Original paper

Triggering drug use in patients with psoriasis: an investigative report from Turkey

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Abstract

Introduction: The patients clinically diagnosed with psoriasis were investigated for drug use that may trigger psoriasis.

Aim: To minimize the triggering drug use and help the medical treatment of psoriasis patients.

Material and methods: The study involved 289 psoriatic patients who attended our clinic in 2010–2012 and were asked to bring their drug lists of the last year, which they obtained from the pharmacy’s record system. They were advised not to use the drugs that may trigger psoriasis. Data analyses were performed using SPSS program version 19.0.

Results: A total of 289 patients were included in the study. Two hundred and twenty-one patients were using non-steroidal anti-inflammatory drugs; 133 patients were using anti-reflux drugs; 35 patients were using antidiabetic drugs; 31 patients were using calcium-channel blockers and 24 patients were using β-blockers. In our study group, there was no significantly difference between median PASI scores of the patients using a triggering drug and those of who are not using a triggering drug. However, there was a positive low correlation between PASI rates and numbers of drugs used ($r = 0.180, p = 0.013$).

Conclusions: Many other factors may trigger psoriasis, therefore the effect of stopping or minimizing the drug use on disease remission is not known. Because of the high triggering drug use rate, it is important to enlighten psoriasis patients about triggering drugs.

Key words: psoriasis, triggering drugs, β-blockers, non-steroidal anti-inflammatory drugs.

Introduction

Adverse drug reactions and medication errors are major public health problems. Therefore, taking a careful medical history, superintend redundant medicine consumption and drug interaction are a critical step for prevention. There are many reports in the literature regarding the initiating, triggering and aggravated roles of drugs in psoriasis etiopathogenesis [1–8]. However, it is difficult to prove in an antidepressant receiving patient whether the stress or drug is a triggering factor. It is the same in the antibiotic use; it is unclear whether the infection or the used antibiotic is the triggering factor.

However, effects of some drugs are more prominent. Triggering effects of drugs are indicative in some drugs, like non-steroidal anti-inflammatory drugs (NSAIDs) and/or β-blockers, because lesions are recovered after the drug discontinuation. The most commonly reported drugs, which trigger psoriasis in the literature, are NSAIDs, β-blockers, synthetic antimalarial agents, lithium and tetracycline [2, 4–6].

Even biological agents, which have been reported as successful in psoriasis treatment in recent years, have also been reported that they may cause exacerbations of psoriasis lesions [8–11].

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Although there are no definite data related to psoriasis incidence, general consensus of dermatologists has been that the number of psoriasis cases has increased in the recent years. Socioeconomic conditions and uncontrolled drug use, which is a new trend, and also easy contamination of diseases in crowded environments are believed to be triggering factors in the psoriasis increase. It has been accepted that drugs act like exogenous antigens and they sometimes play triggering roles in psoriasis pathogenesis [2, 3, 6].

Aim

The goal of this study was to investigate a correlation between triggering drugs used in patients with psoriasis and mean PSI scores, and to draw attention to the triggering drug use in those patients.

Material and methods

Patients, who came to our outpatient clinic between 2010 and 2012 and were diagnosed with psoriasis, were requested to bring their drug lists, which were recorded in the pharmacy’s computer system. After reviewing those lists, we have informed patients about the drugs that may have possibly caused the triggering. We excluded patients, who were not recorded in the Social Security System (SGK), and whose drug lists were only provided from anamnesis information, from the study. A total of 289 cases were included in the study. By using the pharmacy lists, drugs, which were used at least for 3 months and at most for 32 months were reviewed. Time intervals in the lists were related to disease durations.

Statistical analysis

Statistical analysis of data was performed using 19.0 version of the SPSS package program. Normal distribution of data was evaluated by Kolmogorov-Smirnov test. The level of significance was accepted as $p < 0.05$. Descriptive statistics were presented as mean ± standard deviation or median (min-max) values for continuous variables. In addition, frequency ($n$) and percentage (%) values were used for categorical variables. It was evaluated whether there was any difference in median of PASI scores between triggering drug users and non-users in independent groups using non-parametric test (Mann-Whitney $U$ test) analysis. It was evaluated whether there was any correlation between PASI rates and numbers of drugs used using Spearman’s correlation coefficient.

Results

Median age of cases was 45.00 (min: 8, max: 86) years; median age for females was 43.00 (min: 8, max: 84) years and median age for males was 47.00 (min: 8, max: 86) years. In this present study, 156 females (53.98%) and 133 males (46.02%) were included. Disease duration was 12.51 ±15.52; Psoriasis Area Severity Index (PASI) value was 5.50 ±0.45 (min: 0, max: 42) points. Of 289 cases, 221 were using NSAIDs (76.5%), and drug distribution of patients was as follows: 68 patients (30.8%) diclofenac, 70 patients (31.7%) ketoprofen, 37 patients (16.7%) ibuprofen, 61 patients (27.6%) naproxen, 35 patients (15.8%) acetyl salicylic acid, 68 patients (30.3%) flurbiprofen, 1 patient (0.5%) acemetacin, and 21 patients (9.5%) indomethacin. The list of patients, who used those drugs concomitantly, is given in Table 1.

