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ORIGINAL CONTRIBUTIONS

EVALUATION OF FIVE DIFFERENT REGIMES FOR THE TREATMENT OF VITILIGO

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Response of vitiligo patients to five different regimes was evaluated taking only those patients who had either static or progressively increasing lesions. Selection of the regime depended upon the clinical characteristics of the disease. Each regime was tried for at least 4 months and if a patient did not improve with one regime, he was shifted to another regime. A patient was considered to have improved, if the lesions started repigmenting, or the previously progressive lesions stopped increasing further. Regime I consisted of 150 mg levamisole orally on two consecutive days per week; given to 13 cases, it resulted in improvement in 7 (53.8%). Regime II consisted of levamisole in the same dose combined with once a day topical massage with 0.1% fluocinolone acetonide acetate cream; it led to improvement in 27 (81.8%) of the 33 cases. Regime III consisted of 2 mg betamethasone orally on alternate days combined with levamisole and topical fluocinolone; given to 32 cases, it was successful in 28 (87.5%). A combination of 2 mg betamethasone orally alternating with 20 mg 8-methoxypsoralen and sun exposure (regime IV) caused improvement in 17 (85%) of the 20 cases. An oral mini-pulse consisting of 5 mg betamethasone orally twice a week combined with 50 mg cyclophosphamide daily orally (regime V) was successful in 20 (90.9%) of the 22 cases. the remaining two cases showed improvement when the dose of betamethasone was increased from 5 mg to 7.5 mg twice a week. Thus ultimately each one of the 91 patients responded to one or the other regime. The side effects were minimal and insignificant.

The degree of improvement at the time of analysis was 100% in 23.3% cases, 50-100% in 44.2% cases and less than 50% in 32.5%, after 4-14 months of treatment. It is felt that the results may be better after a longer follow-up, although all patients are not expected to get complete repigmentation.

Key words : Vitiligo, Treatment, Levamisole, Corticosteroids, Psoralens, Oral mini-pulse.

Currently, the major therapeutic measures for vitiligo include psoralens and corticosteroids, topically and/or systemically, either singly or in various combinations. The success rates have been about 50% with topical corticosteroids[1,2] 25-75% with oral corticosteroids[3,4] 50-70% with oral PUVA therapy[5,6] and about 93% with a combination of oral PUVA and oral corticosteroids.[7] Since vitiligo has strong social implications, search for more effective regimes continues. We are reporting our results with 5 different regimes used for treating vitiligo patients.

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Materials and Methods

Patients having progressive or static lesions of vitiligo were treated with one of the five regimes mentioned below. The selection of the regime for a patient depended upon the extent of the disease and the rapidity of spread of the lesions. Patients having only a few lesions which were either static or increased very slow-

ly, were treated with levamisole 150 mg (50-100 mg for children) orally daily on two consecutive days per week (Regime I), or combined with a thorough topical massage with 0.1% fluocinolone acetonide acetate cream once daily (Regime II). Patients having more extensive lesions which were static or slowly increasing in size and/or number were treated with levamisole and topical fluocinolone as in regime II combined with 2 mg betamethasone or 20 mg prednisolone as a single oral dose after breakfast on alternate days (Regime III), or oral corticosteroids as in regime III combined with 8-methoxypsoralen (8-MOP) 20 mg (10 mg for children) orally on the alternate days when corticosteroids were not given, followed 2-4 hours after the oral dose, by exposure to sunlight for 15-30 minutes (Regime IV). Patients who had very extensive disease which was spreading very fast were treated with an oral mini-pulse consisting of 5 mg betamethasone orally as a single oral dose after breakfast on two consecutive days a week, combined with 50 mg cyclophosphamide orally daily (Regime V). Patients were re-examined every two months. Each regime was tried for at least 4 months and if the response to one regime was not adequate, the patient was changed to another suitable regime. Photographic records of representative lesions were maintained for objective evaluation of the response to treatment.

Periodic evaluation of weight, blood pressure, blood sugar, urinalysis and the other side effects of topical and systemic corticosteroids, psoralens and cyclophosphamide was undertaken. In addition, all patients were examined for the presence of halo nevi, and if present, the pigmented portion was either excised or electrocoagulated.

Results

Out of 130 patients included in the study, 19 patients did not come for follow up and in 20 patients the follow-up period was less than 4 months. These 39 patients have been excluded from the analysis. Of the remaining 91 patients, 40 were males and 51 females. Their ages ranged from 3 to 60 years. The duration of the disease varied from 10 days to 20 years at the time of presentation and most of them had already received treatment elsewhere before coming to us.

The response to various regimes used by us is shown in table I. If a patient having increasing lesions showed repigmentation, he was considered to have improved, and in case only further spread of the disease was arrested without any repigmentation, he was con-

Table I. Response of vitiligo patients to the different therapeutic regimes.

Regime	Status of disease before treatment	Number of patients with the lesions				Percentage response
		Total	Improved	Static	Increased	
I	Increasing	9	4	1	4	53.8%
	Static	4	2	2	—	
II	Increasing	15	11	3	1	81.8%
	Static	18	13	5	—	
III	Increasing	20	16	3	1	87.5%
	Static	12	9	2	1	
IV	Increasing	13	12	—	1	85%
	Static	7	5	1	1	
V	Increasing	22	14	6	2	90.9%
	Static	—	—	—	—	

Cases of failures with one regime were treated with another regime.

