Academic Sciences Asian Journal of Pharmaceutical and Clinical Research

Vol 5, Suppl 2, 2012 ISSN - 0974-2441

Research Article

PHARMACOVIGILANCE IN 150 CASES OF PLAQUE PSORIASIS AND A CASE FOR CONVENTIONAL THERAPY

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Received:17 January 2012, Revised and Accepted: 10 April 2012

ABSTRACT

Psoriasis is commonest chronic skin disease afflicting 1-2% population and increasingly associating diabetic epidemic. The disfiguring stress, compromise of quality of life and uncertain response to therapy add risks of therapy getting distorted. Conventional medications remain popular with most physicians for treatment despite emergence of attractive biological therapies.

Present study put vigil on the adverse consequences occurring in routine management of plaque psoriasis cases over three month uninterrupted treatment, excluding cases exhibiting noncompliance or dropouts. One fourth of all cases suffered one or more adverse effects stated in the report. Most adverse effects were explainable as known toxic effects of drugs or consequences of disease.

The impact of therapeutic prescription in conformity with or in breach of standard guidelines, patient specific factors of age and sex, personal habits and diabetic co-morbidity were also assessed to comprehend scope for prevention, early detection or management of adverse effects.

The literature is referred on available biological therapies as possible options and lacunae of evidence to their adoption are discussed. In balance, conventional drug therapy will continue to be mainstay of psoriasis therapy for forseable long period and quality care is suggested to best focus on minimizing their adverse effects.

Keywords: Adverse effect, Pharmacovigilance, Psoriasis

INTRODUCTION

Detection assessment and understanding of adverse drug events towards prevention has become indispensable perspective of modern drug therapy. This essentially guides appropriate use of drugs and interpretation of safety information by health care providers. The knowledge of risks associated with observed therapeutic benefits in specific patient population facilitates therapeutic choices to suit individual patient requirements. Prompt recognition of adverse effect will help efficient management and offer indications on epidemiologic associations. Study of adverse effects employes prospective case control, cohort or retrospective database analyses. Scope for generalizing the observations requires study in large population. However, even limited samples can reflect relative risk of available therapeutic options to avoid common adverse reactions. Population in which drug is tested necessarily differs from those in which the therapy is employed, making initial information available on adverse effects insufficient. Distinct perspectives are also desirable for the elderly, the women or people of diverse socioeconomic strata. Psoriasis is major and commonest chronic skin disease requiring prolonged therapy. This is overlaid by unsatisfactory therapeutic response, poor compliance and risks of nagging as well as serious adverse effects. Vast majority of patients have limited resources. Conventional drugs only are prescribed at our centre and perhaps many other[1]. Modern biological therapy is claimed of superior benefit-risk ratio[2].

Attempt has been made to profile adverse effects of conventional therapies employed in cases of plaque psoriasis over uninterrupted three month period. Bearing of adherence to therapeutic guidelines as well as patient's age, sex characteristics is also assessed. The outcomes are evaluated in reference to reported adverse event of biological therapies in psoriasis to envision present pragmatic course to quality care.

MATERIALS AND METHODS

Study covers data on 150 cases of psoriasis excluding 42 cases who were found irregularly complaint to therapy or failed to report for review. Cases seeking medical help purely for psoriasis and not having any other complaint were included in the study. Some of the cases were discovered with abnormal blood sugar and were also referred for care of endocrinologist. Such cases were however not excluded from consideration. After diagnosis and prescription of therapy by clinical specialist, patients were incorporated into the study seeking prior informed consent with assurance of not revealing identity at any stage. Detailed personal and disease history was elicited and particular prescribed therapies were recorded. Examination of total lesion area as percent of body surface was made in order to judge the prescribed therapy for consistency with or otherwise the current therapeutic guidelines[3]. Following table briefly describes drugs employed in present study and there use as per standard therapeutic guidelines for psoriasis.

