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THERAPEUTIC EFFECT OF ASWAGANDHADI COMPOUND IN ASTHI-MAJJA KSHAYA (OSTEOPOROSIS/OSTEOPENIA) - A PILOT STUDY

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INTRODUCTION

Osteoporosis is emerging as a major health problem in view of the increasing number of older people in India. It is estimated that in India 61 million people are affected by Osteoporosis out of which 80% are female. Intervention to prevent bone loss in early postmenopausal women has become the only approach to control the increasing incidence of Osteoporosis (WHOM 1994). Osteoporosis occurs both in male and females in India. Osteoporotic fractures occur more commonly in Indian male than female. In Ayurveda *Asthi kshaya* is a condition in which there is decrease in the *Asthi dhatu* (Bone tissue)¹ leading to many undesirable effects. It can be compared with Osteoporosis in which there is decrease in the Bone Mineral Density (BMD) leading to increased risk of fractures. Two conditions mentioned in Ayurveda as *Asthi kshaya* and *Asthi saushirya*. *Asthi saushirya* is not mentioned as a separate condition but, as a symptom of *Majja kshaya* where as, *Asthi kshaya* is mentioned as an independent

ABSTRACT

Osteoporosis is a systemic disorder that affects entire skeleton, which is a metabolic disease of the bone characterized by low bone mass and micro architectural deterioration of the skeleton, leading to enhanced bone fragility and fracture risk. In Ayurveda, it is correlated with *Asthi-Majjakshaya*. Basing on the concept a formulation "Aswagandhadi Compound" has been selected to observe the possibility of enhancement of bone mass and 30 numbers of patients for 4 weeks, on the basis of symptomatology and confirmed BMD test at Indoor Patients Department (IPD) were put to observational study of National Research Institute of Ayurved Drug Development, Bhubaneswar. It was observed that, BMD (t-score) was increased by 4.3% after completion of treatment duration, which was statistically highly significant ($P < 0.001$). It was observed that the drug is able to enhance the bone cell formation as well as decreasing bone mass desorption. The formulation expected to act by balancing bone remodeling and also preventing bone loss by increasing the bone density. It is interpreted from the above study that, this "Aswagandhadi Compound" is having efficacy on the disease *Asthi-Majjakshaya* (Osteoporosis/Osteopenia) from the evidence of the study which is discussed in details.

Condition (Sushruta *et al.*, 1980). No specific sign and symptoms are seen in *Asthi saushirya* but, the sign and symptoms along with the treatment of *Asthi kshaya* are found described separately. The sign and symptoms of *Asthi kshaya* are. *Asthi-sandhi shula*, *kesha*, *roma*, *nakha*, *danta vikara/pata* and *daurbalya* which are mostly identical as with the updated sign and symptoms of osteopenia/osteoporosis mentioned in the modern medical sciences. Recently, modern scientists have agreed with the observation as definite association between hair, nails and teeth pathology with osteopenia/osteoporosis.

Aims and Objectives: The aim of the study is to find out the probable efficacy of a herbomineral compound drug having expected activities of osteogenesis and ossification.

MATERIALS AND METHODS

A total no. of 30 patients both from Osteoporosis and Osteopenia (*Asthi-Majjakshaya*) were selected from OPD on the basis of clinical features and confirmed Bone Mineral

Density (BMD) Test as per criteria and were admitted in IPD of National Research Institute of Ayurvedic Drug Development, Bharatpur, Bhubaneswar, Odisha irrespective of their sex, religion, etc. Written consent was obtained from each patient after briefing them detailed information about the treatment, Ethical clearance was also obtained from the Institutional Ethics Committee.

Inclusion Criteria: Following criteria was adopted before starting the study as

- Patients with BMD (t-score) were equal to or less than -1.
- Patients presenting with the symptoms of osteoporosis (Asthi-Majjakshaya) as per protocol designed
- Patients between the age group of 35 to 80 years.

Exclusion Criteria

- Patients below the age of 35 above 80 years
- Patients with BMD (t-score) - 1 and above
- Patients with rheumatoid arthritis, gouty arthritis and longstanding systemic disorders
- Known case of diabetes mellitus (DM) uncontrolled hypertension (HTN), thyrotoxicosis, hyperparathyroidism, Addison’s disease, paget’s disease, cushing’s syndrome tuberculosis of bone, Osteomalacia, chronic renal disease, hepatic and cardiac diseases and long term systemic diseases with continuation of modern drugs.

