INDIAN J DERMATOL VENEREOL LEPROL 1986; 52 : 85-88

TREATMENT OF 25 CASES OF PSORIASIS WITH ORAL AROMATIC RETINOID (TIGASON)

M L Khatri and M Shafi

Twenty five cases of different types of psoriasis who were resistant to conventional therapy, were treated with oral aromatic retinoid (Tigason). We observed complete remission in 10, very good improvement in 9 and partial improvement in 4 patients, while 2 cases did not show any improvement. Mild to moderate side effects were noticed in 23 patients.

Key words : Retinoids, Psoriasis, Treatment.

Oral retinoids have been tried in the treatment of psoriasis since 1971.[1] Recently, (etretinate), an aromatic retinoid, has been successfully used for the treatment of this disease.[2-6] This compound is a derivative of vitamin A acid (retinoic acid). Its composition is All-trans-9-(4-methoxylphenyl)-3, 7-dimethyl-2, 4,6,8,-non atetraenoate (etretinate). In the present study, experience with the systemic use of etretinate (Tigason) in selected cases of psoriasis is recorded and discussed.

Materials and Methods

Twenty five cases of different types of psoriasis (psoriasis vulgaris 20, including 2 with arthropathy, erythrodermic psoriasis 3, and palmo-plantar psoriasis 2), who were resistant to conventional therapy were selected from January, 1983 to July, 1985 for this study. Majority of these patients were admitted to the dermatology wards for initial assessment. Investigations included complete blood analysis, ESR, bilirubin, SGPT, alkaline phosphatase, total lipids, triglycerides, cholesterol, serum proteins, electrolytes, urea and sugar, and urine analysis performed in each case before starting the therapy with Tigason. These investigations were repeated every fortnight during the course of initial therapy, and monthly while on maintenance dose.

The age of the selected patients varied from 22 to 80 years except one female patient aged 14 years. Sixteen were males and 9 females. The female patients of child-bearing age were on contraception, either oral pill or IUCD, and they were instructed to observe it strictly till one year after stopping Tigason.

The initial dose of Tigason was 0.75 mg/kg/day. This dose was later reduced to 0.5 mg/kg/day after a considerable improvement or if the patient developed moderate side effects. After clearance of the lesions, this dose was further reduced to 0.25/kg/day as maintenance therapy. The duration of treatment varied from 4 weeks to 20 weeks, while the maximum duration of maintenance therapy was one year. No local treatment was given except emulsifying ointment.

The extent of the disease was recorded approximately as percentage of the body surface. Grading of the severity of the disease was made on the basis of erythema, scaling and infiltration of the lesions, which were recorded as 0 to 4.

Results

The initial improvement was noticed as decrease in scaling and erythema, followed by gradual decrease in infiltration. In 50% of the cases, erythematous patches without scaling and infiltration persisted for a long time. The

From the Department of Dermatology, Central Hospital and Faculty of Medicine, Al-Fateh Universiy, Tripoli, Libya (SPLAJ).

Address correspondence to : Dr. M. L. Khatri, P. O. Box-13457, Al-Fatch University, Tripoli, Libya.

initial improvement was noticed after one week in 15 patients, two weeks in 7 patients and three weeks in 1 patient. Complete clearance of the lesions was noticed in 10 patients and partial clearance with persistence of a few thick lesions was noticed in 9 patients. Four patients showed only 25 to 50% improvement, while 2 patients did not show any improvement even after 6 weeks treatment. The time taken for complete clearance was 4 weeks in 2 patients, 8 weeks in 2, 12 weeks in 4, 16 weeks in 1, and 20 weeks in 1 patient. The three patients with erythrodermic psoriasis showed only mild to moderate improvement after 2-4 weeks as far as erythema and scaling is concerned. One of these with associated arthropathy had significant improvement of joint pain. However, in these 3 cases, the treatment was withdrawn 4 to 8 weeks later because of severe side effects. The other two patients with psoriatic arthropathy also showed considerable relief of pain and reduction of swelling of joints within 4 weeks time.

