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Original Article

Effect of chemical exposure in induction and evolution of vitiligo: Correlation between duration of exposure and disease, site of exposure and onset, and impact upon avoidance

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ABSTRACT

Background: The exogenous oxidants can trigger and lead to progression and chronicity in idiopathic vitiligo similar to chemical leucoderma and contact vitiligo.

Aims: The basic objectives of this study were to study chemical exposure history in vitiligo patients and to correlate this with induction or progression of lesions.

Methods: This prospective observational study with intervention in the form of avoidance of exposure was conducted at MGM Medical College, Bihar at eastern India during the period of September 2010 to April 2012. Detailed record of demographic and clinical features was noted with specific chemical exposure especially duration of exposure, site of exposure, and outcome of the disease upon avoidance of chemicals.

Results: The proportion of cases coming to the OPD with vitiligo was 1.03% ($n = 241$) among total 23,410 outpatients department's dermatological patients. History of household chemical exposure and industrial (occupational) chemical exposure was found in 94.6% ($n = 228$) and 0.4% ($n = 1$) patients, respectively. The duration of disease and duration of chemical exposure had no correlation ($r = +0.1756$). Regarding avoidance of chemical exposure on the progression of vitiligo, the difference between fully compliant versus noncompliant was statistically significant ($p < 0.05$) but between partial compliant versus noncompliant was not significant ($p > 0.05$). Correlation of site of chemical exposure with site of onset of disease was found in 64.9% ($n = 148$) patients.

Conclusions: Chemical triggering factors play very significant role in induction and progression of vitiligo.

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1. Introduction

Vitiligo has a multifactorial, multistep etiology, always characterized by an increase of external or internal phenol/catechol concentrations and reactive oxygen species.¹ Vitiligo is believed to be the net outplay of several endogenous and exogenous factors in a relatively susceptible individual.² Several triggering factors have been elicited in the pathogenesis of vitiligo although exact precipitating causes are still speculative.^{3,4}

Some forms of vitiligo vulgaris are in fact chemical leucoderma caused by unidentified melanocytotoxic chemicals in the environment.⁵ Some persons with 'idiopathic vitiligo' may actually have an environmentally or occupationally induced leucoderma.^{6–8} Some cases of idiopathic vitiligo may be due to unsuspected inhalation or ingestion of chemicals that produce contact leucoderma.⁹ Chemical factors such as food contaminants/additives/preservatives and cosmetic products could aggravate vitiligo because they produce oxidative stress in the skin.¹⁰ Incidence of vitiligo was found to be higher in villagers living near dyeing, printing and carpet industries.¹¹

In some chemical leucoderma patients who, despite the omission of all contributory toxic chemicals for more than one year, still develop vitiliginous patches in different parts of their body. These cases were termed as 'chemical vitiligo' to represent the vitiliginous process, which was switched on initially by the chemicals and continued even after stopping use of the chemicals.¹²

Depigmentation in chemical leucoderma and contact vitiligo occurs from loss of melanocytes in the epidermis. The depigmentation spreads beyond the areas of contact, probably via an immune-mediated mechanism.¹³

Chemical leucoderma, a disease of industrial origin, has subsequently also been seen to be induced by certain domestic consumer products.¹⁴ The reported contributory chemicals in household objects are lip stick, mehendi (herbal hair color), amulet string color, eye liner, lip liner,¹² deodorant, detergent, cleanser, perfume, perfumed oil, herbal oil, insecticide, pesticides, rubber sandal, black socks/shoe,¹³ hair dye,¹⁵ alta,¹⁶ adhesive bindi,¹⁷ wrist watch leather belt,¹⁸ tooth paste (gel, colored),¹⁹ rubber condom.²⁰

