ORIGINAL RESEARCH

Evaluation of efficacy and safety of Vatantak Gold Tablet and Pain Kill Oil in painful inflammatory Musculoskeletal Conditions w.r.t Vatavyadhi: A PMS study

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ABSTRACT

Background: The most frequent global source of chronic pain and disability is musculoskeletal (MSK) conditions. Modern therapies have been evolved for a number of different MSK disorders, but they have a number of drawbacks. In treating chronic MSK conditions, Ayurvedic the rapeutics are safer and performs better than conventional standard care. The present study aimed to abridge evidence on Ayurvedic treatment options in painful inflammatory MSK conditions with Vatantak Gold Tablet and Pain Kill Oil. **Methods:** Multicentric**,** post-marketing, open label, clinical study. Convenient sampling was done and written informed consent acquired from 60 patients aged ≥ 18 years (both male and female) with musculoskeletal pain. End point assessment for efficacy and safety done after 60 days by physical, structured questionnairesalong with haematological and biochemical assessments. Statistical significance was considered at the level of $p < 0.05$. **Results:** Substantial improvements were seen in the parameters ESR, RA Factor, C-Reactive Protein and Uric Acid ($p<0.001$). VAS and PEG Scale also showed highly significant ($p<0.001$) changes on the subjective pain parameters along with QoL improvements mainly over the physical domain. Safety metrics remained within the expected ranges, and no anomalies or clinically significant adverse events were identified. **Conclusion:** Vatantak Gold Tablet and Pain Kill Oil administration are both safe and notably effective for usage in painful inflammatory musculoskeletal disorders due to their potent herbo-mineral composition.

INTRODUCTION

Musculoskeletal (MSK) condition results in temporary or permanent limitations in functioning and involvement. There are over 150 different diseases and conditions that fall under this umbrella. Chronic MSK pain is the leading cause of disability, and 1.71 billion people worldwide suffer from MSK diseases. These can include sudden, transient conditions that severely impair mobility and dexterity, necessitating early retirement from the workforce, decreased levels of well-being, and a reduced capacity to engage in social activities.[1] Although MSK pain is largely somatic in nature, the existence of other pain syndromes, such as neuropathic and/or visceral pain syndromes, is not prohibited. MSK pain comes in a variety of different forms, including sprained muscles, pain from fractures, shoulder pain, and others. Chronic low back pain, neck pain, and pain from osteoarthritis and rheumatoid arthritis are the most common types. MSK pain can strike at any age, although it is more likely as we age. During the course of a lifetime, almost everyone has MSK discomfort in some capacity.[2]

The prevalence of specific types of MSK pain varies widely.[3]Between 15 and 20% of people report having neck or shoulder discomfort, and between 10 and 15% report having knee pain. The prevalence of pain is about 1.5–2 times higher in women than in men, and the ratio is over four females to one male for fibromyalgia. Patterns of MSK pain problems vary greatly by age and sex. Osteoarthritis is extremely common in the elderly, affecting over one-third of people over age 60.[4,5]

MSK pain poses a diagnostic and treatment challenge. MSK pain has sensory repercussions, but it also has effects on the motor control systems and associated biomechanics. The pathophysiological classifications of pain include nociceptive, neuropathic, nociplastic, idiopathic, and mixed types of pain.[6]In patients with MSK, a systematic history taking will aid in identifying chronic pain and assist selection of the most effective therapeutics.[7,8]The use of disability-related metrics of quality-of-life may be particularly pertinent because MSK pain can be persistent and improving pain-related disability appears to be a more significant aim than pain control for some patients.[9]In order to effectively manage a patient's pain, pharmaceutical and non-pharmacological interventions should be combined[10]

