

Pharmacovigilance of conventional therapy in 250 cases of vitiligo at tertiary specialty care

Abstract

Aims and Objectives: Adverse drug reaction (ADR) may infringe upon compliance, which compromises therapy outcomes in chronic diseases. Our study focused on pharmacovigilance in stigmatizing disease vitiligo, concern with improving disease management incorporating current medical knowledge. **Materials and Methods:** Therapies in 250 vitiligo cases were scrutinized over period of six months, examining consistency to consensus approach and profiling of the adverse effects. **Results:** Adverse drug effects occurred in fifth of localized and third of generalized vitiligo patients. Adherence to consensus line of therapy resulted significantly in less adverse effect incidence, and steroid overtreatment was major determinant of risk. **Conclusion:** Consistency of treatment to consensus approach based on disease extent is prudent to reduce adverse drug effects in vitiligo. Increased vigilance, due psycho-social address, and incorporation of safe and efficacious new immunomodulator drugs is emphasized for consideration toward improved current vitiligo management.

Key words: Adverse drug reactions, guideline, pharmacovigilance, vitiligo

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INTRODUCTION

Vitiligo, the stigmatizing skin disease, has prevalence ranging from 0.5% in the east to 4% in extreme west regions in India.^[1,2] Modern therapeutic options include topical immunomodulators, photochemotherapy, excimer laser, and surgery. No single therapy is regarded as the most effective since success varies with type and location vitiligo. Objective of present treatments is to regain pigment in vitiliginous areas rather than controlling the disease process. Treatment is essentially long-term, hence issue of safety remains important consideration. Corticosteroids, both topical and systemic, have been used in vitiligo for over half a century. There is continuing concerns of steroidal efficacy as well as the adverse effects. Corticosteroids and photochemotherapy using combination of psoralen and sun radiation or UV-A exposure are the most widely prescribed conventional therapies for vitiligo. Newer immunomodulators, protective antioxidants, nutrient supplement etc., are proposed as useful in vitiligo treatment. Preferences for time-honored conventional economical therapy has hindered due exploration of new therapeutic options in vitiligo. Nevertheless, adverse effects of steroids and photochemotherapy remain persistent concerns. The efficacy versus adverse effect issues call for focused re-assessment to utilization of alternative rational therapy options. Present study in 250 vitiligo patients explores adverse effect profile of conventional therapy. Scope for alternative options toward better outcomes may be also appraised.

MATERIALS AND METHODS

Two hundred and fifty cases seeking medical help purely for vitiligo and no other complaints were included in the study. Some of these cases were discovered with defective thyroid function and were referred for appropriate endocrinological care but not excluded from study. Diagnosis and therapeutic prescription were at discretion of the clinical specialist. Patients were explained of the study and were assured of keeping their identity secret. Free informed consent was thus obtained for their participation. Detailed personal and disease history was elicited, and prescribed therapies were recorded. Total lesion area as percent of body surface was assessed in order to gauge the prescribed therapy as consistent or otherwise to consensus therapeutic guidelines.^[3,4] This is explicit as described in Table 1.

Patients reporting fresh or those already under management were included. They were followed

over six month period involving monthly visit for review. At each visit, questions were asked to ascertain uninterrupted treatment and any troubling adverse effects proactively. Examination to detect cutaneous adverse effect was next performed. Patients were segregated by the prescribed treatment regimens and conformity of the same to consensus guidelines. Predictable and other adverse effects with the regimens were recorded. Rates of adverse reactions noted to occur in patients stratified by age, sex, duration, and concurrent thyroid disorder were compared and analyzed using Fisher's exact statistic.

RESULTS

The incidence of adverse effects attributable to treatment exhibited increase with increasing disease extent and intensity of therapy from one fifth in localized to one third in extensive vitiligo patients [Table 2].

Psoralen photochemotherapy employed in spread out lesions was particularly associated with ocular photosensitivity as well as systemic malaise of headache, nausea, and vomiting. Skin burns resulted also in one tenth of cases. Milder consequences like inflammation, pruritus, and hyperpigmentation occurred nearly to same frequency [Table 3].

