Role of Ayurvedic Herbo-Mineral Formulation Yograj Guggulu and Agnikarma (Traditional Cautery) in Osteoarthritis of Knee Joint Pain and Their Effects on Blood Levels of Dopamine, Substance-P and β-Endorphins: An Open-Label, Non-Controlled Comparative Randomised Clinical Trial

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Abstract

This study aimed to find out an alternative method e.g. Agnikarma, and some herbal medicine by which pain can be relieved without any side effect but there was no any scientific study on biochemical level yet so for present research work total 40 adult patients of both sex with narrow age, weight and height were selected and divided randomly in two groups containing 20 patients each. Group 1 was given Yograj Guggulu 1000 mg in the morning and evening and follow up- weekly for three weeks. In Group 2 Agnikarma therapy was done weekly for three weeks. The evaluation of β- endorphin, Substance-P & Dopamine in patient serum before treatment & after three weeks i.e. at completion of study were done. Prior to registration of patient for the proposed study, well informed consent of patients were taken after proper ethical approval from our institute. The observation made on response of both groups, were recorded on a standard proforma. The comparison of both the groups was calculated statistically. Substance-P is a pain mediator & it is decreased after treatment in our study & dopamine increases in our study while there is no significant effect on β- endorphin. There are no conflict of interest for this study and we have ethical approval by Institute Ethical Committee (EC Registration no. ECR/526/Inst/UP/2014 Dt. 31.1.14): Dean/2015-16/EC/78.

Key word- Agnikarma, Yograj Guggulu, β- endorphin, Substance-P & Dopamine.

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Introduction

One of the most common degenerative musculoskeletal conditions in the world, osteoarthritis (OA) of the knee joint is a significant contributor to pain, functional impairment, and disability, especially in the elderly. Progressive articular cartilage deterioration, subchondral bone remodelling, synovial inflammation, and osteophyte production are the hallmarks of the syndrome, which eventually results in persistent joint discomfort and decreased mobility.

The global burden of osteoarthritis has increased significantly due to factors such as aging, obesity, sedentary lifestyle, and mechanical stress on weight-bearing joints. Knee osteoarthritis, in particular, is associated with persistent pain, stiffness, and reduced quality of life, thereby posing a substantial socioeconomic and healthcare challenge.

Pain in osteoarthritis is a complex phenomenon involving both peripheral and central mechanisms. In addition to structural changes in the joint, neurochemical mediators such as dopamine, substance-P, and β-endorphins play important roles in pain perception and modulation. Substance-P is a neuropeptide associated with the transmission of nociceptive signals and inflammation, whereas β-endorphins act as endogenous opioids that inhibit pain pathways. Dopamine is involved in reward, motivation, and modulation of pain perception through central nervous system mechanisms. Alterations in the levels of these neurotransmitters have been linked with chronic pain conditions, including osteoarthritis, highlighting the importance of exploring therapeutic interventions that may influence these biochemical markers.

Conventional management of osteoarthritis primarily focuses on symptomatic relief through analgesics, intra-articular injections, nonsteroidal anti-inflammatory medications (NSAIDs), and surgical interventions in advanced cases. Although these approaches can reduce pain and inflammation, long-term use is often associated with adverse effects, limited efficacy in disease modification, and high economic burden. Consequently, there is growing interest in complementary and traditional medical systems that offer safer and holistic therapeutic options for chronic musculoskeletal disorders.

In Ayurveda, osteoarthritis of the knee joint closely resembles the clinical entity described as Janu Sandhigata Vata, a disorder caused primarily by aggravation of Vata Dosha affecting the joints. Classical Ayurvedic texts describe symptoms such as pain (shoola), swelling (shotha), stiffness (stabdhata), crepitus (atopa), and restricted movement of the joint. Management of this condition focuses on pacifying aggravated Vata, nourishing joint tissues, and restoring functional balance through internal medications and external therapeutic procedures.