According to Ayurveda the biological constituent Vata is in charge of forming biological substances, moving them around, and fortifying the body by supporting the bones and muscles, including the action of the other two Doshas (Pitta and Kapha), Vata also controls the way in which any information or system in our body is regulated, signalled, conducted, and controlled.[11]Inferentially, the exacerbated Vata itself, after vitiating the affected other Doshas and Dushya (tissue element), permeates the entire body or a portion of it, causing various sorts of pain, for which the condition is known as Vatavyadhi (Vata disease).Neuro-muscular abnormalities or musculoskeletal disorders/conditions can be correlated to the Nanatmaja Vikaras of Vatavyadhi which has specific pathology of manifestation which refers to conditions that primarily affect the nervous system, musculoskeletal system, and reticuloendothelial system but also affect all other body systems.[12]

Vitiated Vata causes pains, aches and inflammation and the remedy in this case be the pacification of Vata by therapeutic and behavioural changes, accomplished mostly through the preliminary Panchakarma procedures Snehana (oleation) and Swedana (fomentation).[13]Virechana and Basti Karma are the main Panchakarma procedures for the management of Vatavyadhi. Shastra, Kshara and Agnikarma also indicated along with internal medications which help to pacify vitiated Vata.[14]

The vast majority of the Ayurvedic pharmacopoeia are plants and minerals. Modern texts provide a good summary of their therapeutic qualities. Ayurvedic formulations, which are frequently complicated and contain a number of herbal and mineral constituents, are controlled by well-explained pharmacological preparation, compatibility, and administration rules.[13]The conventional approach to treating this illness has its own limitations. It has significant side effects, is very symptomatic, and can be treated surgically or with conservative methods. Yet, the management and techniques of Ayurveda can be used to treat these types of illnesses more effectively.The present study was undertaken to assess the efficacy of Vatantak Gold Tablet (internal) and Pain Kill Oil (local) which are Ayurvedic proprietary medicines developed, manufactured and marketed by Jamna Herbal Research Limited, Bhopal, Madhya Pradesh, India in MSK Conditions w.r.t Vatavyadhi. Local Abhyanga with oil and Ayurvedic Rasayana internally were selected for the present study as it has shown best for Vatavyadhi.

MATERIALS AND METHODS

The present post-marketing, open label, clinical study was undertaken at two Ayurveda establishments situated in Kolkata (The Ayurveda Clinic and Research Centre and Gananath Sen Institute of Ayurvidya and Research). Ethical approval (IECCRI/22-23/13 dated 02/11/2022) was obtained from Independent Ethics Committee (Clinical Research) India, a CDSCO approved independent ethics committee founded by Independent Research Ethics Society. The study was also registered for CTRI (CTRI/2022/11/047342) on 16/11/2022. Objective of the study was to explore the efficacy of relieving painful condition in Musculoskeletal Disorders [Osteoarthritis (OA), Rheumatoid Arthritis (RA), Sciatica, Gout) w.r.t Vatavyadhi.Participants provided written informed consent and was informed about the detailed nature of the study and assurance was provided on voluntary participation. Convenient sampling technique was used to recruit the 60 participants from the outpatient clinic who came for regular health check-ups and consultation.

Patients were included based on age ≥ 18 years (both male and female) with musculoskeletal pain; fit and no need for any hospital administration; willing to perform all study related procedures including the use of study medicine, allow the physical and biochemical assessments. Exclusion criteria was using steroids and/or recreational drugs in the past 6 months; open wounds or infection at the application site; renal impairment; poorly controlled diabetes mellitus; pregnant; unstable medical or psychiatric illness; chronic & acute disorders requiring hospital admission; known HIV-positive, Hepatitis B or C status; inability to carry out visits, maintain current medication regimen and unwillingness to participate in all components of the study. The end point assessment of treatment effect after 60 days of treatment were based on both changes and success on Physical assessment (height, weight, blood pressure, pulse and respiratory rate); Pain Score: Visual Analogue Scale (VAS)[15]; Disease activity based on questionnairesPain, Enjoyment of Life and General Activity (PEG) Scale[15]; Blood tests (Erythrocyte Sedimentation Rate, Rheumatoid Arhritis Factor, C-Reactive Protein, Serum Uric Acid). Along with Quality of Life – WHOQOL-BREF[16]; Drug safety parameters skin test, Renal Function Test & Liver Function Test.

