Original article:

Narrowband TL01 for the treatment of vitamin D deficiency in individuals of Fitzpatrick skin type IV & V.

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Abstract:

Introduction: There is widespread hypovitaminosis D in Indian population. Vitamin D is a naturally synthesized hormone in the skin. TL01 synthesize vitamin D naturally using ultraviolet radiation B. This has been used for lighter skin types (type I & II) but not for darker skin types (type IV & V).This study was under taken as a randomized controlled trial for university population. The sample was a convenient sample from the population comprising of adults from both genders.

Methodology :To check TL01, Philips - as a tool for vitamin D synthesis, in Indian skin type (Skin type IV & V), a total of 44 participants both males and females of 18-70 years of age, were randomly allocated to two groups and studied. Out of them 29 completed the study. One group was given intervention of , 3- 20W TL01 lamps whereas the other was not treated with it, and served as matched control.

Observations : TL01 was easy to administer. 34 % dropouts were seen. No adverse effect or any errythema was seen with a low dose regimen.

Result and Conclusion : Vitamin D level significantly increased in the intervention group as compared to control group (p=0.0032)*.Mean rise was of7.68ng/ml in the intervention group. No change in vitamin D was seen in control group. TL01 is seen as a tool for vitamin D synthesis (in skin type IV & V).

Key words:Vitamin D, TL01, UVR B, Skin type IV &V, TL01

Introduction:

Vitamin D is the earliest hormone, Synthesized naturally in human skin from the sunlight – as part of physiology, using UVR B [(1)]. Lack of natural sun exposure (<30% skin surface area, or less UVRB) can cause its deficiency, it was reported in medical history that during rickets epidemic –actinotherapy was used[(2)]. Presently, due to modern lifestyle there are many reports of the considerable prevalence (>80%) of hypovitaminosis D[(3)], leading to significant mortality [(4)]. More over darker skin type variants IV & V commonly found in Indian locations are reported to be prone for this due to high melanin content[(5)], thus making actinotherapy a therapeutic tool, to be considered again.

Etymologically “Actinotherapy” is derived from Actin(o) meaning ray, ray shaped or radiation. UVR B part of solar radiation is used for the synthesis of Vitamin D. Technological advancements in lamps (narrowband TL01, Philips) , has made low dose and comparative high yield possible for this vis a vis to the previous broad band lamps. TL01 lamps have output spectrum specific[255-320] for serum vitamin D synthesis. The wavelength peak equivalent to 295-311 nm.The output peak is specified by the manufacturer. Philips inc.

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Aims &Objectives: Aim of this study was to check action therapy by TL-01 as a tool & specifically objective was the evaluation of — the effect of TL01 lamps (20 watt, 3 lamps, applied over ~33% of body surface area (BSA) i.e. over back, upper extremity dorsal surface and back of neck & head), for significant change in plasma vitamin D levels in studied participants.

Materials and Methods:

- **Trial design:** Single blinded randomized controlled trial.
- **Participants:** participants were from Guru Nanak Dev University employees and their family members**. Screening-**Screening was done as per the inclusion & exclusion criteria. Skin reaction to sunlight was checked. Skin sensitivity checking was done to check the skin reaction to the TL01 lamps. Screening to any physical damage to skin by local inspection of the treatment site was also done. Only Skin Type IV&Vwere included.
- **Interventions–**
- **UVR Dose details – Protocol-** The effective dose was given as irradiance at theskin surface. The treatment area was selected for safety of eyes, and to prevent tanning of face.It was - back, head and arms.Three 20 W [power consumption]TL01 florescent lamps of two feet length, were mounted on a wooden frame. Incident rays at 90 degree were applied at a distance of two feet or 60 cm [as per inverse square law it reduces the irradiance]to the back, arms and head ~ 33% BSA. The total out was very low. This body area was also not expected to be exposed to sunlight generally, thus it made it a useful site of application rather than the face. The irradiated area was most sensitive to the photobiological effect, but was not usually exposed to sunlight. TL01 are known to have a bioactive peak at 311 nm- {the physical irradiance and photobiological effect is highly dependent upon wavelength}. Which made total bioenergy availability very good in respect to total exposure as compared to the other sources for e.g. total physical irradiance dose was very low in this design as compared to other sources like - Waldmann lamp that is known to haves 24 to 40 TL01s of 6 feet length with a 100 watt [power consumption each].
- **25% progression of Dose by time**- As per the treatment protocol given for sub-errythemal dose for skin type V and IV, to achieve effectiveness of subsequent session the dose was increased by time - 25%. As there are adaptive changes due to UVR this progression was recommended in standard protocols - Low and Reed 2000[(7)]. It is as per the Bunsen - Roscoe reciprocity law.
- **Sample collection, storage**- Baseline values were obtained from the venous sample kept in EDTA & centrifuged to be kept in freezer for ELISA analysis. Next four sessions of actinotherapy using TL01 lamps were given to the back while the participants were in high sitting position, protective goggles were used for the therapist and the patient throughout the treatment session, and again the venous sample was taken in EDTA centrifuged, kept in freezer for ELISA analysis.

