported
H Kuvettu et.al	A randomized single blind clinical study with pre-test and post-test design	462 20-60 years	Gouty arthritis	**Group A** -234 patients were administered *Karma Basti*prepared with for 30 days. **Group B** - 228 patients were administered *Kaisoraguggulu* 500 mg 2 tablets thrice daily for 30 days. .	The signs and symptoms of gout-burning sensation, pain, swelling, stiffness, mobility, deformity of joints were assessed under symptom grade parameter. Objective parameters included haemoglobin percentage, ESR and serum uric acid.	Marked improvement was found for 56% of patients in group A, whereas in group B it was only 33%. The study showed statistically highly significant results for all subjective and objective parameters in both the groups. The study concluded that Guduchi Sadhita Grithawas more effective than Kaisoraguggulu in the management of gouty arthritis.	Not reported
Dr Vikas Rana et.al(2017)	Non-randomized-comparative parallelgroup design	30 20-70 years	Vatarakta.	**Group 1-** 15 patients were administered with *Sadya Mrudu Sneha Virechana*of *Erand Taila*10-50 ml with *Ksheera*for 3-5 days for *Koshtasuddhi* followed by administration of 2 tablets of *Punarnnava Amarita Guggulu*500 mg with *Amrithadi Kvath* 24 g as *Anupana*for 8 weeks. **Group 2** - 15 patients were given only 2 tablets of *Punarnnava Amarita Guggulu*500 mg with *Amrithadi Kvath*24 g as	The subjective criterias assessed were *sandhi soola, sandhi shotha, sparshasahyata, raga, vidaha, twak vaivarnya, stabdata, shithilta, hritspanadan* and *sandhi vikriti.* The objective parameter was serum uric acid.	In group 1, 80 % got moderate improvement and 20 % got mild improvement. In group B, 20% got marked improvement, 53.3% got moderate improvement and 26.6% got mild improvement. The study found, group 1 and group 2 were equally effective in symptoms like *sparshasahyata, raga and shithilta. Sandhi shotha, ra*ga and *vidaha* were improved to greater extent in group 1, whereas *sandhi soola, twak vaivarnya* and *stabdata* were better controlled in group 2.	No adverse effect was noted during the trial and follow up period in this trial.

				*Anupana*for 8 weeks.			
Asok Kumar Panda et.al	non randomized controlled pilot study	22 Mean age 47	*Gambheera Vata-Rakta*diagnosed as acute gout.	**Study group-**12 were treated with leech for 7 days with 4 weeks follow up **Control group-**10 patients who were not willing to participate in leech application were given local diclofenac application for 7 days	Pain, joint swelling, joint tenderness, joint erythema, patient's global assessment to response to therapy and investigator's global assessment to response to therapy.	leech application is effective in reducing pain, joint swelling, joint tenderness and joint erythema.	The statistical assessment used was unclear in this study.
Dr V Balendu Krishnan et.al (2018)	Comparative clinical trial wth Pre-test and post-test design	40 18-60 years	Gouty arthritis	**Group A-** amapachana with Sunti churna, Kalavasti with vasaguluchyadi kashaya and guluchyadi gritha (anuvasana), Moorchita tila taila for abhyanga with mrudu swedana followed by shaman oushadis- punarnnavadi guggulu 2 bid with kokilakshakam kashaya (30-45 ml). **Gropu B-** amapachana with Sunti churna , snehapana with guduchyadi gritha followed by virechana withNimbamrutadi eranda taila and Moorchita tila taila for abhyanga with mrudu sweda followed by shaman oushadis- rasnaguggulu 2 bid with manjishtadi kashaya (30-45 ml) Follow up-48 days for Group A, 30 days for group B.	*Sandhigraha, Sandhi Shoola, Sandhi Shotha*, joint colour, *Sparshasahatva* and serum uric acid	Both groups were highly significant in reducing the subjective and objective criteria's. In group A, the percentage of relief was 77.74% and in group B, it was 56.50%. The study concluded that both the groups were having significant role in gouty arthritis, but Vasti has more contributory effect compared to Virechana. The statistical analysis was also unclear in this study too.	Not reported
Harbans Singh et al 2017	Prospective open-label multicentre study with pre-post design	100 25-60 years	Primary gouty arthritis	Amrita guggulu tab 2 Tab of 500 mg twice daily with luke warm water for 12 weeks and Pinda taila external application on affected joint(s)	Serum uric acid, QOL, using SF-36, Health Survey Questionnaire, Patient's Global Assessment scale, Physician's global assessment scale,VAS, LFT, KFT	Statistically significant result of Serum uric acid, VAS score, QOL, Patient's Global Assessment Scale, Physician's global assessment scale. LFT and KFT were performed at baseline and at the end of the treatment. Though some	Not reported

