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EFFICACY OF VITAMIN D SUPPLEMENTATION IN PATIENTS WITH CHRONIC LOW BACKACHE – A PROSPECTIVE STUDY

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ABSTRACT

Background: Chronic low back ache (LBA) is one of the commonest and expensive ailments of youngsters with ambiguous pathophysiology leading to a significant loss of productivity. Studies established that the vitamin D is a proven anabolic hormone for the entire musculoskeletal system. This study was designed to evaluate the differences in outcomes with various oral formulations of vitamin D available in the market. **Methodology:** This study is a randomised, prospective, open label analytical study of a cohort of patients with LBA and hypovitaminosis D from June 2022 to August 2022. Patients were sequentially randomized to one of the three treatment subgroups (Granule group, Nano Syrup group, Soft gel capsule group) named after the vit.D formulation they received after establishment of clinical, radiological and biochemical eligibility. Total number of 145 subjects were screened, among them 119 subjects were eligible and 87 have completed the study. Vitamin D supplementation of 60,000 IUs per dose for ten consecutive days (pulse-D therapy) was given in form of granule (1 g sachet) or nano syrup using aqueous nanotechnology (5 mL bottle) or soft gel capsule. Adverse drug reaction recording chart was provided to all patients and was reviewed regularly. The patient's weight was measured on day 0, week 3, week 6, week 9 and week 12. **Results:** Hypovitaminosis D is a potential causative factor for LBA in addition to the other known factors. The results obtained with nano syrup formulation were significantly better compared to other formulations. **Conclusion:** Vitamin D can play an important role in pathogenesis and treatment of LBA. Nano formulations developed with aqueous technology have shown enhanced stability, water solubility, bioavailability, significantly better improvement in vitamin D level and functional outcome in low back pain.

KEYWORDS : Hypovitaminosis D; Mechanical low back ache;

INTRODUCTION:

Chronic low back ache (LBA) is one of the commonest and expensive ailments of youngsters with ambiguous pathophysiology leading to a significant loss of productivity. Because of many modifiable and non-modifiable risk factors, the dynamic stabilisers of the spine are prone to acute and chronic strain.[1–3] 90% of them improve after six to eight weeks of treatment with 60% recurrence in two years to follow.

While studies established that vitamin D (vit.D) is a confirmed anabolic hormone for the entire musculoskeletal system, hypovitaminosis D is still an overly underestimated, avoidable, and correctable etiological component for LBA.[4,5]

The study was taken up to compare the outcomes of several oral vitamin D formulations available in the market.

MATERIAL & METHOD:

This is a randomized, prospective, open label analytical study of a cohort of patients with Low back ache & hypovitaminosis D. Patients were sequentially randomized to one of the three treatment subgroups (Granule group, Nano Syrup group & Soft gel capsule group) named after the vitamin D formulation they received after establishment of clinical, radiological and biochemical eligibility.

Ethical committee approval and informed consent were taken before commencing the study. 140 subjects were screened. 119 subjects were eligible to participate and 87 have completed the study. Patients of both the genders between 18 and 50 years of age were included.

Pregnant and lactating women, patients on vitamin D supplements for the past three months, patients on drugs altering vitamin D metabolism, medical or surgical disorders affecting vitamin D metabolism, pre-existing co morbidities, neurological back ache, congenital or developmental malformations of spine & patients with history of trauma were excluded. Pain and functional disability were assessed with visual analogue scale (VAS) and Modified Oswestry low back pain disability questionnaire (MODQ) respectively. Treatment with analgesic (aceclofenac), muscle relaxant (thiocolchicoside) and antacid (ranitidine) were given to all the patients uniformly for five days.

Vitamin D analysis was done and Vitamin D < 30 ng/ml was considered as hypovitaminosis D, 20-29.9 ng/ml as insufficiency, <20 ng/ml as deficiency and 30-100 ng/ml as sufficiency. Pain beyond three months was considered as chronic.

Fit for study candidates were allotted to one of the treatment subgroups sequentially as per the randomization chart and vit.D supplementation of 60,000 IUs per dose for ten consecutive days (pulse-D therapy) was given in the form of granule (1 g sachet) or nano syrup using aqueous nano technology (5 ml bottle) or soft gel capsule.

Adverse drug reaction recording chart was provided to all patients and was reviewed regularly. Review analysis was done at three weeks to conclude the findings. Additional blood sample was collected from willing subjects after three months to study the decline of vitamin D level.

P value <0.05 taken as statistically significant. Paired student T test, Independent sample T test were used for comparisons of two groups and one/two way analysis of variance (ANOVA) was done for multiple comparisons. Nominal variable (VAS) was analysed by Chi-square test.

The prefix "Pre" implies variable before treatment and "Post" implies variable after treatment, suffix "D" implies vitamin D. The term improvement/Diff. in vitamin D implies "Post. D minus Pre. D".