Mild to moderate side effects were observed in 23 out of 25 cases (Table I). All patients except 2, developed mild to moderate dryness of lips. Out of 3 patients of erythrodermic psoriasis, 2 showed increase in erythema after 4 weeks, while one patient showed increase in erythema and developed hyperpyrexia after 8 weeks.

Abnormal laboratory parameters were observed in 6 patients after 2-4 months of therapy. Three patients showed a moderate rise in SGPT. One of them also had an increase in the level of alkaline phosphatase. Four patients had elevation of lipids—one with rise in total lipids (1120 mg%) and triglycerides (260 mg%), another with increase in total lipids (1320 mg%) and cholesterol (375 mg%), the third with elevation of total lipids (1126 mg%), while the fourth patient showed rise in triglycerides (205 mg%) only. Among these, the first patient also had increased SGPT.

Table I. Side effects of etretinate.

	Number of patients having side effects after the on-set of treatment		
	2 weeks	4 weeks	8 weeks
1. Dryness of lips	7	23	18
2. Dryness of mouth	—	8	4
3. Dryness of nose	—	5	2
4. Epistaxis	—	—	1
5. Cheilitis	—	—	6
6. Thinning of the healthy skin	—	—	4
7. Desquamation of the healthy skin	—	6	2
8. loss of hair	—	—	2
9. Itching	—	—	3
10. Stomach pain	1	2	—
11. Sweating	—	4	—
12. Increase in erythema	—	3	1
13. Hyperthermia	—	—	1
14. Laboratory parameters : Elevation of			
1. SGPT	—	—	3
2. Alkaline phosphatase	—	—	1
3. Total lipids	—	—	3
4. Triglycerides	—	—	2
5. Serum cholesterol	—	—	1

Eight patients were followed upto 1 year, while 12 were seen regularly upto 6 months. Five patients did not turn up for folow up after 4 to 8 weeks initial treatment. In 5 patients the treatment was stopped after 4 to 8 weeks because of severe side effects. Out of 10 patients with complete remission, relapse was observed in 3, two patients showed recurrence of lesions 3 months after stopping Tigason and one developed a few lesions even after 2 weeks. Rest of the 7 patients did not show any recurrence upto 6 months. The patient who showed recurrence after 2 weeks was again given the maintenance dose of 25 mg/day, and she was free from lesions for the last 6 months on this dose without any side effect.

Comments

The mechanism by which retinoids regulate the growth and differentiation of the human epithelial tissue is still unknown. In the past,

naturally occurring retinoids have been tried topically[7,8] and orally[9] with minimal improvement in psoriasis. Later, 13-cis-retinoic acid was tried, which was less effective than aromatic retinoid.[10,11] Lately, Lassus[6] has tried aromatic retinoid in a double-blind cross-over fashion and concluded that most of the patients showed complete remission. In our experience, complete remission was observed in only 40% of the patients.

Moderate to excellent results were observed in cases with psoriasis vulgaris, while the patients of erythrodermic psoriasis did not show satisfactory response except the one with arthropathy who felt considerable relief in joint pain. Other studies have suggested a more promising response with oral Tigason in erythrodermic psoriasis.[12,13] In psoriatic arthropathy, the results obtained by various authors are not consistent. Orfanos and Georz[14] reported negative results while Brackertz and Muller,[15] Rosenthal[16] and Stollenwerk et al[17] have observed satisfactory improvement. We have also noticed considerable relief in joint pain in all the three cases of psoriatic arthropathy.

Mild to moderate side effects were noticed in majority of the cases in this study. This observation has been consistently recorded in the literature.[3-6,13,18] A larger percentage of our cases had elevation in the liver enzymes as compared to previous studies.[6,18] Four of our cases showed increase in the lipid profile, while the earlier studies did not record such changes. However, Peck[19] has observed comparable elevation of triglycerides in 10% of his cases and Mohammed and Kamal[18] have noticed triglyceridemia in one out of 36 patients. All the side effects were reversible either on reduction of the dose or after stopping the treatment.