Steroid monotherapy in regimen 1 also had skin complaints as major adverse consequence including pruritus and skin inflammation as well as atrophy. Incidence of skin atrophy increased in sequential regimens in combination with photochemotherapy. Steroid did associate also with systemic complaints of headache, nausea, and skin hyperpigmentation in some patients [Table 3].

Extent-wise prescription of therapy as per consensus rules very significantly prevented the incidence of adverse effects overall. Adverse effects also occurred significantly less frequently in younger patients. There was no significant difference in rate of adverse effects among sexes or in regard to early or late stages of disease. Though thyroid dysfunction was found only in 12% of cases, there was significant reduction in adverse effects associated with vitiligo treatment [Table 4].

DISCUSSION

Adverse effects play important role in poor compliance to therapy. Reported high non-compliance rates in vitiligo may be due to such adverse effects.^[5] Ocular problems, headache, nausea, and vomiting are recognized adverse effects of oral steroids and PUVA therapy.^[6,7] These occurred most frequently in regimen 3, whereas the frequencies are less in regimen 2. Skin atrophy was more frequent in regimen 3 followed by regimen 2, and may be due to added strong topical corticosteroid. Steroids cause biochemical changes in skin lipids, disturbing water homeostasis.^[8] The least adverse reactions in regimen 1 may be due to use of mild potency topical corticosteroid. Frequent hyperpigmentation in regimen 3 followed by regimen 2 may be due to exaggerated reaction to sun light. Drug in vitiligo patients are singularly the major determinants of adverse effects risk.

Prescribed treatment was examined for conformity with the referred guidelines stated in method section.^[3,4] Digression of guideline for

Table 1: Therapeutic guidelines for different treatment regimens

Regimen	Number of cases	Drug used (alone or in combination)	Consensus or guideline
Regimen 1	60	Topical fluticasone propionate 0.05%	Adequate for under 3% BSA affliction
Regimen 2	99	Topical fluticasone propionate 0.05% clobetasol propionate 0.05% in combination with oral methoxsalene (0.6 mg/kg, E.O.D.) with sun light exposure	For lesions exceeding 3% and up to <10% BSA but not aggressively progressive
Regimen 3	91	Oral methoxsalene (0.6 mg/kg, E.O.D.) with sun light exposure+topical clobetasol propionate 0.05% with or without topical mometasone furoate 0.01% + oral prednisolone (0.5 mg/kg as pulse therapy)+ antacids and antioxidant 1 capsule per day (containing lycopene 3 mg)	Progressive lesions afflicting more than 3% BSA or any lesion exceeding 10% BSA

Table 2: Occurrence rate of any adverse effects under different treatment regimens

Regimens	Total number of patients	Patients affected with any ADR	Percent incidence
Regimen 1	60	12	20
Regimen 2	99	26	26.26
Regimen 3	91	30	32.96

ADR = Adverse drug reaction

Table 3: Percent-frequencies of specific adverse effects as per therapeutic regimens

Adverse effects	Drug regimens			
	Regimen 1 n=60	Regimen 2 n=99	Regimen 3 n=91	All combined n=250
Hyperpigmentation	3.33	8.08	12.09	8.4
Pruritus	8.33	9.09	6.59	8
Sun sensitivity and sun burn	5	10.10	13.19	10
Skin eruptions and inflammation	1.67	7.07	8.79	6.4
Skin atrophy	5	11.11	12.09	10
Ocular irritation	1.67	20.20	26.37	17.2
Headache, nausea, and vomiting	5	18.18	20.88	16

regimen 1 represents overtreatment while that for regimen 2 and regimen 3 drugs is undertreatment. Greater depigmentation area increases anxiety in patient, and overtreatment decision by clinical may be compelled. Such decisions significantly caused increase in risk of adverse effects. The evidence is prohibitive to digression from standard therapeutic guideline based on disease extent. Patients under 16 years significantly suffer less adverse effects, this aspect requires in-depth exploration.

