Original Contributions

ROLE OF ORAL VITAMIN D3 ANALOGUES IN THE TREATMENT OF PSORIASIS

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Oral vitamin D_3 analogues 1 alpha hydroxy cholecalciferol and 1,25 dihydroxy cholecalciferol were compared with placebo in the treatment of psoriasis. Three groups of 15 patients each were given 1 α hydroxy cholecalciferol at 1 ug/day 1,25 dihydroxy cholecalciferol at 0.5 ug/d and multi vitamins other than Vit A and Vit D, respectively. Patients were followed up for 3-6 months. Assessment of severity and response was done by Psoriasis Area Severity Index (PASI). Both Vit D_3 analogues 1 α hydroxy vitamins D3 and 1,25 (OH)2 D_3 were found to be effective. Serum and urinary calcium remained within normal limits.

Key Words : Psoriasis, Vitamin D_3 Analogues

Introduction

Morimoto et al conducted a study which demonstrated the possible efficacy of biologically active metabolites of Vit D_3 for treatment of patients with psoriasis vulgaris and indicated that oral administration of 1 - α hydroxy vitamin D_3 and topical application of 1,25 dihydroxy vitamin D_3 (1, 25 - (OH) 2 - D3) are useful in the treatments.

With the role of vitamin D_3 and its analogues having been established, topical calcipotriol i.e. 1,25(OH) 2-D_3 has been extensively studied for treating different types of psoriasis.[1] However this form of therapy is very expensive and can cause local irritant reaction as compared to oral vitamin D_3 analogues. Systemic vitamin D_3 analogues have been studied because of the expected increase in serum calcium levels. No toxic alterations in serum calcium were noticed by Morimoto et al.[2] The present study was conducted to determine the efficacy of oral vitamin D_3 analogues in the treatment of psoriasis vulgaris.

Materials and Methods

Forty-five patients of biopsy proven psoriasis vulgaris were divided in to 3 groups of 15 each. Group A was given 1- α hydroxy cholecalciferol at 1 ug/d at bedtime. Group B was given 1,25 (OH) D_3 0.5 ug/d in two divided doses. Group C patients were given multivitamins other than vitamin A and vitamin D.

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Assessment of severity and response to treatment was done by Psoriasis Area Severity Index (PASI).[3] All patients were subjected to a battery of tests including haemogram, liver function test, renal function tests, serum calcium and 24 hour urinary calcium. The patients were instructed to take plenty of water and to consume a low calcium diet during therapy. The patients were followed up weekly for the first two weeks then fortnightly for 3-6 months or till complete remission, which ever was earlier.

Results

Group A included 11 male and 4 female patients aged 22 to 45 years (mean 29.7 $\pm$ 9.42 year). Group B included 10 male and 5 female patients with ages ranging from 22 to 68 years (mean 33.57 $\pm$ 13.73). Group C consisted of 9 male and 6 female patients with ages 20 to 45 years (mean 27.33 $\pm$ 5.62), (Table 1).

One patient each from group 1 α hydroxy cholecalciferol and group B had worsening of the disease during the study period and were shifted to methotrexate whereas six patients in the control group had worsening of the disease during the study period.

Mean PASI scores at the beginning of the study in group A, B and C were 6.81 + 3.92, 6.42 $\pm$ 1.84 and 6.43 $\pm$ 0.89 respectively (Table II).

PASI scores after treatment were 0.83 $\pm$ 0.96,

1.38 ± 1.43 and 4.79 ± 1.44 in groups A, B and C respectively. PASI percentage improvement was 87.54 ± 13.59, 76.89 ± 27.15 and 24.22 ± 19.90 in groups A B and C respectively.

Vit D_3 analogues were significantly more effective than placebo, however difference in efficacies of 1 α (OH) D_3 and 1,25 (OH)2 D_3 was statistically not significant. Mean serum calcium and 24 hour urinary calcium increased significantly but remained within normal limits. The initial improvement was noticed at approximately 4 weeks with oral vitamin D_3 analogues.

Table I. Assessment of various parameters in different groups.

Group	Before treatment			After Treatment			Improvement (%)
	PASI	Serum Ca. (mg/dl)	24 hr Urinary Ca.(G/day)	PASI	Serum Ca. (mg/dl)	24 hr urinary Ca. (G/day)	
1 OH Vit D3	681± 3.92	9.17± 0.42	0.15± 0.07	0.83± 0.96	9.66± 0.46	0.22+ 0,08	87.54± 13.59
Rocaltrol	6.42± 1.184	9.40± 0.43	0.13± 0.08	1.38± 1.43	9.72± 0.43	0.19± 0.07	76.89± 27.15
Placebo	6.43± 0.89	9.26± 0.18	0.14± 0.03	4.79± 1.44	9.19± 0.21	0.13± 0.03	24.22± 19.9

Discussion

Psoriasis is a common disorder of keratinization. It is characterized by chronic hyperproliferation, incomplete differentiation of epidermal keratinocytes, elongation and dilatation of capillaries in the papillary dermis and migration of activated neutrophils and lymphocytes into both epidermis and dermis.[4]

Two basic mechanisms are responsible for the action of Vitamin D_3 analogues-nuclear mechanism and transmembrane signalling. Nuclear mechanisms involve Vitamin D_3 receptor (VDR), which belongs to nuclear receptor superfamily. Possible mechanisms include (a) modulation of transcription of target genes (b) regulation of growth and differentiation possibly by proto-oncogene products (c) decreased target cell sensitivity to growth factors and (d) increased transcription of transforming growth factor B in epithelial cells[5] thus enhancing anti inflammatory and anti proliferative effect.

Transmembrane signalling is suggested by increased influx of calcium into the cell via a non-nuclear mechanism.The increased intracellular concentration of calcium results in differentitation of keratinocytes. Possible mechanisms are (a) Rapid hydrolysis of phosphatidyl inositol phosphate [6] (b). Translocation of protein kinase C from cytosolic to membrane position (c) increased activity of transglutaminase which is a calcium dependent enzyme responsible for cross linking the proteins of cornified envelope.

Vitamin D_3 also has an effect on cutaneous inflammation [7] by (a) inhibition of IL 1, IL 2, IL 6, (b) induction of IL 10, (c) decreased IL 8 binding and IL8 induced HL ADR expression (d) decreased activity of cytotoxic and natural killer cells, promotion of suppressor cells.

The present study found Vitamin D_3 analogues to be effective in the treatment of mild-moderate psoriasis. There was an increase in the serum and 24 hour urinary calcium levels but it remained within normal limits. Further studies should be undertaken on larger number of patients with longer follow up.

Table II. Severity of psoriasis and mean percentage improvement

Severity of Psoriasis	1 OH D3	Rocaltrol	Placebo
Mild (PASI) < 10)	85.7	75.9	24.2
Moderate (PASI 10 - 15)	93.9	89.3	
Severe (PASI) > 15)	94.6		

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