Criteria for Diagnosis

The criteria of diagnosis was based on clinical and radiological parameters. A total no.of 30 patients fulfilling the criteria of diagnosis of Osteoporosis/Osteopenia (Asthi - Majjaskhya) were selected for the study and were treated with the trial drug Aswagandhadi Compound for 30 days.

Drug, Dose and Duration

Aswagandhadi compound a combination of five ingredients i.e. Awagandha Churna (Powder of Withenia somnifera) 5 gms, Guduchi Satva (Aqueous extract of Tinospora cordifolia) 500 mg, Godanti Bhasma(Purified Gypsum) 250 mg, Sudha Guggulu (Purified Gum Resin of commiphora wightii) 1 gm & Mukta Sukti Bhasma (Purified Corel) 500 mg, mixed together made into a mixture at a dose of 7 gms 250mgs given each dose for 3 times a day after food with Luke warm milk for one month. All the individual drugs were purchased from Indian Medical Pharmaceuticals Corporation limited with S.O.P. and R&D certificates.

Dietary Regimen

The patients were advised as per Ayurvedic fundamental principles to avoid Apathya diet and were provided recommended hospital diet till the course is completed.

Criteria for assessment

Improvement in the patients was assessed on the basis of relief in sign and symptoms along with BMD score. All the sign and symptoms were noted giving score marking depending upon their severity to assess the effect of the treatment.

Parameters of the study: Subjective parameters

Shoola (Pain)

- Grade 0 - No Pain

- Grade 1 - Mild Pain
- Grade 2 - Discomforting pain
- Grade 3 - Distressing pain
- Grade 4 - Horrible

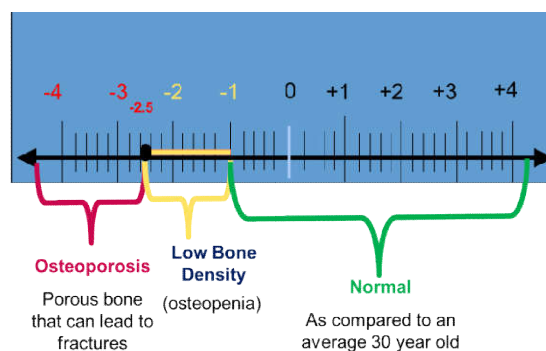
Sparsha asahisnuta (Tenderness)

- Grade 0 - No Tenderness
- Grade 1 - Mild Tenderness without any sudden response on pressure
- Grade 2 - Wincing of face on pressure
- Grade 3 - Wincing of face with withdrawal of the affected part on pressure
- Grade 4 - Resistance to touch.

Dourbalya (General debility)

- Grade 0 - No Dourabalya
- Grade 1 - Not able to perform strenuous activity
- Grade 2 - Not able to perform moderate activity
- Grade 3 - Cannot perform moderate activity but can perform mild activity without any difficulty
- Grade 4 - Mild activities cannot be performed even.

Objective parameter On the basis of BMD score scale



Bone mineral density (t-score): WHO criteria for assessing osteoporosis

- Normal - “t” Score greater than - 1
- Osteopenia - “t” score between - 1 and - 2.5;
- Osteoporosis - “t” score less than or equal to - 2.5
- Severe osteoporosis - “t” scoreless than - 2.5 with fracture.

Overall effect of therapy has been assessed through parameters adopted

Marked improvement > 75-100% of improvement Moderate improvement 50 to 74% of improvement Mild improvement 25 to 49% of improvement Poor improvement less than 25% of improvement.