  Outcomes- Plasma Vitamin D **was the main outcome measure. It** is a mediator of multiple health outcomes.

  Sample Size —A pilot study was undertaken during winters to check whether the target population has vitamin D deficiency and the serum Vitamin D data was obtained for 20 volunteers. (Participants) [(6)]

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`Sample Size has been calculated by referring to the Pilot Study. The Probability of making type 1 Error i.e. Alpha was assumed to be 0.05 and the risk of type II error i.e. 1-beta was 0.80.Which assumed that the risk of a Type II error could be four times as great as the risk of Type I error. In calculation the difference of means was 10 as base line value was 20 and sufficiency reported is 30.The pooled SD is taken as 9.The obtained result is of sample size=14[each group] for RCT(parallel design - independent sample) with actual power=0.808``

To get to 14 each group sample size a total of 44 subjects were taken and there are total 15 drop outs leaving 29 who were randomly allocated to two groups (15 in intervention group and 14 as control).

Randomization - Randomization of the sample selected from the target population is done by random number table generated from internet.

Blinding – Participants were blinded to the grouping.

Statistical Methods - Descriptive statistics was used to summarize data. Inferential statistics was used to check the objectives using Independent and paired t test for vitamin D levels between and within the groups respectively. Nevertheless, Significance level (p value) was checked for them and interpreted.

Observation and Results:

Participant Flow – From various departments of Guru Nanak Dev University. Data was collected during months of winter Baseline

Table 1.1 descriptive baseline data for All Included and Randomized - (N=44 individuals)

SN	Variable	Mean ± SD
1	**AGE**	**42.16±13.22 years**
2	**M:F**	**29:15**
3	**VITD**	**18.37±8.17 ng/ml**
4	**BMI**	**25.42±3.57**

Numbers analyzed- A total of 29 participants completed the study and were analyzed.

Table 1.2 - Descriptive Statistics in between the two Groups of participants studied (N=29).

SN	Variables	Group 1 (15 participants)	Group 2 (14 participants)
1	Age	37.33±14.13 Yrs	46.28±10.53 Yrs
2	M:F Ratio	13:2	9:5
3	Vit D	18.54±6.98 ng/ml	17.96±8.32 ng/ml
4	BMI	24.81±3.28 kg/m2	26.05±4.37 kg/m2
5	SBP	129.9±10.81 mm of Hg	128.1±18.25 mm of Hg
6	DBP	83.87±6.65 mm of Hg	82.43±13.52 mm of Hg

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Control group baseline Vitamin D (17.96±8.32 ng/ml) was comparable (p=0.84) to experimental group's(18.54±6.98ng/ml). Post actinotherapy a significant (p=.003) change in experimental group was found with a mean difference of 8.64±7.18ng/ml after four sessions with TL01 in between the group analysis.For within the group analysis of pre, and post 25 (OH) D values, the t-test is statistically highly significant ($p < 0.0001$).