Once the case record form had been completed, the data was checked and corrected by the investigator.

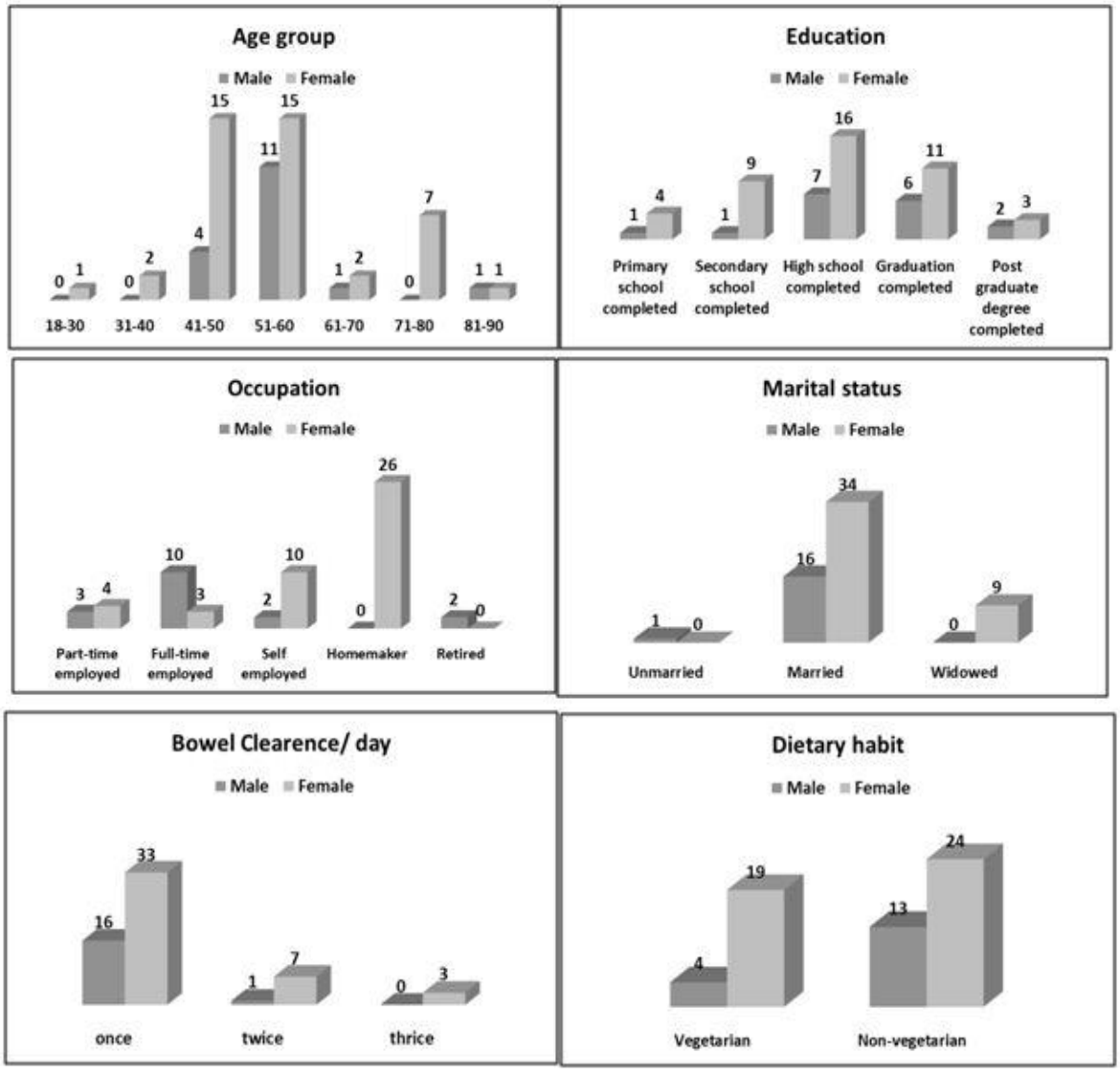
After coding, cleaning and editing data was entered into the computer through Statistical Package for Social Sciences (SPSS version 25) software for analysis. Statistical significance was considered at the level of $p < 0.05$ in all the efficacy parameters. Before and after treatment was compared by Paired Samples t-Test.