Observations

Table-1 Showing the sex ratio

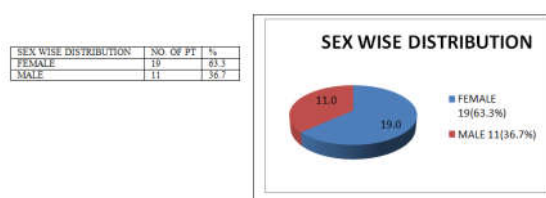
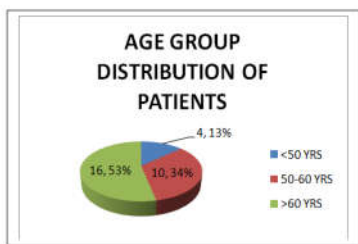
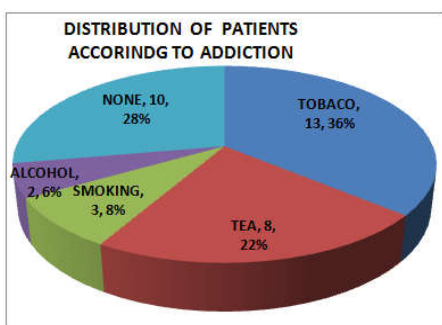


Table 2. Showing the age ratio

AGE GROUP	NO OF PTS	%
<50 YRS	4	13
50-60 YRS	10	34
>60 YRS	16	53



From the Table no-1 it is observed that out of 30 no's of patients selected for trial, 19(63.3%) no. of patients were female and 11(36.7%) no of patients were from male, So far age ratio is concerned from the Table no-2, 4(13%) no. of patients were less than 50 years, 10(34%) no. of patients were within the age group of 50-60 years and 16(53%) no. of patients were within the age group of more than 60 years of age.



It has been observed from the above table that out of 30 no's of patients 10(36%) nos. of patients were having addiction of tobacco and 7(22%) nos. of patients with tea. Whereas 3(8%) no of patients were smoker and 2(6%) no of patients were addicted with alcohol that signifies that addiction have major role for aggravation of diseases.

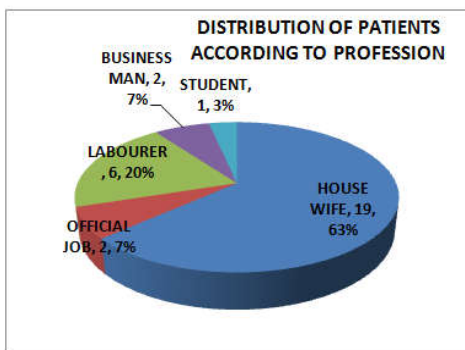


Table no 3. Showing the personal addiction habits & profession

It has been observed from the above diagram no-2 that out of 30 no's of patients 19(63%) no of patients were house wife which clearly signifies that in India 61 million people are affected by Osteoporosis, out of which 80% are female due to their post menopausal condition (Davis *et al.*, 1999). It has been observed from the above table that the 19 nos of female patients and 11 no of male patients complaining of, Asthi dourballya before treatment; but 30 days of treatment with Aswagandhadi compound the the nos of posive patients reduced this signifies that the medicine significantly reduced the Asthi dourballya in case of both male and female patients.

Table 3.

THE DIFFERENCE OF BT & AT IN ASTHIDOURBALYA			
	BT	AT	% of change
FEMALE	19	18	5.3
MALE	11	9	18.2

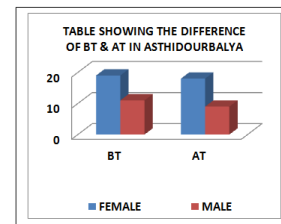
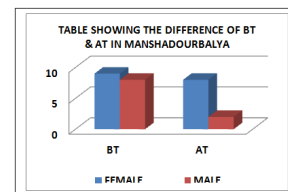


Table-4

THE DIFFERENCE OF BT & AT IN MANSHADOURBALYA			
	BT	AT	% OF CHANGES
FEMALE	9	8	11.2
MALE	8	2	75



It has been observed from the above table that, the no of patients suffered with Mamsha dourbalya reduced in case of male than female patients before treatment i.e. 8 positive patients reduced to 2 patients. This signifies that, the drug effectively working in case of Mamsha dourbalya in case of both male and female.

Overall effect of therapy

It was observed that, out of 30 no. of patients Moderate improvement was found in 3(10%) no. of pts, Mild improvement was found in 26(86.87%) no. of pts, where as poor improvement in 1(3.33%) patients which indicates the better efficacy of compound drugs.