| Drug              | Number of triggering drugs (n) |
|-------------------|--------------------------------|
|                   | Diclofenac | Ketoprofen | Ibuprofen | Naproxen | Acetyl salicylic acid | Flurbiprofen | Acemetacin | Indomethacin |
| Diclofenac        | 68         | 28         | 10        | 15       | 12                   | 21          | 0          | 5           |
| Ketoprofen        | 28         | 70         | 13        | 20       | 10                   | 21          | 1          | 8           |
| Ibuprofen         | 10         | 13         | 37        | 11       | 4                    | 5           | 0          | 3           |
| Naproxen          | 15         | 20         | 11        | 61       | 9                    | 21          | 1          | 8           |
| Acetyl salicylic acid | 12      | 10         | 4         | 9        | 35                   | 11          | 0          | 2           |
| Flurbiprofen      | 21         | 21         | 5         | 21       | 11                   | 68          | 1          | 5           |
| Acemetacin        | 0          | 1          | 0         | 1        | 0                    | 1           | 1          | 0           |
| Indomethacin      | 5          | 8          | 3         | 8        | 2                    | 5           | 0          | 22          |
diseases were 31 (10.7%), and 113 (39%) respectively. Seventeen (6%) patients were taking terbinafine, and 40 (14%) were taking corticosteroids. None of patients was receiving antimalarial drugs, whereas 16 (5.6%) patients were receiving sulphonamide; 10 (3.5%) were on salazopyrin and 7 (2.4%) were on trimethoprim sulfamethoxazole. Of patients, 111 (38.4%) were taking penicillin, and 8 (2.8%) were taking tetracycline. The number of antidiabetic users was 31 (10.7%). Concomitant use of NSAIDs with β-blocker agents was detected in 22 cases (7.6%), and concomitant use of NSAIDs with antidiabetic agents was observed in 27 cases (9.3%). Concomitant intake of NSAIDs with antibiotics was observed in 91 cases (31.5%), whereas NSAIDs-gastric agent combination was observed in 118 cases (40.8%).

NSAID-antibiotic-β-blocker combination was observed in 12 cases (4.2%); NSAID-antibiotic-antidiabetic agent combination was observed in 5 cases (1.7%); and NSAID-antibiotic-β-blocker-antidiabetic combination was used in 2 cases (0.7%). Mean disease duration of patients was 12.5 ±15.5 years.

Median value of PASI score was 5.55 ±0.45 points in the total patient group. In patients, who received none of triggering drugs, the median value of PASI score was 6.15 (min: 2, max: 22) points. Median PASI score of patients, who took more than one drug was 5.50 (min: 0, max: 42) points (p = 0.835). There was a positive low correlation between PASI rates and numbers of drugs used (r = 0.180, p = 0.013).

Discussion

In our study, we investigated the rate of triggering drugs used by patients with psoriasis. The most commonly used drugs were NSAIDs, antibiotics and antidepressants, and gastric medications (cimetidine, famotidine, ranitidine) were following them. Antidiabetic agents, β-blockers, CCBs and ACE inhibitors, which have been increasingly used for type II diabetes and hypertension that are metabolic syndrome components related to obesity in the recent years, have also made up a significant problem in psoriasis. Because medications for hypertension and diabetes should be used permanently, their selection has become much more important. In line with the literature, although we observed that the rate of triggering drug use was increased, the PASI rate was also increased in our study.

There are many studies, which have indicated that NSAIDs trigger psoriasis [1–8, 12, 13]. It was defined that ketoprofen (70 cases, 24.2%), diclofenac (68 cases, 23.5%), flurbiprofen (68 cases, 23.5%) and naproxen (61 cases, 21.1%) were the most commonly used NSAIDs; and they were followed by ibuprofen (37 cases, 12.8%), acetyl salicylic acid (35 cases) and indomethacin (22 cases) in our study. Moreover, there were many patients, who were taking one or more of those drugs together. Median value of PASI score was 5.55 ±0.45 points in the total patient group. In patients, who received none of triggering drugs, the median value of PASI score was 6.15 (min: 2, max: 22) points. Median PASI score of patients, who took more than one drug was 5.50 (min: 0, max: 42) points. There was no statistically significant difference in median PASI scores between triggering drug users and non-users.

β-Blockers have been frequently reported as triggering drugs for psoriasis in the literature [14–18]. β-Blocker use was observed in 26 of our patients. ACE inhibitors have also been reported as triggering drugs for psoriasis [19–22]. Our 63 patients (22%) were receiving ACE inhibitors. In our study group, 14 patients (4.9%) were receiving the ACE inhibitor-β-blocker combination.

It was reported in previous studies that also calcium channel blockers triggered psoriasis [23–26]. In our study, 31 patients (11%) were taking calcium channel blockers. Seven of our patients (2.4%) were taking CCB-ACE inhibitor combination, whereas 7 patients (2.4%) were taking CCB-β-blocker combination.