Regimen	No. of Cases	Drug Used (in combination)
Regimen 1	50	Who received topical salicylic acid 3% in combination with coal tar 6% once daily. Suitable for mild disease extent under 5% BSA
Regimen 2	52	Who received Regimen 1 in combination with topical corticosteroids (strong; clobetasol propionate 0.05% or halobetasol propionate 0.05%. and weak; betamethasone dipropionate 0.01% or mometasone furoate 0.01%) 3 week twice daily followed 1 week rest and so on. Suitable for moderate disease extent above 5% but under 10% BSA
Regimen 3	48	Who received Regimen 2 in combination with systemic methotrexate (5 to 15 mg once in week). Suitable for more extensive disease

Patients reporting fresh or those already under management were included. They were followed over three month period involving monthly visit for review. At each visit questions were asked to ascertain uninterrupted treatment. Patients were segregated in accordance to prescribed treatment regimens and specific questions were asked to scrutinize complaints suggesting adverse drug effects. Confirmatory examinations for physical sign was taken up. General profile and rates of various adverse reactions as per predictable adverse effect profile of employed drug was made. Combined rates of adverse reactions for each treatment regimen were prepared. Rates of adverse reactions noted to occur in patients stratified by

age, sex, personal habits and concurrent diabetes were compared and analyzed using Fisher's exact statistic.

RESULTS

Incidence of adverse effects under various adapted treatment regimens is presented under Table 1. Which ranges between 1/4th to around 1/3rd cases of psoriasis.

Table 1: Occurrence rate of any adverse effects under different treatment regimens

Regimens	Total number of patients	Patients affected with any ADR	Percent incidence
Regimen 1	50	12	24
Regimen 2	52	18	34.6
Regimen 3	48	16	33.3

Table 2 describes the kind of adverse effects and their frequencies. Local irritation occurred frequently under regimen 1, while stria and skin thinning as well as burning sensations under regimen 2. Rash occurred more frequently in regimen 1, while photosensitivity in both regimen 1 and 2. Gastric upsets did occur even in regimen 1 but most frequently in regimen 3 employing methotrexate. Folliculitis did not occur in cases treated with regimen 3. Nausea, vertigo, abnormal liver function test and abnormal blood cell count occurred remarkably with higher frequency under treatment regimen 3 employing methotrexate.

Table 2: Percent-frequencies of specific adverse effects as per therapeutic regimens

Adverse effects	Drug regimens			
	Regimen 1 n=50	Regimen 2 n=52	Regimen 3 n=48	All combined n=150
Local irritation	16	13.46	6.25	12
Stria or skin thinning	---	13.46	10.42	8
Burning sensation	2	19.23	12.5	11.33
Rash	16	11.54	6.25	11.33
Photosensitivity	12	13.46	6.25	10.67
Folliculitis	4	3.85	---	2.67
Nausea	---	7.69	10.42	6
Gastric disturbance	8	5.77	22.92	14
Vertigo	---	9.62	12.5	7.33
Abnormal liver function test	---	---	18.75	6
Abnormal blood cell counts	---	---	22.92	7.33

Table 3 analyses differential rates of adverse effects in patients stratified by distinct variables which may influence the same. It is seen that treatment decision in conformity with standard guidelines yielded very significantly lower incidence of adverse effects as compared to that in cases not treated as per guidelines (undertreated or overtreated). Patients above age of 40 years also suffered very significantly higher incidence of adverse effects. There were no sex dependent differences in rates of adverse effects.

Although only 27 of 150 reported cases had abnormal blood sugar control, such cases suffered significantly higher rates of adverse effects to antipsoriatic medications. Smoking or tobacco habit did not significantly increase adverse effect rate. While history of alcohol surprisingly, associated with significantly lower adverse effects rates. However, the number of patients giving history of alcohol use is much lower.

DISCUSSION

Observed frequencies of adverse effects to conventionally employed pharmacotherapy in psoriasis is pretty high. Adverse effects play important role in poor compliance to therapy. The same may be important bases for generally reported high rates of non compliance in psoriasis[4]. Local irritation, rash and photosensitivity are recognized adverse effects of coal tar and salicylate topical therapy, which occurred most frequently in regimen 1. Reduction of their frequencies in regimen 2 and 3 may have been due to concomitant use of corticosteroids. Particularly high burning sensation in regimen 2 may be attributed to added steroids which also did not abet photosensitivity. The adverse effects of steroids in causing stria or skin thinning also shows the most in regimen 2. Biochemical changes in skin lipids caused by steroids disturbing water homeostasis is well known[5]. The same may be at least partly responsible for such adverse effects. The decline of many such adverse reactions in regimen 3 may be due to added anti-inflammatory and cellular effects of methotrexate. Gastric disturbances occured less frequently under regimen 1 and 2 that employ topical therapies, stress may also cause such effects which is recognized in patients of psoriasis[6]. Gastric disturbances and vertigo as well as liver function test and blood cell count disorders occurred predominantly with methotrexate usage as expected. Such occurrences showed up in nearly 1/5th of recipients which is cause of major concern.