2. Materials and methods

The study was conducted at the department of Dermatology, Venereology and Leprology, M.G.M. Medical College & L.S.K. Hospital, Kishanganj, Bihar at eastern India. The study was done during the period extending from the month of September 2010 to April 2012. Inclusion criteria of the patient would be all morphological variants of vitiligo pre-treated or untreated. There was no selection bias in inclusion of cases. The number of investigator was one thus avoiding inter-observer variation/bias. Exclusion criteria are (a) post-inflammatory leucoderma, (b) post-burn leucoderma and (c) congenital hypomelanotic or depigmentary disorders. The reason for attending the OPD was cosmetic and social stigma associated with the disease. A patient was included once only but

followed up to know the impact of avoidance of chemical exposure. This was ensured by giving specific registration number to each vitiligo patient and maintaining detailed record of demographic and clinical features in 'Case Record Proforma' with clinical relevant photographs. The study was prospective observational with intervention in the form of avoidance of exposure. The study was done after getting proper institute ethical committee's approval. Each patient or parent/guardian (in case of minor) was explained about the nature of the study in his/her own language, and official informed consent form was signed by every one of them prior to the study. In case of minor, consent form was signed by parent/guardian.

2.1. Chemical triggering factors¹²

Detailed history of specific chemical exposure, which has been reported as contributory agents of chemical leucoderma especially duration of exposure, site of exposure, and outcome of the disease upon avoidance of chemicals were meticulously noted. Histories of industrial chemicals as well as household chemicals were taken into account. Meticulous history taking/ noting and examination were done to corroborate the chemical exposure (in household objects) and development of chemical leucoderma. The criteria used to assess the stability were stable (no fresh lesion, no change in shape and size of the existing lesion), partial unstable (no fresh lesion but change in shape and size of the existing lesion) and totally unstable (appearance of fresh lesion, change in shape and size of the existing lesion). The criteria for compliance were fully (complete avoidance of industrial chemicals and/or predisposing household chemicals), partial (occasional exposure of industrial chemicals and/or predisposing household chemicals), none (no avoidance of industrial chemicals and/or predisposing household chemicals).

Statistical analysis has covered correlation with site of onset and site of exposure of contributory chemicals, correlation of duration of chemical exposure with duration of disease to detect correlation coefficient (*r* value) and finding the effect of avoidance of chemical on the progress of the disease (student *t*-test to detect *p* value).

3. Results

The proportion of cases coming to the OPD with vitiligo was 1.03% (*n* = 241) among total 23,410 outpatients department's dermatological patients. Mean age of the patients was 25.43 ± 16.97, male:female ratio being 1:1.31 and baseline characteristics of patients are shown in Table 1. Reason for attending the OPD was cosmetic (*n* = 140, 58%) and psychosocial (*n* = 101, 42%). The decade distribution and month of recruitment are depicted in Figs. 1 and 2 respectively. Confetti macules were present in 26.1% (*n* = 63) cases. Presence of pruritus and leucomelanoderma was seen in 5.8% (*n* = 14) and 0.4% (*n* = 1) respectively.

History of household chemical exposure was noted in 94.6% (*n* = 228) patients (Table 2). History of industrial (occupational) chemical exposure was noted in 0.4% (*n* = 1) patient. The commonest offending chemical was colored toothpaste (57.3%, *n* = 138) (Fig. 3) and least common being deodorant,

Table 1 – Baseline characteristics of patients.

Occupation	Gender (n = 241)	
	Male (n = 104) 43%	Female (n = 137) 57%
Student	30 (28.9%)	62 (45.2%)
House wife	0	49 (35.8%)
Labor	24 (23.0%)	1 (0.8%)
Farmer	24 (23.0%)	0
Not working	6 (5.8%)	18 (13.1%)
Business	13 (12.5%)	1 (0.8%)
Service	7 (6.8%)	6 (4.3%)

rubber condom, wrist watch leather strap (each 0.42%, n = 1) (Fig. 4). The duration of disease and duration of chemical exposure showed no correlation (r value = +0.1756) (Fig. 5).