Yograj Guggulu, a classical Ayurvedic herbo-mineral formulation described in traditional texts, is widely used in the management of Vata-dominant musculoskeletal disorders. The formulation contains Guggulu (Commiphora mukul) along with multiple herbal ingredients that possess anti-inflammatory, analgesic, and Vata-shamaka properties. Previous studies suggest that Yograj Guggulu may help reduce joint pain, improve mobility, and support metabolic processes involved in tissue repair.

Agnikarma, a traditional Ayurvedic therapeutic procedure involving controlled therapeutic cauterization using heated metallic instruments, is recommended in classical texts for the management of chronic pain conditions. Agnikarma is believed to alleviate pain by removing obstruction in channels (srotas), improving local circulation, and balancing aggravated Vata. From a modern perspective, the thermal stimulation produced by Agnikarma may influence nociceptive pathways, enhance blood flow, and stimulate endogenous pain-modulating mechanisms.

Despite the widespread clinical use of these therapies, scientific evidence explaining their effects on biochemical pain mediators remains limited. Understanding the relationship between Ayurvedic interventions and neurochemical markers such as dopamine, substance-P, and β-endorphins may provide valuable insights into their mechanisms of action and contribute to evidence-based integrative pain management.

Thus, the current study was conducted to assess the effectiveness of the Ayurvedic herbo-mineral formulation Yograj Guggulu and Agnikarma in the treatment of knee osteoarthritis, with special emphasis on their effects on clinical symptoms of pain and biochemical markers including dopamine, substance-P, and β-endorphins. The study was designed as an open-label, non-controlled comparative randomized clinical trial to assess both the therapeutic efficacy and possible neurochemical modulation associated with these traditional Ayurvedic interventions

Material & Methods

There are no any analgesics which are free from side effects. Therefore, we decided to find out some alternative source to relieve pain. There are some well-known methods e.g. Agnikarma, and some herbal medicine by which pain relieve but there was no any scientific study on biochemical level yet so for. In Ayurvedic medical science, various modalities of treatment are explained for the management of pain. Agnikarma chikitsa is said to be superior among all. Now a days the process of Agnikarma done by

using gold, silver, Panchadhatu and iron shalaka etc. The procedure of Agnikarma does not have side effect. It is cost effective and it can be managed with patients as ambulatory and can be performed in OPD also. Yograj Gugglu is also a well known ayurvedic drug and we have tried to evaluate it on biochemical level for joint pain management.

For present research work total 40 adults patients of both sex with narrow age, weight and height were selected and divided randomly in two groups containing 20 patients each. Group 1 was given Yograj Guggulu 1000mg in the morning and evening and Follow up- weekly for three weeks. In Group 2 Agnikarma therapy was done weekly for three weeks. The evaluation of Substance-P, Dopamine and β-Endorphin in patient's serum before treatment & after three weeks i.e. at completion of study, were done. Prior to registration of patient for the proposed study, well informed consent of patients were taken.

Agnikarma

Agnikarma is the process used to treat a variety of illnesses by applying Agni (heat) i.e. therapeutic use of Agni is called as Agnikarma. It is described in Sushrut Samita- Sutra sthan-12. Acharya Sushrut has included Agnikarma in the Anushastra karma i.e. parasurgical procedure. Maharshi Sushruta has told that Agnikarma is superior to all parasurgical procedures.

Agnikarma is a para-surgical procedure in Ayurveda, detailed in texts like the Sushruta Samhita, utilized for chronic pain management. It employs controlled heat from metallic instruments to alleviate pain by pacifying Vata and Kapha Dosha, enhancing circulation, and removing obstructions in physiological channels.

From a modern biomedical perspective, its analgesic effects may arise from thermal stimulation, modulation of nerve signals, activation of the gate control mechanism, release of endogenous opioids, and enhanced blood circulation which aids tissue repair.