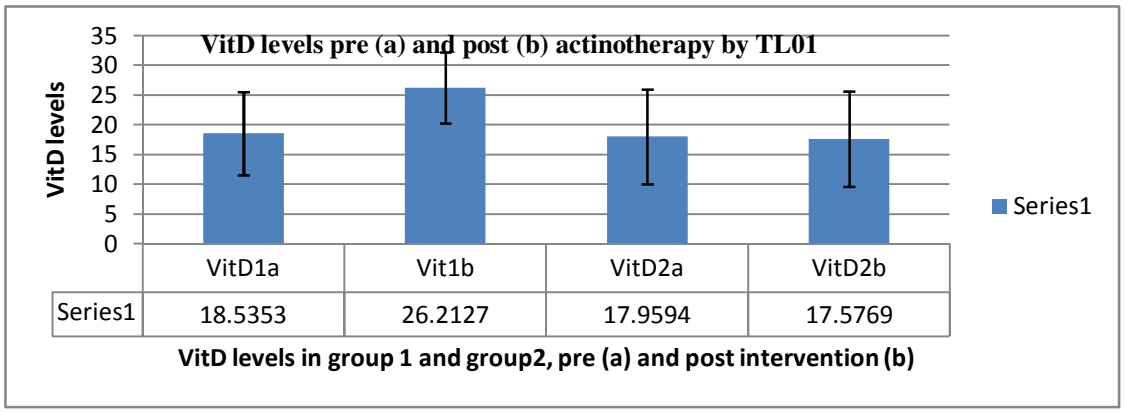

Figure 1.1 - Pre and post intervention of UVRB VitD levels in the two (intervention & control) groups.

A mean increment of 7.68 ng/ml has been seen in this study. The mean value of intervention group was within the deficiency range with mean of 18.5 ng/ml that rose to mean of 26.21 ng/ml after the four sessions of TL01 as seen in (Fig 1.1).

Discussion:

The target population was studied (in pilot study for it); as the vitamin D (18.06±9.06 ng/ml) level found was location specific & season specific, sample size calculation was done from pilot study.

Studies on very small sample (5 only) like **Chandra P** in 2007 have been reported,[8] where treatment of vitamin D deficiency in case of malabsorption syndrome was completed; **Bogh** *in* 2011[9] have studied four group with 15, 14, 12 & 14 participants in each group where they reported on effectiveness of a low dose regimen. Recently **Farrar et al.**in, 2013 [10] have reported a total sample of 60 with 10 participants in each dose group of south Asian individuals where increments in VitD are seen. In present study 15 & 14 participants have completed the study thus making it comparable to contemporary studies as far as participants in each group are considered improvements of a mean value of 7.68 ng/ml is observed in the present study in the intervention group with a sub-errythemal dose . Vitamin D assay are ELISA based and were done by using a German kit DLD. This had a coefficient of variation of 2.4 to 4.4 % for intra-assay variation.

Philips TL01was effective in increasing serum vitamin D levels using TL01 narrowband lamps when exposure was given to ~33 % of body surface area. This was achieved in four sessions of therapy. Increasing the dose by 25% of time in each session, thus [10 minutes, 12.5 minutes, 16 minutes & 20 minutes]. No adverse reaction was reported using three 20 Watt lamps as they kept the dose with the recommended levels.

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For most of the world population UVR- B is the primary source of vitamin D. Vitamin D is a potent mediator for various health factors. Bone and blood vessels just being two related target organs for them where the finds of arthrosclerosis were found to relate to bone density **(Hyder, 2009)**[11]. A plethora of diseases are associated with its deficiency and may improve with its sufficiency**(Grant, 2005)**[12].The geographical distribution and seasonal variation of sunlight where the ultraviolet index falls may lead to a variation in occurrence rates of such diseases, from summer to winter and from south to north **(Levis 2005, Maxwell 1994)**[13,14]. In present study the UV Index was of ~ 3 at given location (Amritsar) during winters.It is located at latitude of 31° 37' N andlongitude of 74° 55' E. 70% of the participants were deficient(<20ng/ml) and 24% had insufficient vitamin D (<30ng/ml) as seen in (Fig 1.2.)