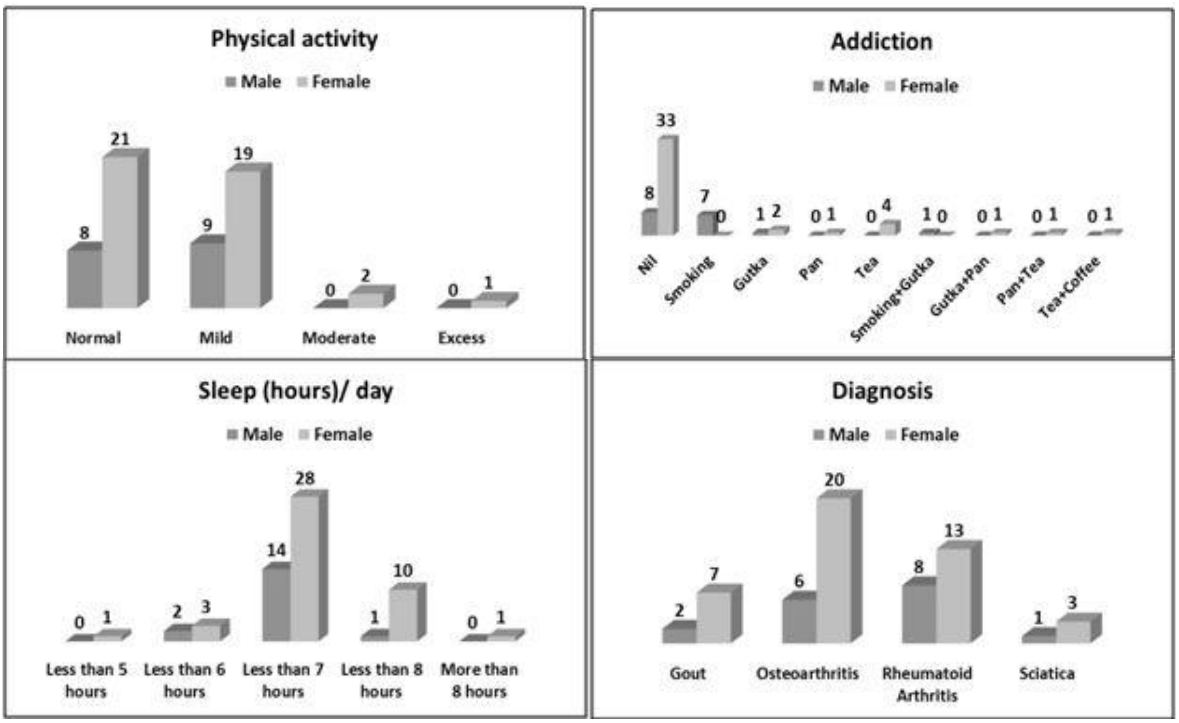
Jamna Herbal Research Limited has developed and marketing both the products (Vatantak Gold Tablet and Pain Kill Oil) after getting manufacturing licence from Office of the Drug Controller (AYUSH), Bhopal, Madhya Pradesh, where observed the effects and communicated on label and promotional materials. The drug review as mentioned in Ayurvedic Pharmacopoeia of India[17], Ayurvedic Formulary of India[18] and Ayurvedic texts[19]shows their effectiveness. These Ayurvedic drugs are scientific formulation of herbo-mineral compounds and natural oils intended to evaluate the efficacy on the musculoskeletal disorders with local application of Pain Kill Oil (twice daily) and oral intake of Vatantak Gold Tablet (2 tablets twice daily after food with milk or lukewarm water). The study adhered to the Good Clinical Practice and New Drug &Clinical Trial Rules, 2019.