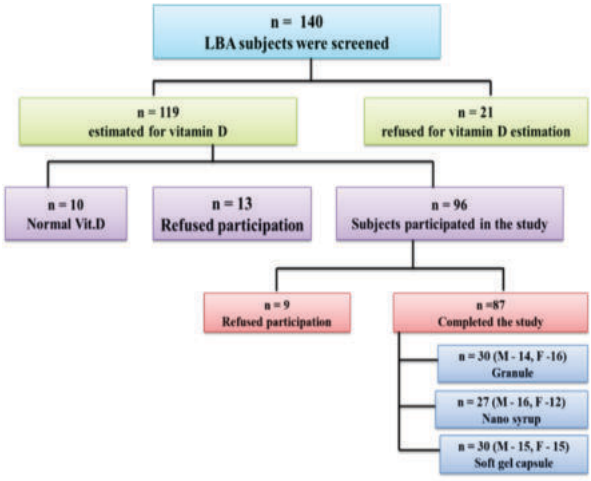

Figure 1: Showing the study design

RESULT:

Out of the 119 eligible subjects, 87 could complete the study (Fig. 1). Mean age of the total cohort was 31.32 ± 7.02 years and the mean BMI was 25.77 ± 3.18 kg/m^2. Highest increase of mean vit.D was noted in nano syrup group i.e. from 17.75 ± 7.46 ng/ml to 99.12 ± 24.64 ng/ml (Table 1). Significant difference in VAS was noted in all the three treatment subgroups and total cohort with adjunctive nano syrup therapy (Table 2). The difference in vit.D and MODQ was significant in each of the study groups after treatment (Table 3). Significant difference in vit.D was noted between the nano syrup group and the other two groups after treatment. There was no significant difference between the genders in pain (VAS) before and after treatment. Women had significantly lower vit.D before treatment and men had significantly better functional improvement after treatment. The difference in vit.D between deficiency vs. Insufficiency groups after treatment was not significant. Subjects living indoors had lower vit.D and subjects with chronic LBA had significantly better improvement with nano vit D syrup therapy. Majority of these subjects were in normal BMI category and the gender variation of BMI was insignificant. Analysis of the drug content in all the three formulations of vit.D was done in an independent accredited laboratory. 129.40, 118.10 and 149.05% of drug for granule, nano syrup and soft gel capsule respectively per unit was noted. There were no adverse effects attributable to nano syrup therapy. Eighteen subjects had Post.D > 100 ng/ml (Fig. 3). Only two of them consented for the estimation of serum calcium levels as none of them had any complaints of vit.D toxicity and both of them had normal serum calcium levels (9.6, 9.7 mg/dl respectively).

Table.1. Summary statistics of the study group (n= 87)

Variable	Total study cohort (n = 87)		Granule (Sub group n = 30)		Nano syrup (Sub group n = 27)		Soft gel capsule (Sub group n= 30)	
	RANGE	Mean ± SD	RANGE	Mean ± SD	RANGE	Mean ± SD	RANGE	Mean ± SD
Age (years)	18 - 50	31.32 ±7.02	20 – 48	29.45 ± 6.82	19 - 50	30.82 ± 7.19	20 - 49	36.56 ± 7.04
BMI (kg/m2)	16.93 - 38.26	25.77 ±3.18	17.1 - 36.31	27.16 ± 4.19	16.03 - 32.25	25.16 ± 4.28	16.53-31.72	24.58 ± 3.71
Pain (months)	0.2 – 60	11.65 ± 12.76	0.2 – 45	10.39 ± 11.44	0.25 - 59	9.24 ± 10.45	0.71 - 48	13.02 ± 14.04
Pre-MODQ%	12 – 100	45.73 ±16.05	15 – 72	39.21 ±14.02	25 - 100	54.09 17.83	20 - 67	40.46± 12.41
Post-MODQ%	0 – 55	14.12 ±11. 7	0 – 48	16.25 ± 12.14	0 - 30	13.24 ± 9. 38	0 - 53	18.28± 11.30
Diff. MODQ%	6 – 70	31.61± 15.87	8 – 46	22.96 11.43	12 - 72	40.85 ± 17. 26	6 - 56	22.18 ± 13. 53
Pre-Vit.D ng/ml	4.62 - 29.43	17.01 ±7.22	4.50 - 27.83	16.91 ± 6.44	5.40 - 27.47	17.75 ± 7.46	5.89-27.60	16.15 ± 6.21
Post-vit.D ng/ml	23 – 150	75.07 ± 26.9	26.68 – 150	69.73 ± 28. 11	30 - 147.30	99.12 ± 24.64	24 - 105	68.5 ± 16.27
Diff.in vit.D	14. 4-130.2	58.06 ± 27.58	14.7 - 131.49	52.81 ± 27.49	15.4 - 131	81.37 ± 26.32	14.7 - 129.43	52.35 ± 17. 30

BMI= Body Mass Index, Prefix Pre=Variable before treatment, Prefix Post=Variable after treatment measured at 3 weeks, MODQ=Modified Oswestry low back pain disability questionnaire (Index in %), Diff=Difference.