References

1. Schumacher A and Stuttgen G : Vitamin A Saure bei Hyperkeratosen, epithelialen Tumoren und Akne, Deutsche Medizinische Wochenschrift, 1971; 96 : 1547.
2. Ott F and Bollag W : Behandlung der Psoriasis mit einem oral wirksamen neuen Vitamin A Saure Derivat, Schweizerische Medizinische Wochenschrift, 1975; 105 : 439-441.
3. Orfanos CE and Runne U : Systemic use of new retinoid with and without local diathranol treatment in generalized psoriasis, Brit J Dermatol, 1976; 95 : 101-103.
4. Dahl B, Mollenbach K and Reymann F : Treatment of psoriasis with a new retinoic acid derivative Ro 10-9359, Dermatologica, 1977; 154 : 261-267.
5. Fredrikson T and Petterson V : Severe psoriasis —Oral therapy with a new retinoid, Dermatologica, 1978; 157 : 238-244.
6. Lassus A : Systemic treatment of psoriasis with an oral retinoic acid derivative (Ro-10-9359), Brit J Dermatol, 1980; 102 : 195-202.
7. Frost P and Weinstein GD : Topical administration of vitamin A acid for ichthyosiform dermatoses and psoriasis, JAMA, 1969; 207 : 1863-1868.
8. Kaidbey KH, Petrozzi JW and Kligman AM : Treatment of psoriasis with topically applied tretinoin and steroid ointment, Arch Dermatol, 1975; 111 : 1001-1003.
9. Burgoon CF Jr, Graham JH, Urbach F et al : Effects of vitamin A on epithelial cells of skin : The use of vitamin A in the treatment of diseases characterized by abnormal keratinization, Arch Dermatol, 1963; 87 : 63-80.
10. Peck GL and Yoder FW : Treatment of lamellar ichthyosis and other keratinizing dermatoses with an oral synthetic retinoid, Lancet, 1976; 11 : 1172-1174.
11. Orfanos CE, Pullman H, Runne V et al : Behandlung der Psoriasis mit Vitamin A, vitamin A saure und oralen Retinoiden, Hautarzt, 1979; 30 : 124-233.
12. Guilhou JJ, Malbos S and Meynadier J : Traitment oral des psoriasis graves par un nouveau retinoide aromatique (Ro-10-9359), Ann Dermatol Venereol, 1978; 105 : 813-818.
13. Konstantinovic SV : Clinical aspects and side effects of therapy by oral administration of retinoids in various skin diseases, in: Retinoids, Editor Orfanos CC et al : Springer, Berlin, 1981; pp 479-481.
14. Orfanos CE and Goerz G : Orale Psoriasis Therapis mit einem neuen aromatischen Retinoid, Dtsch Med Wschr, 1978; 103 : 195-199.

15. Brackertz D and Muller W : Die Beeinflussung der Arthropathia psoriatica und der chronischen poly arthritis durch ein oral wirksames aromatisches Retinoid, Verch Dtsch Ges Inn Med, 1979; 85 : 1343-1346.
16. Rosenthal M : Retinoid in der Behandlung von Psoriasis-Arthritis, Schweiz Med Wschr, 1979; 109 : 1912-1914.
17. Stolenwerk R, Fischer Hoinkes H, Komenda K et al : First results in the treatment of psoriatic arthritis with a new vitamin A acid derivative Retinoid (Ro 10-9359) Paper, International Symposium on the treatment of Psoriasis-Arthritis, Tel Aviv, 1979; 18-25.11.
18. Mohammed Mohy El-Din Selim and Kamal Abdel Hafez : The oral aromatic retinoid Ro 10-9359 (Tigason) in the treatment of selected dermatoses, Arab J Med, 1983; 1-9 : 27-37.
19. Peck GL : (Unpublished data, September, 1981) as quoted by Elias PM and Williams ML : Retinoids, Cancer and the Skin, Arch Dermatol, 1981; 117 : 160-180.