RESULTS

Socio-demographic information showed 60 participants, comprising both male (28.3%) and female (71.7%). Participants' ages ranged from 30 - 82, with a mean age of 54.93 (±11.004 SD) years. The patients' levels of education varied; 91.67% (55) of them had completed their schooling, while only 8.33% (5) of the study participants had completed less than grade 10. Work status shows that the majority of them (43.33%) were homemakers, constituted of females. Marital status showed 83.33% were married. Dietary habits revealed non-vegetarian diet was consumed by 61.67% participants. Mid to normal physical activity was reported by 95%. Bowel was found normal in 81.67% along with 80% reported sleep less than 7 hours/day. Among the participants with MSK conditions 43.5% were diagnosed as suffering from Osteoarthritis followed by Rheumatoid Arthritis constituting 35.5% (Figure 1).

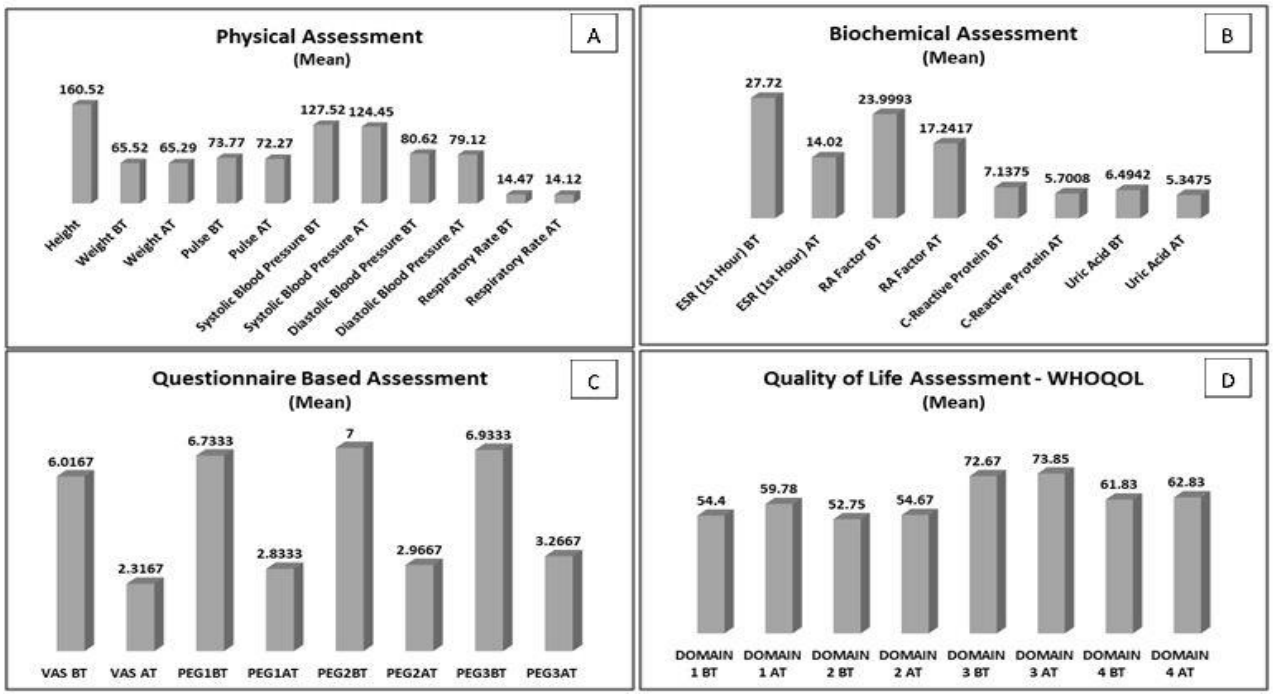
Figure 1: Socio-demographic distribution of the participants along with diagnosis





Physical assessment: showed that the physical parameters regarding weight, pulse, blood pressure and respiratory rate remained maintained before and after treatment and there were not much noticeable changes in their mean, even though statistically significant changes were observed in weight, pulse and blood pressure parameters (Figure 2 and Table 1).