						changes were observed, they were within the normal range.	
Shashank Jha et.al 2014	Non-comparative trials with pre-post design	10 20-65 years	signs and symptoms of *Vatarakta* and serum uric acid level	Leech therapy -3 times at intervals of 3 weeks. Treatment schedule:	*Sandhishoola, Sandhishopha, Sandhivaivarna Sandhidaha,Serum uric acid*	Statistically significant result.	Not reported
Upadhyaya GP et.al.,2010	Non-comparative trials with pre-post design	*35* Not mentioned	signs and symptoms of *Vatarakta* and serum uric acid level	*Punarnnava Guggulu tab -2 tab (500 mg each) after meals with water for 45 days and follow-up were done for 15 days.*	Subjective criteria-signs and symptoms of *Vatarakta Objective criteria-Serum uric acid, ESR, TLC, DLC, Urine routine, and microscopic examination.*	Statistically significant result. Maximum effect was observed in kandu(itching), Sparsasahatva (tenderness). Casts and epithelial cells were found reduced significantly from urine.	Not reported
L Prasannakumar et.al	Non-comparative trials with pre-post design	5 16-70 years	signs and symptoms of *Vatarakta* and serum uric acid level	*Guduchyadi ksheera vasthi* as *yoga vasthi*	Pain, burning sensation, malaise, sleep, tenderness, oedema, walking ability	For four patients, uric acid came to normal. No patient got complete relief from symptoms. 20 % remained unchanged.	Not reported
Harsh Segal et al., 2018	Non-comparative trials with pre-post design	31 20-60 years	signs and symptoms of *Vatarakta (Gout), Serum uric acid level 5.5 to 10.0 mg/dl*	Two grams of powder of Andrographis paniculata thrice daily with water.	Subjective criteria-Oedema, stiffness, inflammation, itching, heaviness, numbness, piercing pain, fatigue, pallor, thirst, indigestion Objective criteria-serum uric acid	Except symptom pallor, the p value was either <0.05 or <0.01.	
Sharma Usha et al., 2014	Non-comparative single blind trials with pre-post design	30 20-60 years	signs and symptoms of *Vatarakta* and serum uric acid level	Tablet Amrita Guggulu 500 mg thrice daily with anupana of amritadi Kashaya 72 ml.	Subjective criteria Sandhi shola (pain in joints), Sandhi shotha (swelling in joints), Raga (Redness), Kandu (Pruritis), Vidaha, Twak vaivarnyata, Sparsasahishnuta (tenderness) Objective criteria-Serum uric acid, Hb, TLC, DLC, ESR, RA factor	Statistically significant result.	Not reported
Sharma Usha et al.	Non-comparative single blind trials with pre-post design	30 20-60 years	signs and symptoms of *Vatarakta* and serum uric acid level(>6 mg/dl)	Tablet Punarnnava amrita Guggulu 500 mg thrice daily with anupana of amritadi Kashaya 72 ml.	Subjective criteria Sandhi shola (pain in joints), Sandhi shotha (swelling in joints), Raga (Redness), Kandu (Pruritis), Vidaha, Twak vaivarnyata, Sparsasahishnuta (tenderness) Objective criteria-Serum uric acid, Hb, TLC, DLC, ESR, RA factor	Statistically significant result.	Not reported
Yogita Deepak Khore et.al.	Pre-post design	10 20-60 years	signs and symptoms of *Vatarakta* and	Virechana with draksha kashaya (40 ml) and	Subjective criteria-Shotha, shola, aaraktata, kathinya,	60 % relief in stiffness & tenderness, 50 % relief in swelling and	Not reported