Material used for Agnikarma

There are so many materials which are used for Agnikarma like drugs, articles and substance used to produce therapeutic burns (samyakadagdha) during Agnikarma therapy. They are classified as follows-

1. **Vanaspatija** (Herbal origin)- Pippali (Piper longum), Yasti Madhu (Glycerrhizaglabra), Haridra (Curcuma longa), Sneha Tail etc.
2. **Praanija** (Animal Origin)- Godanta, Sring, Aja's hakrita etc.
3. **Metallic and others-** Panchdhatu (Silver, Copper, Iron, Tin& Zinc), Swarnshalaka, Soochi, Stone etc.

Triphala Decoction, Aloe vera & G.glabra powder Different type of Shalaka including Panchdhatu Shalaka

Agnikarma in Different Vikaara

Acharya Sushrut described Agnikarma in following four types of Vikaara-

1. Tvakgata Vaata Vikaar (Skin)- By Pippali, Godant, SwarnShalaka, Aja's hakrita etc.
2. Maasagata Vikaar (Muscles)- By Jambavausht, panchadhatu shalaka etc.
3. Sira,Snayu (Vessels &ligaments, tendon) – By madhu, Gud (Jaggery), Sneha etc.
4. Sandhi & Asthi (joints & bones)- Panchdhatu shalaka, Sneha etc.

Indications for Agnikarma

- Sciatica pain, Peri-arthritis shoulder joint, Frozen shoulder, in early stage Osteoarthritis of knee joint, Cervical pain, Tennis elbow, Plantar fasciitis, Planter corn, Viral warts, Arsha, Arbuda, Bhagandar, Asthisandhigat vat vikaar, Gridhrasi , Apachi, Granthi, Shlipada, Nadivran etc.

Different kits used during Study

1. Dopamine ELISA Kit-

The range of the detection of this kit is 31.25 to 2000pg/ml. It is used for quantitative determination of Dopamine in serum, plasma and other biological fluids. I have used it for determination of concentration of dopamine in serum.

2. Substance P ELISA Kit-

The range of the detection of this kit is 78.13 to 5000pg/ml. This kit is used for quantitative determination of Substance-P in serum, plasma and other biological fluids. I have used it for determination of concentration of Substance-P in serum.

3. β–Endorphin ELISA Kit-

The detection range of this kit is 15.63 to 1000pg/ml. This kit is used for quantitative determination of β–Endorphin in serum, plasma and other biological fluids. I have used it for determination of concentration of β–Endorphin in serum.

Yograj Guggul

Yograj Guggul is a famous herbomineral drug in tablet form. It is widely used for the treatment of various type of musculoskeletal pain. Osteoarthritis of the knee joint is referred to in Ayurveda as Janu Sandhigata Vata, a disease mostly brought on by an aggravation of Vata Dosha that affects the joints (Sandhi). Joint tissue deterioration, dryness (rukshata), lubrication loss, and discomfort (shoola) are all part of the degenerative process. A traditional Ayurvedic herbo-mineral combination called Yograj Guggulu is frequently used to treat musculoskeletal conditions that are dominated by Vata. Guggulu (Commiphora mukul) and many herbal components with analgesic, anti-inflammatory, and vata-pacifying qualities make up Yograj Guggulu. Classical Ayurvedic writings state that the formula works by:

Calming the agitated Vata Dosha
Increasing digestion and Agni (metabolic fire)
Eliminating metabolic poisons called Ama that block physiological channels (srotas)
Joint tissue strengthening and nourishment (Asthi and Majja Dhatu)
Increasing joint range of motion and decreasing rigidity

Thus, Yograj Guggulu helps restore balance within the musculoskeletal system and alleviates pain associated with degenerative joint disorders.

From a pharmacological standpoint, the therapeutic effects of Yograj Guggulu are attributed to its bioactive substances, notably guggulsterones from Commiphora mukul, which exhibit analgesic, antioxidant, and anti-inflammatory properties. Key mechanisms include inhibition of inflammatory processes, modulation of pain perception through neurochemical changes, reduction of nociceptive signalling by affecting Substance-P activity, and protective antioxidant effects against oxidative stress in joint tissues. Collectively, these attributes may alleviate pain, enhance joint function, and positively affect biochemical markers related to pain modulation.