DISCUSSION

Vitiation of Vata and deterioration of all Dhātu is a natural phenomenon occurs in old age. Provocation of Vata occurs by two processes, both Santarpana and apatarpana. Provocation of Vata causes by Apatarpana is due to taking diet and regimen which causes the depletion of dhatus via ruksha,laghu etc.and mainly during the Jara vashtra, Reviewing all the available literature related to Asthidhatu and Majja Dhātu, the final diagnosis of the disease was given as Asthi soushirya. Vata Dosha contributes large for occurrence of Asthi related diseases because of unique relationship of Vata and Asthi. Gambhira Dhātu (deep-seated tissue), Svabhava Balapravritta Vyadhi (Natural Phenomemon due to old age) and Bhedawastha (complicated stage) make this disease Asadhya (incurable). Management of established bone porosity is difficult. Hence, prevention of the condition becomes very important. The disease can become Yapyā by intervention at proper level, followed with Pathyapathaya. Prevention of Asthi saushirya should be commenced at the level of Asthi-Majjakshaya which is precursor of Asthi Saushirya (bone porosity). The bone density in the form of more osteoblast cells is of prior concern. Apart from improvement of nutrition and life style changes for the control of osteoporosis, prevention of fractures of the vertebrae, non-vertebral bones and hips by correction of the bone density and it is also necessary to reduce the loss of Calcium which is required for healing of old fractures.

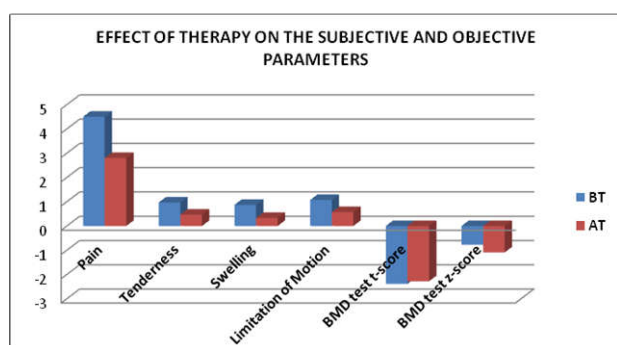
Table 5. Effect of therapy on the subjective and objective parameters of the 30 patients in osteoporosis (Asthi-Majjakshaya)

Parameters	Mean SD		Change		“t” Value
	BT	AT	Mean	%	
Pain	4.5±0.63	2.8±0.6	1.73	38.5	14.8*
Tenderness	0.97±0.41	0.47±0.5	0.5	57.7	5.4*
Swelling	0.87±0.68	0.33±0.48	0.53	61.5	4.6*
Limitation of Motion	1.07±0.64	0.57±0.5	0.5	46.88	6.1*
BMD test t-score	-2.39±0.77	-2.28±1.1	0.01	4.3	5.8*
BMD test z-score	-0.77±0.76	-1.09±0.76	0.23	30.6	5.1*

* p≤0.001 shows statistically highly significant. BT- Before treatment, AT- After treatment

Effect on Pain

Pain is the cardinal symptoms of vitiated *Vata Dosha*. Pain does not arise in the absence of *Vata*⁸. Therefore this compound formulations can relieve pain only by pacifying vitiated *Vata Dosa*. It was observed that the changes of pain 4.5±0.63 after 30 days of treatment which was reduced to 2.8±0.6, and a total relief of 38.5% was found in pain after 30 days of therapy with “t” value of 14.8, which was statically highly significant (P<0.001).



Effect on Tenderness

It was observed in the present study that the changes of Tenderness were 0.97±0.41 after 30 days of treatment which was reduced to 0.47±0.5, and a total relief of 57.7% was found in Tenderness after 30 days of treatment with “t” value of 5.4 which was statistically highly significant (P<0.001) (Table-5).

Effect on Swelling

It was observed that the changes of Swelling were 0.87±0.68 after 30 days of treatment which was reduced to 0.33±0.48, and a total relief of 61.5% was found in Swelling after 30 days of treatment with “t” value of 4.6 which was statistically highly significant (P<0.001).

Effect on limitation of motion

It was observed that, the changes in limitation of motion of were 1.07±0.64 after 30 days of treatment it was reduced to 0.57±0.5, and a total relief of 46.88% was found in Swelling after 30 days of treatment with “t” value of 6.1 which was statically highly significant (P<0.001).