Table 3: 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	93	16.13	<0.0001
As per guidelines	57	54.39	
Not as per guidelines			
Age			
Up to 40 years	106	19.81	<0.0001
>40 years	44	56.82	
Sex			
Males	98	30.61	NS
Females	52	30.77	
Alcohol habit			
Present	47	19.15	<0.028
Not present	103	35.92	
Smoking or tobacco habit	79	36.62	NS
Present	71	25.32	
Not present			
Diabetes			
Present	27	62.96	<0.0001
Not present	123	23.58	

Drug related risk of conventional psoriasis therapies are widely recognized and particular monitoring investigations are adapted as routine. There is much less evidence to predict other determinants for increased adverse effects risk. Prescribed treatment was examined for conformity with the referred guidelines[3] stated in method section. Digression of guideline for regimen 1 was undertreatment while all instances of digression for regimen 2 and regimen 3 drugs were those of overtreatment. Frequently, greater apparent sufferings of the patient may tempt overtreatment decision by clinician. It is observed that such decisions would significantly increase risk of adverse effects. The evidence is therefore prohibitive of digression from standard therapeutic guideline and suggests keen measurement of disease extent. Patients above 40 years significantly suffer more adverse effects of therapy. This aspect requires in depth exploration. The relative neglect of self care, nutrition, disease duration and social stress all may be important besides physiological changes, with aging.

Although a minority of patients were diabetic, they suffered significantly higher rates of adverse effects. As such cases were referred simultaneously for care of endocrinologists, role of interaction with antidiabetic drugs, can form logical basis for increased adverse effects, partly. Diabetes however poses state of subtle inflammation and cytokine disturbance.

Smoking and tobacco use are well known to aggravate inflammatory skin disease like psoriasis[7,8], but had only insignificant minor effect on incidence of adverse reactions. Alcohol habit in the patients was mostly in form of occasional consumption. Such cases however had significant reduction in adverse effects rate to psoriasis medication. Alcohol is generally damaging to nutritional and physiological homeostasis[9]. Mild occasional alcohol usage may differ in this regard. As such, beer use reducing peptic ulcer risk as well as cardiovascular risk is reported[10,11].

The entirely conventional therapies used at specialty clinic of tertiary care centre is it self a pointer to their effectiveness and better cost benefit for use at large. Severe psoriasis is a chronic disease and concerns remain on major adverse effect of drugs. Modern immunopathologic understanding has led to availability of biological agents. Large clinical trials have established their efficacies. There simultaneous use in other immunologic disorders, like rheumatoid arthritis and chrons disease, besides in psoriasis suggests quite low incidence and mild severity of the adverse effects. The nature of adverse effects are however threatening, like activation of latent infection specially tuberculosis, due to dysfunction and decline of T cell. Some cases of allergic demyelination, thrombocytopenia and haemolytic anaemia, excess weight gain and heart failure and even development of lymphoma have been documented. Obviously, high costs and dread of such adverse effects mandating sophisticated monitoring have precluded their adoption in a developing country like India. Their clinical use must rise only through large scale application, especially in diverse populations. There are no concrete understanding on their short course in combination with conventional therapies to improve benefit/risk ratios. Even limited observation in European countries indicate adverse effects among 5 -20% of patients prescribed these drugs. Peculiar problem of emergence of fresh lesions at unaffected sites or conversion to guttate or pustular form of psoriasis by biological therapies is also seen occasionally[1,12]. The scenario leads to preference for conventional agents. Observations of the study thus, dictate need for improved vigilance and regular monitoring of conventional treatment to detect early organ damage and other risks. Uncertainties of therapeutic response may be difficult to overcome but due psychological address to stress of stigmatizing disease and avoidance of nagging adverse effects can improve therapeutic compliance and better the scenario of clinical management of psoriasis.

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