			serum uric acid level(>6 mg/dl)	eranda taila (40 ml)	sparshasahatva, daha Objective criteria- Serum uric acid	pain, uric acid level decreased slightly.	
Sivaprasad Huded et.al	Randomized single blind study with pre-test post-test design	20 18-60 years	Vatarakta, acute gouty arthritis- Hyperuricemia	Guduchi yoga (aqueous extract of Guduchi and Trapusha) 2 g bid with luke warm water after food for 12 weeks .	*Subjective parameter- Sandhishula, daham, sandhisotha, sparshasahatwam, twaklohita Objective parameter-serum uric acid*	Statistically significant results along with attainmaent of normal serum uric acid and improvement in general well being of the patients.	Not reported
Pundapal Amitkumar B et.al	Single blind trials with pre-post design	20 16-70 years	Vatarakta	Lekhana basti as Kalabasti protocol-16 days Vataraktantaka Rasa-250 mg tds for 30 days.	Pain, burning sensation, malaise, disturbance of sleep, tenderness, walking ability, peripheral pulse, lipid profile.	Statistically significant results	Not reported

Table 1: Characteristics of Studies

Figures

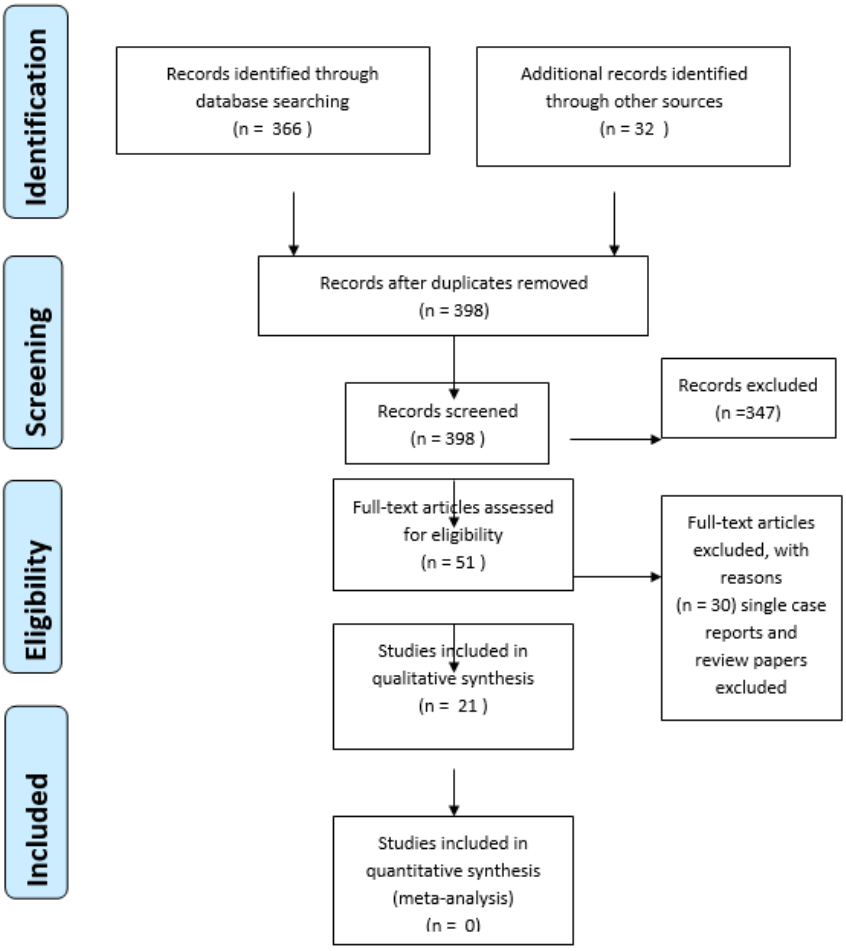

Figure 1

PRISMA 2009 Flow Diagram

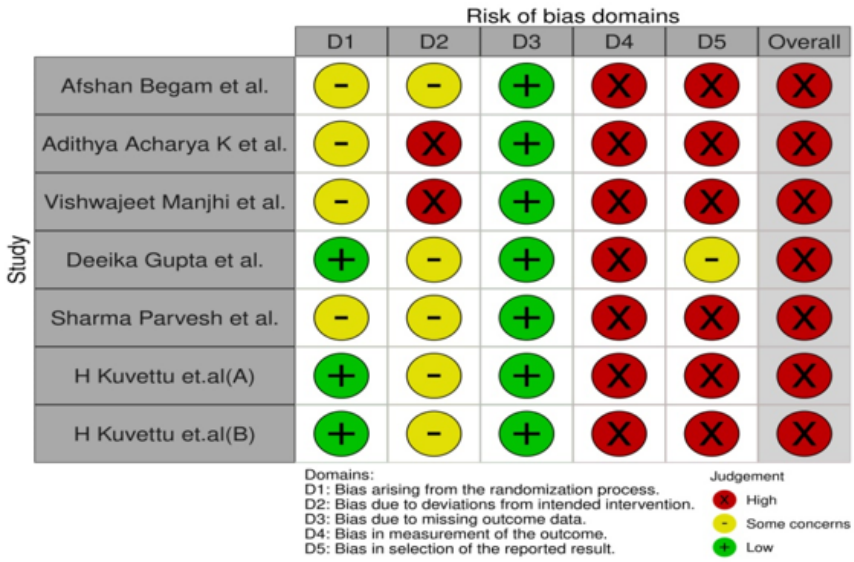

Figure 2

Risk of bias graph

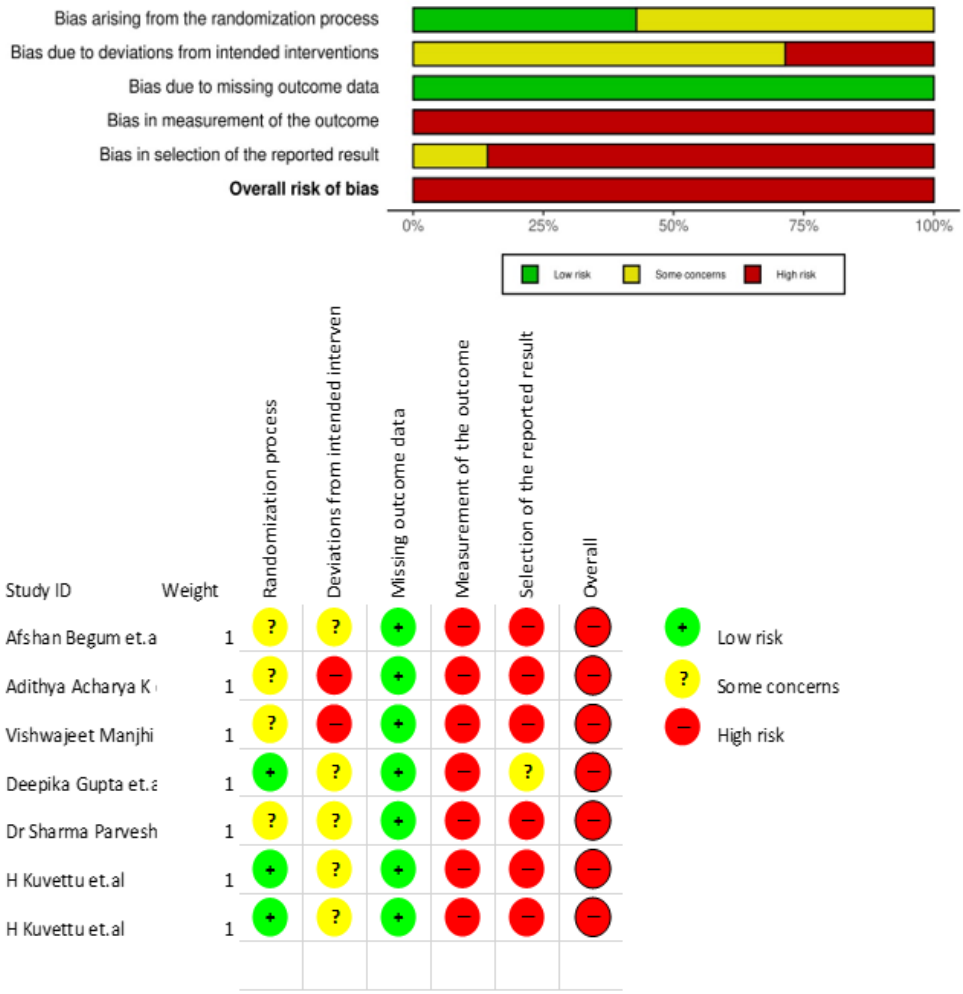

Figure 3

Risk of bias summary

Figure 4

Bias assessment for non-randomized studies