Effect on BMD Score

It was observed that the changes in BMD “t” score were -2.39±0.77 and after 30 days of treatment which was reduced to -2.28±1.1, In the present study, BMD (t-score) increased by 4.3% after completion of duration, which was statically highly significant (P<0.001).

This indicates that the drug is enhancing bone formation as well as decrease bone desorption. Although the change in percentage from before treatment to after treatment in case of t-score is low but that low percentage of improvement in almost all cases.

The Pharmacokinetic effect of Aswagandhadi compound

A compound formulation the combination of Aswagandha (*Withania somnifera*), Guduchi (*Tinospora cordifolia*), Mukta sukta Bhasma (Calcinated pearl), Godanti Bhasma (Calcinated Gypsum), Guggulu (*Commiphora wightii*) is hoped to repair the calcium deficiency related to Osteoporotic bone. In Ayurveda Guggulu has been considered for Vata dosha, Guduchi has considered as a Rasayana and Aswagandha as a anti inflammatory and immune modulator and Mukta Shukti and Calcium are natural calcium indicated in Asthi kshaya in some articles in Ayurveda. *Withania somnifera* is an analgesic, helps relieve in pain associated with osteodystrophic disorders⁷, and the results showed that *Withania somnifera* possessed potent anti-inflammatory activity². *Withania somnifera* is a potent antioxidant and causes a significant inhibition of NO synthetase, protein synthesis and nuclear factor-kappaB (NF-kappaB) activation.

Agarwal *et al.* studied *Withania somnifera* for anti-inflammatory activity in immune mediated inflammation. *Commiphora wightii* contributes in the critical process of bone remineralization (Singh *et al.*, 2003) investigated *Commiphora wightii* for reduction of pain, stiffness and joint mobility in older patients with OA of the knee and reported significant improvement in the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) total score with symptomatic improvement (Fatope *et al.*, 2003). The active ingredients of *Commiphora wightii* are flavanones (muscanone and naringenin) (Meselhy, 2003; Zhu *et al.*, 2001) observed the scavenging effect of *Commiphora wightii* against DPPH radicals (Zhu *et al.*, 2001). *Withania somnifera* is an analgesic, which helps relieve pain associated with *Tinospora cordifolia* have been reported to affect the proliferation, differentiation and mineralization of bone like matrix on osteoblast Alcoholic extract of *Tinospora cordifolia* have been shown to stimulate the growth of osteoblasts, increasing the differentiation of cells into osteoblastic lineage and also increasing the mineralization of bone like matrix. As calcium supplements Mukta pisti and Godanti Bhasma and other sudha varga dravyas are mild organic form of calcium carbonate and are beneficial osteoporosis as calcium supplement at minimal dose of 125 - 250 mg (1-2 ratti). Calcium compounds are alkaline in nature.

The natural calcium preparations like bhasmas are more effective than synthetic calcium due to the reason that, they contain easily absorbable and assailable form of oxide and they contain other trace elements such as magnesium, copper, zinc etc. Irrespective of the gastrointestinal condition they do exhibit

their efficacy unlike synthetic molecules which cannot be absorbed in unhealthy gut conditions such as indigestion, chronic gut motility disorders and hormonal imbalances¹².

Pharmacodynamic Effect

Looking to the individual response of the drug, it is expected that, the drug acts as an antagonist to the glucocorticoid receptor and promotes good bone health. It shows anabolic steroid properties for healing of fracture. It increases intramuscular creatinine level. It blocks the muscle damaging effect of control and leads to the formation of new muscles. It shows significant inhibition of DPPH free radical.

Conclusion

From above study, it was observed that Aswagandhadi compound showed encouraging effect in the management of Osteoporosis/Osteopenia (Asthi-Majjakshaya) and it also improves the general health of the patients due to the anabolic effect (Rasayana) properties. Most of the ingredients are considered as Rasayana in Ayurveda like Aswagandha, Guggulu, Guduchi having anti oxidant properties. The calcium supplement through Godanti and Muktasukti are added value of the drug for Osteoporosis /osteopenia. It is hoped that the compound may show more effect if continued for a longer duration. The trial still continuing to find out the effect in more no of samples for longer duration, which was evident from the above study by changing the BMD value with 't' score and 'z' score.

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