Comparing two data (fully compliance versus non-compliance) by Student t -test ($p < 0.05$) is statistically significant, whereas comparing two data (partial compliance

Fig. 1 – Decade distribution of total number of patients. **Fig. 2 – Month of recruitment.****Table 2 – Reported contributory chemicals in household objects.**

Household objects	Contributory chemical	%	n
Deodorant	para-Tertiary butyl phenol	0.42	1
Detergent/cleanser	para-Tertiary butyl phenol	8.3	20
Hair dye	p-Phenylenediamine	13.3	32
Mehendi (herbal hair color)	p-Phenylenediamine	34.5	83
Alta	Azo dye	11.2	27
Perfume	para-Tertiary butyl phenol	2.5	6
Lip stick	Azo dye	10	24
Adhesive bindi	para-Tertiary butyl phenol	18.7	45
Tooth paste (gel, colored)	Cinnamic aldehyde	57.3	138
Eye liner	Azo dye	5.4	13
Insecticide	para-Tertiary butyl phenol	11.6	28
Pesticides	para-Tertiary butyl phenol	9.5	23
Rubber sandal	Monobenzyl ether of hydroquinone	40.7	98
Black socks/shoe	p-Phenylenediamine	1.7	4
Rubber condom	Mercaptobenzothiazole	0.42	1
Amulet string color	Azo dye	32.8	79
Lip liner	Azo dye	0.42	1
Perfumed oil/herbal oil	Phenolic catecholic derivative	29.5	71
Wrist watch leather belt	Azo dye	0.42	1

Fig. 3 – Vitiligo on lip: from colored toothpaste.

Fig. 4 – Vitiligo on wrist: due to wrist watch leather strap.

Fig. 5 – Graph showing correlation between duration of disease and duration of chemical exposure.

versus non-compliance) using Student t-test ($p > 0.05$) is statistically not significant.

Correlation of site of chemical exposure with site of onset of disease was found in 64.9% ($n = 148$) patients.

4. Discussion

Among the contributory chemicals, our study showed similar pattern like Ghosh and Mukhopadhyay's study¹² of preponderance of household chemicals over industrial chemicals as causative factors. However our study differs with the above study¹² regarding the pattern of contributory chemicals including the commonest and the least common causative factors probably due to the reason of our one being rural based study having different social, economic and cultural background as compared to the urban setup of the other study.

Duration of disease had no correlation with the duration of chemical exposure in our study. Thus, understanding the mechanism(s) by which 4-TBP (tertiary butyl phenol) causes melanocyte death may elucidate the pathology underlying contact vitiligo in specific and idiopathic vitiligo in general.²¹

Complete avoidance of exposure to offending chemicals has definite impact on the progression of the disease process. Full exposure or even partial exposure can ultimately trigger the dermatosis. Thus, our study is in tune with the recent observation by Glassman²² that exogenous oxidants induce chemical leucoderma and contact vitiligo and shared mechanisms might elucidate trigger factors and reasons for progression and chronicity in idiopathic vitiligo.

As par Gellin⁸ and Fisher,⁹ some persons with “idiopathic vitiligo” may actually be an environmentally or occupationally induced leucoderma, and as par Cummings and Nordlund,⁵ chemical leucoderma is caused by unidentified melanocytotoxic chemicals in environment.

Progression of chemical exposure occurred in 4.8% ($n = 11$) of existing vitiligo patients and vitiligo appeared in remote areas in 46.5% ($n = 106$) of cases. This can be supported by similar study,¹² whereas in chemical leucoderma, even withdrawing toxic chemicals for a year, newer patches appear in remote areas, termed as 'chemical vitiligo'.

Study limitations: (i) our study was cross-sectional, hospital out-patients-based study, (ii) the sample size was not vast, (iii) patch test with the chemicals could not be done due to ethical and medico-legal reasons as well as lack of standard protocol for patch testing method in chemical leucoderma, (iv) our study was a pilot and open one; in future we would like to execute a case-control study, and (v) chemical analysis was not feasible due to lack of facility.

What's already known about this topic is that exogenous oxidants may have some role in progression and chronicity of some form of idiopathic vitiligo. Vitiligo might have some chemical triggering factors in certain cases. What does this study add is vitiligo has definite contributory factors from chemical exposure in good number of patients. Idiopathic vitiligo in many cases by proper history taking and clinical pattern analysis has been identified as chemical leucoderma. Complete avoiding has definite impact by controlling the progression of the disease.

Conflicts of interest

The authors have none to declare.

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