Table 4: Percent incidence of adverse effects with regard to probable determinants

Probable determinants	n	% incidence of adverse effects	Fisher's exact test P value
Treatment decision			
As per guidelines	167	12.57	<0.0001
Not as per guidelines	83	56.63	
Age			
Up to 16 years	80	17.5	<0.0121
>16 years	170	31.76	
Sex			
Males	112	22.32	NS
Females	138	31.16	
Disease duration			
Up to 5 years	129	25.58	NS
>5 years	121	28.93	
Thyroid disorder			
Present	30	20.91	<0.0001
Not present	220	73.33	

NS = Not significant

Few patients who reported thyroid disorder had significantly less rate of adverse effects. But, such cases were few, and acquired parallel care of endocrinologists.

Vitiligo is a chronic disease provoking concerns over major adverse effect of drugs. Immunopathologic understanding has led to new options, tacrolimus and pimecrolimus.^[9] These agents were not prescribed despite reported impressive success in vitiligo therapy. Local large scale studies with these therapies in diverse people may be necessary to convince traditional dermatologists. Short course of such drugs in combination with conventional therapies and evaluation of benefit/risk ratios may be reasonable way of their incorporation in routine management.

Possibly adverse effects may be less if innocuous adjunct therapies, such as pseudocatalase and ginkgo biloba extract, are included where feasible. Placental extract melagenina may also seem safe as adjunct and deserves evaluation.

In the present scenario, there is preference solely for conventional agents. Similar was noted in respect of psoriasis therapy (Gupta *et al.* 2012).^[10] Observations of the study suggest need for vigilance and regular monitoring of conventional treatment to detect unwanted effects and risks. Uncertainties of therapeutic response may be reduced by addressing social and psychological stress and by minimizing adverse effects. Consequent improvement of therapeutic compliance would definitely add to quality clinical management of vitiligo.

REFERENCES

1. Kent G, Al'Abadie M. Psychologic effects of vitiligo: A critical incident analysis. *J Am Acad Dermatol* 1996;35:895-8.
2. Ongenaes K, Beelaert L, Van GN, Naeyaert JM. Psychosocial effects of vitiligo. *J Eur Acad Dermatol Venereol* 2006;20:1-8.
3. Taieb A, Picardo M. Clinical practice. Vitiligo. *N Engl J Med* 2009;360:160-9.
4. Gawkrödger DJ, Ormerod AD, Shaw L, Mauri-Sole I, Whitton ME, Watts MJ, *et al.* Therapy Guidelines and Audit Subcommittee, British Association of Dermatologists; Clinical standards department, Royal college of physicians of London; Cochrane Skin Group; Vitiligo Society. Guideline for the diagnosis and management of vitiligo. *Br J Dermatol* 2008;159:1051-76.
5. Al-Aboosi MM, Ajam ZA. Oral photochemotherapy in vitiligo: Follow-up, patient compliance. *Int J Dermatol* 1995;34:206-8.
6. Tegner E. Oral 8-methoxypsoralen photochemotherapy of psoriasis. *Acta Derm Venereol* 1983;107:107-10.
7. Bourkes RJ, Balen ATM, Bruynzeel DP. A retrospective study of ocular findings in patients treated with PUVA. *Dot Ophthalmol* 1985;59:11-9.
8. Patel T, Bhutani T, Busse KL, Koo J. Evaluating the efficacy and safety of calcipotriene/betamethasone ointment occluded with a hydrogel patch: A 6-week bilaterally controlled, investigator-blinded trial. *Cutis* 2011;88:149-54.
9. Hossani-Madani AR, Halder RM. Topical treatment and combination approaches for vitiligo: New insights, new developments. *G Ital Dermatol Venereol* 2010;145:57-78.
10. Gupta AK, Pandey SS, Pandey BL. Pharmacovigilance in 150 cases of plaque psoriasis and a case for conventional therapy. *Asian journal of pharmaceutical and clinical research. Asian J Pharm Clin Res* 2012;5:87-9.

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