Figure 2: Assessment parameters before and after treatment



BT = Before Treatment; AT = After Treatment

B: ESR= Erythrocyte Sedimentation Rate; RA= Rheumatoid Arthritis

C: VAS = Visual Analogue Scale; PEG 1 = What number best describes your pain on average in the past week?; PEG 2 = What number best describes how, during the past week, pain has interfered with your enjoyment of life?; PEG 3 = What number best describes how, during the past week, pain has interfered with your general activity?

D: Domain 1= Physical Health; Domain 2= Psychological; Domain 3= Social Relationships; Domain 4= Environment

Table 1: Assessment parameters findings before and after treatment, (Vatantak Gold Tablet & Pain Kill oil)

	Paired Differences			Sig. (2-tailed)
	Mean	Std. Deviation	Std. Error Mean	
Physical Assessment				
Weight	0.23167	0.41762	0.05391	0.001
Pulse	1.5	2.56773	0.33149	0.001
Systolic Blood Pressure	3.06667	5.60831	0.72403	0.001
Diastolic Blood Pressure	1.5	4.48916	0.57955	0.012
Respiratory Rate	0.35	1.91183	0.24682	0.161
Haematological & Biochemical Assessment				
Erythrocyte Sedimentation Rate (1st Hour)	13.7	5.924	0.765	0.001
Rheumatoid Arthritis Factor	6.75767	8.45836	1.09197	0.001
C-Reactive Protein	1.43667	1.44864	0.18702	0.001
Uric Acid	1.14667	1.0062	0.1299	0.001
Questionnaire Based Assessment (VAS & PEG)				
Visual Analogue Scale	3.7	0.84973	0.1097	0.001
PEG 1	3.9	0.93337	0.1205	0.001
PEG 2	4.03333	0.97366	0.1257	0.001
PEG 3	3.66667	0.79547	0.10269	0.001
Quality of Life Assessment (WHOQOL-BREF)				
DOMAIN 1 (Physical Health)	-5.383	9.922	1.281	0.001
DOMAIN 2 (Psychological)	-1.917	7.805	1.008	0.062
DOMAIN 3 (Social Relationships)	-1.183	4.608	0.595	0.051
DOMAIN 4 (Environment)	-1	3.866	0.499	0.05

PEG 1 = What number best describes your pain on average in the past week?
PEG 2 = What number best describes how, during the past week, pain has interfered with your enjoyment of life?
PEG 3 = What number best describes how, during the past week, pain has interfered with your general activity?

Biochemical assessment: marked reduction (improvement) on the parameters ESR (49.42%), RA Factor (28.14%), C-Reactive Protein(20.17%) and Uric Acid (17.57%) was comparably noticed before and after treatment. Also, highly statistical significance was notedat the level of $p<0.001$ level showing efficacy of administered drugs on the biochemical parameters of MSK conditions (Figure 2 and Table 1).

Questionnaire based assessment: VAS on pain scoring showed improvement of 61.46%. PEG Scale Assessing Pain Intensity and Interference showed mean pain on average in the past week improved by 57.95%; pain interfering with enjoyment of life for the past week enhanced by 57.57%; and pain interfering with general activity for the past week bettered by 52.81%. The parameters VAS and PEG were prominently statistically highly significant at the level of $p<0.001$ compared before and after treatment depicting the efficacy of the administered drugs (Figure 2 and Table 1).

Quality of life assessment: The WHOQOL domains showed perceivable improvements related before and after treatment. Mostly the Domain 1 on physical health was remarkably improved by 9.89% ($p<0.001$) followed by the Domain 2 on psychological by 3.64%. To some extent improvements were also observed on the other domain social relationships and environment (Figure 2 and Table 1).

Complete Blood Count, Liver Function Test and Renal Function Test stayed within the normal limits (Table 2), no abnormalities and no clinical adverse events were observed after 60 days of Vatantak Gold Tablet and Pain Kill Oil administration.