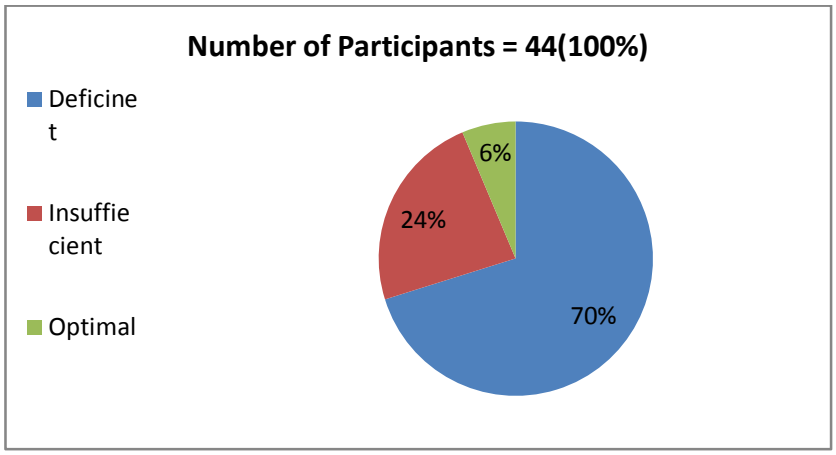

Figure 1.2 -VitD Levels in all 44 participants included in this present study.

Globally it has been identified that lack of vitamin D is associated with increased bone loss; giving vitamin D supplementation has been linked to improvement in health outcome **(Lips 2001)**[15].In a meta- analysis of 18 randomized controlled trials with a total of 57,311 participants it has been shown that regular and normative increase in vitamin D levels can decrease total mortality in general population **(Autier 2007)**[16]. The protocol used can achieve such improvements. India has been reported to have a large number of vitamin D deficiency mediated cases of osteoporosis and other diseases of the same origin have also been identified **(Malhotra , 2008)**[17]. *Thus this is useful for Indian skin types IV and V.*

The Photobiochemical conversion of 7 Dehydrocholestrol to Pro - Vitamin D 3 is mainly dose - rate dependent upon the photo-energy of UVR B. Thus there are numerous studies where in the location, season, and ozone level and even pollution is considered for the adequate production of VitD. The substrate 7DHC is not reported to be a limiting factor till 70 yrs it falls in 77 yr old as reported by **McLaughlin, 1985**[18] ; in present study maximum age is 68 yrs though the mean age being 42.16±13.22 years .Though few studies have reported total cholesterol as a factor determining the synthesis rate of vitamin D. The thinning of subcutaneous fat layer may produce changes from very young to very old, but this is not investigated in the present study. Gender differences are not reported though the melanin content which is usually lower in case of females may favor them for photo conversion but that is mainly skin type dependent. In Indian population mainly skin type V and IV are seen and they are any considered in the present study. Evolutionary and genetic factors may as well affect the synthesis rate though they were not the objective of this study. Specifically the effectiveness of TL 01 for Indian skin type is checked. There are reports that the Indian skin type IV &V takes 5-6 times longer for same photo production than the

western skin types - Type I & II; also the area irradiated is of significance as already exposed areas are photo–adapted and produce less of it. **Rhodes 2010**[19] , reported no association with age(p=0.94), sex, (p=0.79), BMI, (p=0.16) and significant association with base line / pretreatment 25(OH D) (p=0.0001). Base line vitamin D is a major determinant of synthesis rate. If baseline levels are as higher as toxic - UVR B converts the available Vitamin D to in active forms. Uninhibited exposureproduces a level of 60ng/ml[20]. Further in the present study use of UV index as a measure for the vitamin D production efficiency measure has been proposed.

Interpretation- Is by checking the vitamin D levels twice - To fulfill the objective as per the protocol for effectiveness of Actinotherapy as a Tool.

There are various guidelines for sunlight exposure, considering the beneficial effects of Serum Vitamin D over the skin cancer risk; flexibility is increasing in them **(Lucas , 2006 WHO bulletin)** [21].

Conclusion- Low dose regimen can produce incremental change 25 OHD over a period of 10-15 days with 4 sessions.The value was in deficiency range and it increased to insufficiency range but could not reach the required optimal range. Protocol is effective in increasing the plasma vitamin D levels.So , TL01 is a tool for vitamin D synthesis.

Limitations- In present study Multiple parameters[Ca, Parathormone, lipid levels, markers of bone formation] that are involved in vitamin D to bones and blood vessels are not checked that can establish a direct relationship confirming the implication on health factors.

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