Does- 1000mg two times a day.

Observation

Table-1, Concentration of Dopamine in Blood

Groups	Pre-treatment Mean±SD	Post-treatment Mean±SD	Within the group comparison (Paired t-test) Pre-post
Group-1 (n=20)	2646.80 ±743.47	2851.79 ±746.06	-204.99±1213.67 t=0.755 p=0.459
Group-2 (n=20)	2740.47 ±358.77	2988.12 ±344.32	-247.65±379.09 t=2.922 p=0.009
Between the group comparison Unpaired t- test	t=0.507 p=0.615	t=0.742 p=0.463	

Above Table-1 shows that mean value in group-1 are 2646±743.47 & 2851.79±746.06 respectively in Pre & Post-treatment period while in group-2 mean value are 2740.47±358 & 2988.12±344.32 respectively in Pre & Post-treatment period.

Table -1 also shows that statistical comparison within the group-1 is statistically insignificant while in Group-2, the statistical comparison within the group is significant.

Table-1 also shows that statistical comparison between the groups is insignificant.

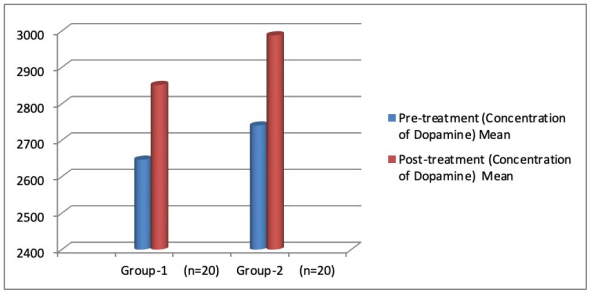


Table-2, Concentration of Substance-p in Blood

Groups	Pre-treatment Mean±SD	Post-treatment Mean±SD	Within the group comparison (Paired t-test) Pre-post
Group-1 (n=20)	4586.21 ±1378.77	4314.84 ±1062.44	271.37±1405.11 t=0.864 P=0.399
Group-2 (n=20)	5809.48 ±1427.01	5608.27 ±1635.50	201.21±1991.39 t=0.452 P=0.656
Between the group comparison Unpaired t- test	t=2.757 P=0.009	t=2.966 P=0.005	-

Above Table-2 shows that mean value in group-1 are 4586.21±1378.77 & 4314.84±1062.44 respectively in Pre & Post-treatment period while in group-2 mean value are 5809.48±1427.01 & 5608.27±1635.50 respectively in Pre & Post-treatment period.

Table -2 also shows that statistical comparison within the group-1 & Group-2 are insignificant while statistical comparison between the groups are significant.

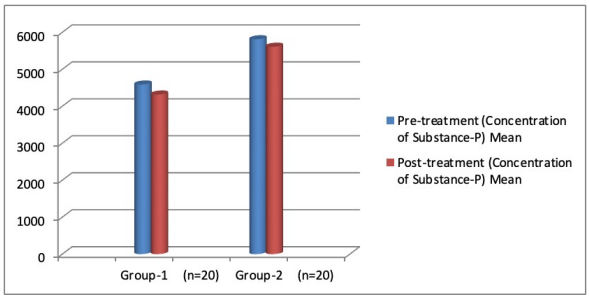
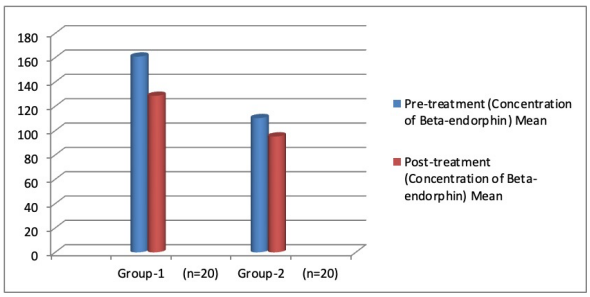