Table 2: Safety parameters findings before and after treatment, (Vatantak Gold Tablet & Pain Kill oil)

	Paired Differences			Sig. (2-tailed)
	Mean	Std. Deviation	Std. Error Mean	
Fasting Blood Glucose	1.600	10.208	1.318	0.230
Serum Urea	1.383	2.799	0.361	0.000
Serum Creatinine	0.03800	0.09993	0.01290	0.005
Total Bilirubin	0.01333	0.09545	0.01232	0.284
Conjugated Bilirubin	0.01617	0.07232	0.00934	0.089

Unconjugated Bilirubin	-0.00283	0.10353	0.01337	0.833
SGOT / AST	3.867	6.537	0.844	0.000
SGPT / ALT	8.867	12.409	1.602	0.000
Alkaline Phosphatase	1.900	12.495	1.613	0.244
Total Protein	-0.0833	0.5253	0.0678	0.224
Albumin	-0.0550	0.2861	0.0369	0.142
Globulin	-0.0273	0.4427	0.0572	0.634
Albumin Globulin Ratio	-0.01017	0.18445	0.02381	0.671
Haemoglobin %	-0.42500	1.59434	0.20583	0.043
Erythrocytes	-0.13333	0.51836	0.06692	0.051
Leucocytes	686.667	1089.972	140.715	0.000
Neutrophils	0.867	5.222	0.674	0.204
Lymphocytes	-1.300	4.303	0.556	0.023
Monocytes	0.450	2.004	0.259	0.087
Eosinophils	0.050	0.999	0.129	0.700
Platelet Count	-0.19750	0.73591	0.09501	0.042

DISCUSSION

Musculoskeletal pain is a growing contributor to decreased quality of life and rising healthcare costs.[20]Many therapies exist to address musculoskeletal pain. Trials and systematic reviews have shown that most therapies for musculoskeletal pain have minor to moderate short-term benefits, but there is insufficient data to support their long-term efficacy.[21]Data suggests that NSAIDs, Cox-2 selective inhibitors, and opioids alleviate pain in the short term, but the impact size is moderate, and it is important to take into account the possibility of side effects such gastrointestinal bleeding and opioid-induced hyperalgesia. Injections provide temporary pain relief for knee and shoulder pain, but their efficacy for back and neck pain is debatable. The best method (e.g. guided vs. unguided), frequency, dose, and active ingredient of the injections are still unknown for many musculoskeletal pain presentations for which pharmacological injections including corticosteroids may be administered for pain treatment. Moreover, there was insufficient evidence to support the clinical efficacy of the majority of additional therapeutic modalities, including ice/hot packs, ultrasound, laser, and acupuncture.[22]

Structures of musculoskeletal system have a strong correlation with Marma Asthi Sandhi Vyadhis, which is covered by Madhyama Rogamarga in Ayurvedic concept and the main culprit which leads to the pathogenesis of Vatavyadhi is Vata. MSK disorders are considered as Kashta SadhyaVyadhi as they include Marma, Asthi, Sandhi.[23]Despite the fact that multiple contemporary therapies have been developed for a variety of musculoskeletal disorders, they have a number of shortcomings, including low efficacy, significant side effects, and high cost. Treatment for musculoskeletal problems typically lasts the patient's entire lifetime; as a result, it must be efficient, comfortable, secure, and affordable.[2] For the treatment of MSK disorders, Ayurveda provides appropriate Shamana and Shodhana Chikitsa.