Stress factor is important as an initiator and booster for lesions. Antipsychotic drug use has been increasing recently because of stress [27–33]. In the literature, it has been indicated that activation of psoriasis lesions has been caused especially by lithium use [27–29]. In our study, there was no lithium receiving patient, but antidepressant distribution among the cases was as follows: citalopram = 50 (17.3%), fluoxetine = 9 (3.1%) and trazadone = 5 (1.7%).

Also antibiotics are one of uncontrollably used drug groups. There are publications about their triggering roles of psoriasis. Especially commonly used penicillin [34], tetracycline [35] and sulfonamides [36] have been reported as triggers. In our study, 111 patients (38.4%) were using penicillin, whereas 8 patients (2.8%) were taking tetracycline. Among sulfonamide using 16 patients (5.6%), 9 were taking salazopyrin and 7 were taking trimethoprim sulfamethoxazole. However, because those drugs were used for a short time and infections were triggers for psoriasis, drugs which were used for infection treatments were not mentioned as frequently as analgesics, antihypertensive and antidiabetic agents in the literature [1–8].

In the literature, it was reported that antidiabetic drugs could also trigger psoriasis [37–40]. In our study, the number of patients on antidiabetic agents was 35 (12%), and other drugs, which our patients used and were known as triggers, were terbinafine [41–43] and antimalarial drugs [1–8]. Terbinafine was used by 17 cases (6%). There was no patient on the antimalarial agents. There are contradictory publications in the literature about gastric medications. Although there have been publications, which indicated that they could cause psoriasis-like skin rash [44], there were also publications, which indicated that they were not triggers, even they could be used in the treatment [45–48]. In our study,
the number of patients on gastric medications was 113 (39%). It has also been reported that alcohol and its metabolites might be triggering skin lesions of psoriasis [49, 50]. Moreover, as alcohol use increases liver toxicities of systemic antipsoriasis drugs, patients should be warned about alcohol use. In our study, we asked about alcohol drinking habits of patients, and informed them about its triggering effect. In our study, 86 cases (31%) were taking alcohol. Two of our cases were hospitalized and received treatment for drinking alcohol, and it was observed that numbers of their lesions were decreased.

As concomitance of psoriasis with metabolic syndrome is a known fact, patients should also be warned about obesity. Health problems, which appear along with obesity, and drugs used for those conditions (antihypertensives, antidiabetics) complicate struggling against the disease.

The aim of this present study was not to define which drugs triggered the disease, but to direct attention of patients with psoriasis to possible triggers. Moreover, healthcare personnel also have important responsibilities. Existence of psoriasis should be definitely reviewed and investigated before recommending or prescribing especially a triggering drug. In the literature it was reported that roles of triggering drugs could be encountered not only after the first use but months after the use, so that drug effect could be missed [8, 9, 23–25, 30]. Even after treatment with biological agents, drug effects, which might increase lesions, might be observed months after the use [8, 9]. Increased PASI score in patients with many drugs use has indicated roles of drugs. Multiple drug use and high PASI scores of advanced age patients (over 50 years) may be an indicator.

In our study group, there was no significantly difference between median PASI scores of the patients using a triggering drug and those of whom are not using a triggering drug. This result in our study may be caused by taking into consideration only drugs reported as triggering in the literature not the others. Some drugs which are used by our patients and not reported as triggering drugs. In our study, 86 cases (31%) were taking alcohol. We focused on the use of drugs which are used by our patients and not reported as triggering drugs.

Conclusions

Treating psoriasis patients, who are receiving psoriasis triggering drugs (77% NSAIDs, 8.3% B-blocker, 37% antidepressants), is similarly difficult as treating a subject with the strawberry allergy using only antihistaminics.

According to pharmacogenetic studies, the same drug may not show the same effect in all subjects, but careful use of drugs and increasing awareness of patients against the disease are important. Thus, we believe that we can be more helpful to our patients. If we emphasize that the drugs they are using can also trigger their diseases and we provide that they are more careful about the issue, then we may also reveal drugs, which are not on the list yet. Physicians working at the primary healthcare settings should be warned about this issue. We believe that especially a warning in the patient leaflet sheet, which underlines that B-blockers should be carefully used in subjects with psoriasis, is not being read by patients.

Currently, we observe that many psoriasis patients accept their diseases with some localized plaques on their bodies, and they continue living by using topical preparations from time to time. We can inform our patients about triggering factors in a very limited time at the outpatient clinic visits with the help of a newsletter or a copy of the text about drugs prepared by the dermatology association. Sunny climate and thermal springs of our country as well as easily and cheaply reached seafood facilities provide conditions helpful for psoriasis treatment. We can be more helpful to our patients by using protective, rehabilitative and life quality increasing methods like group therapies instead of antidepressants, struggling against obesity, and using drugs from other groups rather than psoriasis triggering ones. We believe that another important topic is that healthcare trainings should be given to parents with psoriasis how to protect their children (with genetic susceptibility background) from triggering drugs.

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