Table II. The extent of recovery of pigmentation with different regimes.

Regime	Number of patients with (the time in months) taken for recovery			
	Total	Complete (100%)	50-100%	Less than 50%
I	6	2 (8-10)	2 (4-8)	2 (4-6)
II	24	6 (6-12)	14 (6-8)	4 (4)
III	25	7 (8-14)	10 (8-10)	8 (6-8)
IV	17	5 (8)	8 (10-12)	4 (6)
V	14	—	4 (6-8)	10 (4)
		20 (23.3%)	38 (44.2%)	28 (32.5%)

sidered to have become static. Both these groups indicated response to the treatment. In case, the lesions continued to increase, the treatment was considered to be a failure. In the case of patients with static lesions, repigmentation of the patches indicated improvement while status quo (no change) or increase in the size or number of lesions indicated failure. Based on these criteria, the response rates were 53.8% (7 out of 13) with regime I, 81.8% (27 out of 33) with regime II, 87.5% (28 out of 32) with regime III, 85% (17 out of 20) with regime IV and 90.9% (20 out of 22) with regime V.

Three of the 6 patients who failed to respond to regime I, improved with regime III, while the other 3 improved with regime IV. Similarly, of the 6 failures with regime II, 3 improved with regime III and the remaining 3 with regime V. Of the 4 failures with regime III, 2 improved with regime IV and the remaining 2 with regime V, whereas of the 3 failures with regime IV, 2 improved with regime III and the other with regime V. There were 2 patients who had not responded to regime V, but increasing the dose of betamethasone to 7.5 mg led to improvement. Ultimately thus, all the 91 patients responded to one or the other regime.

Of the 86 patients who started repigmentation, the extent of repigmentation and the time taken to achieve that degree of pigmentation are shown in table II. The side effects noticed with different regimes are given in table III. Most of the side effects were seen with regime III only, but none of these necessitated discontinuation of therapy. Halo nevi were seen in 7 patients and 6 of these patients were less than 14-year-old.

Comments

There is a general belief that vitiligo is an untreatable disease, whereas each one of our patients responded to one or the other regime. Although such a universally good response may not be reproducible in a larger series, it is important to realise that a very high percentage of patients can be benefited by selecting an appropriate regime, giving it an adequate

Table III. Side effects noticed with different regimes.

Side effects	Number of patients having the side effect with regime				
	I	II	III	IV	V
Nausea	2	3	—	6	—
Vomiting	—	—	—	3	—
Weight gain	—	—	7	4	1
Cushingoid facies	—	—	3	1	—
Hypertrichosis	—	—	2	1	—
Acneform eruption	—	—	3	1	—
Raised blood sugar	—	—	2	—	—
Hypertension	—	—	2	1	—
Transient diffuse alopecia	—	—	—	—	4
Menstrual irregularities	—	—	1	1	1

trial, and modifying the regime if the response is not adequate.

Psoralens are known since long. We did not use topical psoralens, because the incidence of blistering is high. Corticosteroids have been used only recently and the response is at least comparable to psoralens, if not better. If the auto-immune theory for vitiligo is correct, then treatment with corticosteroids can be claimed to be based on the aetiopathogenetic mechanisms. Topical corticosteroids have however, been known to produce hypopigmentation in hyperpigmented or normal skin, as also repigmentation in depigmented skin. The mechanism of this duel action is not known.

To the best of our knowledge, levamisole has not been used previously for vitiligo. We have been using levamisole for a variety of conditions including vitiligo and the results are not uniform in all patients. Still for patients having only a few lesions, a trial with levamisole and/or topical corticosteroids for 4 months or so is worth. A reasonable response in approximately 50% of the patients is not bad.

Response to oral corticosteroids is better, but the chief disadvantage is their side effects on prolonged usage. A combination with oral psoralens on alternate days has therefore been considered the most suitable regime, especially when the disease is extensive.[6] However, it must be borne in mind that in some vitiligo patients, the lesions spread very fast every time they take psoralens.[6] Such patients must not be given psoralens.

The oral mini-pulse (Regime V) is an arbitrary derivation of the dexamethasone-cyclophosphamide pulse therapy used for pemphigus patients.[8] Generalised hyperpigmentation is a known side effect of cyclophosphamide.[9] Such a regime is known to produce almost no side effects, and as can be seen from our results the response is the best.

The extent of improvement in a patient is likely to depend upon several factors. Mere arrest of a fast-spreading disease can be quite satisfying to several patients, though repigmentation of the lesions is definitely better. Since the response to any of the regimes is quite slow, there may be no indication of improvement in the first 2 months. An adequate duration of trial with each regime is therefore mandatory. Once repigmentation starts, the regime should be continued till complete pigmentation or maximum pigmentation is achieved. This is likely to take even 2-3 years, depending upon the extent of involvement, and this may explain the sizeable proportion of our patients in whom the response was not complete. It is however, understood, that every patient especially those with extensive disease may not achieve 100% repigmentation, and therefore, if further repigmentation stops at any stage, even after a trial with more intensive regimes, surgical procedures may be considered according to the well-known criteria.

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