Table-3, Concentration of β-Endorphin in Blood

Groups	Pre-treatment Mean±SD	Post-treatment Mean±SD	Within the group comparison (Wilcoxon signed Rank test)
Group-1 (n=20)	160.88 ±140.25	128.64 ±87.09	Z=0.037 P=0.970
Group-2 (n=20)	110.33 ±45.07	95.25 ±43.12	Z=1.045 P=0.296
Between the group comparison Mann-Whistney test	Z=0.325 P=0.745	Z=0.866 P=0.387	-

Above Table-3 shows that mean value in group-1 are 160.88±140.25 & 128.64±87.09 respectively in Pre & Post-treatment period while in group-2 mean value are 110.33±45.07 & 95.25±43.12 respectively in Pre & Post-treatment period. Table- 3 also shows that statistical comparison within the group-1& group-2 are insignificant and statistical comparison between the groups are also insignificant.



Results

- In our study dopamine is increased in both the group. But in group-II, it is statistically significant i.e. Agnikarma is more effective.
- In our study mean value of substance-p are decreased in both the group and it is

statistically significant also. It shows that our treatment is effective in both the groups.

- In this study though the concentration of β-endorphin decreases after treatment but it is statistically insignificant.

Discussion

- Decreased level of dopamine is associated with painful symptom while everybody feels happy when concentration of dopamine is increased. Relief of pain is normally stimulates the release of dopamine in healthy individuals. When we experience pleasure, dopamine is released in our body. In this study not only Dopamine is increased in both the group but it is also statistically significant also.
- Substance-p is a pain mediator and it should be increased in patient having pain. Substance P is an important element in pain perception.Substance P is present in higher concentration in the synovial fluids of arthritispatients. It decreases after treatment in both the groups. This shows that both the treatment is effective in both the groups.
- β-endorphin is one of the happiness hormone. It is studied for its opoid activity. β-endorphins are the endorphins involved in stress relief and pain management. In this study though the concentration of β-endorphin decreases slightly after treatment but it is statistically insignificant.

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- ***Research involving Human Participants and/ Animals***- *Human*

References

1.Biochemistry and the Central Nervous System.- Mcllwain/Bachelard (Fifth edition)

2.Fundamentals of Biochemistry -Dr. A. C. Deb

3.Principles of Biochemistry-Second Edition-H. Robert Hortn, Laurence A. Morgan, Raymond, J. David, K. Gray

4.Susrut Samhita Sutrasthan Chapter-12-Ambikadatt Shastri

5. Bhaishajya Ratnavali- Vaidya Govind Das.

6. Felson, D. T. (2006). Osteoarthritis of the knee. New England Journal of Medicine, 354(8), 841–848. https://doi.org/10.1056/NEJMcp051726

7. Hunter, D. J., & Bierma-Zeinstra, S. (2019). Osteoarthritis. The Lancet, 393(10182), 1745–1759. https://doi.org/10.1016/S0140-6736(19)30417-9

8. Kidd, B. L., & Urban, L. A. (2001). Mechanisms of inflammatory pain. British Journal of Anaesthesia, 87(1), 3–11.

9. Melzack, R., & Wall, P. D. (1965). Pain mechanisms: A new theory. Science, 150(3699), 971–979.

10. Rang, H. P., Dale, M. M., Ritter, J. M., & Flower, R. J. (2012). Rang and Dale's pharmacology (7th ed.). Elsevier.

11. Sharma, R. K., & Dash, B. (2001). Charaka Samhita (Vol. 1–6). Varanasi: Chowkhamba Sanskrit Series Office.

12. Shastri, K. (2016). Sushruta Samhita with Ayurveda Tattva Sandipika commentary. Varanasi: Chaukhamba Sanskrit Sansthan.

13. Tripathi, B. (2017). Ashtanga Hridaya of Vagbhata. Varanasi: Chaukhamba Sanskrit Pratishthan.

14. Patwardhan, B., Warude, D., Pushpangadan, P., & Bhatt, N. (2005). Ayurveda and traditional Chinese medicine: A comparative overview. Evidence-Based Complementary and Alternative Medicine, 2(4), 465–473.