Table2: Showing the comparison of VAS score between the groups

Statistical data on VAS among different treatment subgroups					
Study group	Variable	Chi square	Contingency co- efficient	Df	p value
Total	Pre V AS vs Post V AS	198.17	0.802	54	<0.0001
Granule	Pre V AS vs Post V AS	126.94	0.879	99	= 0.02
Nano syrup	Pre V AS vs Post V AS	83.22	0.76	19	<0.0001
Soft gel capsule	Pre V AS vs Post	115.86	0.893	45	<0.0001

Prefix Pre = Variable before treatment, Prefix Post = Variable after treatment measured at 3 weeks, VAS= Visual analogue scale Significant increase in vit D levels and difference in pain measured by VAS before and after treatment after treatment in group treated with nano syrup compared to sub-groups treated with other oral formulations (Table 2).

Statistical data on vitamin D across different treatment subgroups before and after treatment.

Table 3: Comparison of the vitamin D across the groups before and after treatment.

Comparision	Independent Pre.D	sample T test Post.D
Nano syrup vs Soft gel capsule	t = - 0.57, Df = 44, p = 0.511	t = -5.12, Df = 44, p < 0.0001
Nano syrup vs Granule	t = -0.85, Df = 57, p = 0.421	t = - 4.01, Df = 57, p = 0.0003
Soft gel capsule vs Granule	t = 0.39, Df = 59, p = 0.844	t = 0.39, Df = 59. p = 0.725

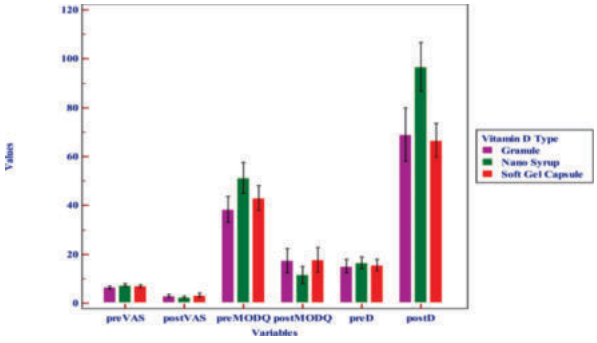

Fig. 2 Clustered multiple variable graph comparing VAS, MODQ and Vit. D levels before and after treatment among the three treatment subgroups.

DISCUSSION:

Vitamin D is essential for growth, development and maintenance of multiple organs in our body and its deficiency will profoundly affect the musculoskeletal system.[6,7] Hypovitaminosis D can be a potential causative factor for LBA in addition to the other known causes. Proper evaluation and adjunctive vit.D supplementation can effectively break the vicious cycle of low back ache with significant improvement in serum vit.D level, effective relief of pain and significant functional improvement without any adverse effects. Improvement in vit.D was not significantly related to its initial status and obese individuals have shown significantly lesser improvement.

In study by Faraj SA et al., In regions where vitamin D deficiency is common, it is a key contributor to persistent low back pain. Screening for vitamin D insufficiency and supplementation should be made mandatory in this situation. Serum 25-OH cholecalciferol measurement is sensitive and specific for detecting vitamin D insufficiency and hence assumed osteomalacia in individuals with persistent low back pain.[5]

In their respective investigations, Ghai B et al. found a high incidence of hypo.D (86%, 82%) in patients with cLBP with a mean age of 43.8, 44 years and a mean vit.D level of 18.4 ng/ml,12.8 ng/ml. After weekly treatment of 60,000 IUs of vit.D for eight weeks,[4,6] 66% achieved normal vit.D, with a mean vit.D of 36.07 ng/ml and substantial clinical improvement in VAS and MODQ at two, three, and six months.[6] Given the considerable improvement in pain and functional level following correction of hypo.D across all treatment categories, supplementary vitamin D supplementation can be regarded as a way of successful LBA therapy. This discovery is contemporary with and adds to the existing literature.[4–6,8] Vit.D has a proven role in the improvement of muscle strength, neuromuscular coordination, pain, sleep and mood modulation.

In present study the results shown with the nano syrup formulation were markedly better compared to the other formulations. Formulation based dosage adjustments assume significance in view of these results. Previously, the diverse outcomes of various formulations, doses, and dosage patterns of vitamin D utilized as an adjuvant for customized therapy of LBA had not been examined.

Nano engineered lipophilic molecule delivery methods have demonstrated improved stability, water solubility, and bioavailability.[9,10] significantly better increase in vit.D and functional outcome with nano syrup in this study demonstrates that the absorption, assimilation, and the potential outcome with nano formulation made with aqueous technology is comparably better for any given dose. As a result, dosage changes for a specific formulation must be examined in light of these findings.

In one trial, daily supplementation with 5500IU & 11000IU of vitamin D given for two weeks has shown peak rise of 64 and 88 ng/ml of vitamin D, respectively.[11] Similarly, after 8 weeks of 60,000 IUs of vitamin D therapy given weekly, 43.48% of the subjects have remained low D.[12] The primary barriers to successful therapy is low dosage daily & high dose weekly & monthly regimens were prolonged treatment time, lack of compliance, and poor improvement.[6,12–15]

CONCLUSION:

Vitamin D can play a significant role in pathogenesis and treatment of LBA. Nano formulations developed with aqueous technology have shown enhanced stability, water solubility, bioavailability, significantly better improvement in vitamin D level and functional outcome in low back pain.

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Conflict of interest: *Nil*

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