The purpose of this study was to offer proof of the efficacy of Ayurvedic herbo-mineral drug therapies (Vatantak Gold Tablet and Pain Kill Oil) for patients with the most prevalent musculoskeletal conditions in terms of reducing pain and/or improving function. The ingredients in Vatantak Gold Tablets that relieve pain and inflammation are Brihat Vatchintamani Ras, YograjGuggulu, Enakgveer Ras,[18]Nirgundi (*Vitex negundo* Linn.), Rasna (Pluchealanceolata C. B. Clarke.), Ashwagandha (With aniasomnifera Linn.), Katuki (Picrorhizakurroa Royle ex Benth) and Dashamool [Bilva (Aeglemarmelos L. Correa ex Roxb.), Agnimantha (Clerodendrumphlomidis Linn. f.), Gambhari (Gmelinaarborea Roxb.), Shyonaka (Oroxylumindicum Vent.), Patala (Stereospermumsuaveolens DC), Brihati (Solanumindicum Linn.), Shalaparni (Desmodiumgangeticum DC), Kantakari (Solanumxanthocarpum S. & W.), Gokshura (Tribulusterrestris Linn.), Prishnaparni (UrariapictaDesv.).[17,19]

On the other hand Pain Kill Oil composed of Rasna (Pluchealanceolata C. B. Clarke.), Akarkarabh (Anacyclus pyrethrum DC.), Katphala (Myricaesculenta Buch.-Ham. ex D. Don), Bharangi (ClerodendrumserratumLinn.), Shukla Jeeraka (Nigella sativa Linn.), Jyotishmati (Celastruspaniculatus Willd), Vatsanabha (Aconitum ferox Wall. ex Ser.), Mustaka (Cyperusrotundus Linn.), Devdaru (Cedrusdeodara (Roxb.) Loud.), Kupilu (Strychnosnux-vomica Linn.), Sarshap (Brassica campestris Linn.) Dhatura (Daturametel Linn.), Shunthi (Zingiber officinale Rosc.), Maricha (Piper nigrum Linn.), Pippali (Piper longum Linn.), Karpoor (Cinnamomumcamphora (Linn.) Nees & Eberm.), Ashwagandha (With aniasomnifera Linn.), Nirgundi (Vitexnegundo Linn.), Rakta Punarnabha (Boerhaviadiffusa Linn.), Shatavari (Asparagus racemosusWilld.), Neelgiritaila (Eucalyptus globules Labill.), Dashamool, [17,19]and Saindhav Lavana.[17]

Vatantak Gold Tablet and Pain Kill Oil reduced the painful inflammatory conditions of MSK Disorders

(OA, RA, Gout, Sciatica) due to their unique composition. There was a highly significant ($p<0.001$) reduction in the mean score for inflammatory haematological markers [ESR (49.42%), CRP (20.17%), RA Factor (28.14%) and Uric Acid (17.57%)]. Also, highly significant ($p<0.001$) reduction of the pain parameters VAS (61.46%) & PEG (57.95%; 57.57%; 52.81)along with improvements on WHOQOL-BREF parameter for QoL. There were no clinically significant changes physical assessment (weight, height, blood pressure and respiratory rate). Likewise, a significant decrease of SGOT, SGPT, Urea and Creatinine indicative of hepato-renal protection was observed and any of the other haematological and biochemical parameters had no significant deviations from normalcy. Moreover, no such clinically significant adverse reactions (either reported by patients, or observed by the investigators), and the overall compliance to the treatment was excellent.Ayurveda formulations have been shown to be efficient and safefor chronic diseases of the musculoskeletal system.[24] Existing non-surgical medication therapies (particularly NSAIDs), which have a variety of drawbacks that make them unsuitable for long-term use.[25-29]Correspondingly, the population size of this study was extremely tiny. This might be a barrier to achieving larger clinical significance. This may be proven in additional patients using a cross-over design along with Panchakarma to produce a more ameliorating therapeutic result.

CONCLUSION

Ayurvedic holistic approach perform better than conventional standard therapy while treating persistent MSK diseases by assembly of sophisticated, personally designed interventions, such as physical therapy, dietary supplements, medication, yoga, and purifying techniques. The constitution-based Ayurveda approach has the relics of treating Vatavyad his with myriad forms of treatment, such as Shodhana and Shamana and avoids using mean-value based medical treatments. Ayurveda treatment with Vatantak Gold Tablet and Pain Kill Oil in this trial exhibited a great deal of pain reduction along with improved general quality of life.

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