Knowledge of Safety Rules during Isotretinoin Acne Treatment – Survey in Women in Childbearing Age from Polish Population

Zuzanna Lewicka, Justyna Mrówczyńska, Monika Raczkowska-Golanko*, Karolina Górska, Aneta Szczerkowska – Dobosz and Michał Milewski

Department of Dermatology, Venereology and Allergology, Medical University of Gdańsk, Poland

*Corresponding author: Monika Raczkowska-Golanko, ul. Korczaka 16/13 81-473 Gdynia, Poland, Tel: +48505259813, E-mail: mraczkowskagolanko@gmail.com

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Abstract

Background: Oral isotretinoin is very effective in severe acne treatment. Due to a large number of its adverse effects and necessity of the long-term use, patients have difficulties in complying with the therapy. In order to provide successful and safe healing, patients must be aware of recommended precautions.

Methods: The study included 412 women (age 15-45 years). It was based on the anonymous, on-line questionnaire, designed in Polish and it contained 30 multiple-choice questions. The data was collected through social-networking service, web logs, isotretinoin Internet forum and from out-patient clinic.

Results: On average, 78.6% of isotretinoin cured patients believe to be clearly informed by their physician about possible side-effects during the therapy. 65.3% attended medical appointment once a month and had blood tested regularly. 94.2% were aware of the risk of serious fetal malformation. Before isotretinoin administration 39.3% were told to exclude pregnancy by test at home and 28.2% were referred for gynecological consultation. 48% did not have pregnancy excluded. 34.3% of sexually active females used two methods of contraception, 56.7% used one method, but 9% did not use any.

Conclusions: The results of our study indicate that the majority of females gained some information about side-effects, basic safety rules and teratogenicity of isotretinoin. Nevertheless, women do not fully understand the risks of the treatment and underestimate necessary precautions, mainly those regarding pregnancy exclusion and effective contraception. Physician counseling is crucial to achieve appropriate patients’ compliance during the isotretinoin treatment.

Keywords: Isotretoin; Safety rules; Acne treatment; Childbearing age; Acne

Introduction

Acne is one of the most common skin disorder [1]. It affects almost all teenagers. 14% to 20% of young people has moderate to severe form of acne [2]. In women the peak prevalence is in the adolescence, but acne may also affect significant percentage of older females [3]. Isotretinoin (13-cis retinoic acid), a vitamin A derivative, remains the most effective acne medication [4], giving a long-lasting remission after the first course of treatment in more than 50% of patients [5]. It is the only treatment that counteracts all of the major mechanisms of acne pathogenesis [6]. The European Medicines Agency approved isotretinoin in severe forms of acne (like nodular or conglobate acne, acne with great risk of scarring) that are not responding to oral antibiotics and topical agents [7]. According to the Consensus of the Polish Dermatological Society isotretinoin can be also used in less severe variants of acne [1]. Although indications for its use are expanding, isotretinoin treatment must remain under accurate medical surveillance [6]. As a known teratogen it should be always prescribed to women of childbearing potential in accordance with the Pregnancy Prevention Programme (PPP) [8]. There is little data on patients’ awareness and about their compliance with the prescriber during isotretinoin therapy [9-11]. Those studies performed among patients, reported that large number of women do not follow the pregnancy prevention recommendations and physicians do not always advise females according to the guidelines. The aim of the present study was to assess basic knowledge of safety issues, side-effects and teratogenicity among the isotretinoin treated and to analyze collaboration with their physicians during the course of treatment.

Material and Methods

The cross-sectional study was conducted among Polish women from January to June 2013. It covered 412 females in childbearing age (15-45 years) that underwent isotretinoin acne treatment. Among women, 59% had higher education or were university studies. The data collection was carried by on-line questionnaire which was designed in Polish language and contained 30 multiple-choice questions. Questionnaires were distributed through social-networking services, such as Facebook, web logs, and the isotretinoin Internet forum (http://www.izotek.fora.pl). The leaflets about the survey were placed in chosen dermatology clinics in big Polish cities (Gdańsk, Gdynia, Bydgoszcz, Warszawa) with population range from 250,000 to 1,700,000. Most of questions concerned patient’s knowledge and their adherence with recommended safety issues during isotretinoin treatment. Women’s self-reports were used to asses physician’s practice. Females were asked about cooperation with their doctor, whether they received sufficient information about isotretinoin side-effects, teratogenicity and necessary precautions - like need of the UV protection and avoidance of certain cosmetic procedures. 10 out of 30
questions applied to principles of the Pregnancy Prevention Programmes for women of childbearing potential treated with isotretinoin. The questionnaire requested about patient’s knowledge and obedience with those principles. Women were asked whether they were advised to exclude pregnancy prior to the initiation of the isotretinoin treatment, if they gained knowledge of contraceptive measures and whether they used contraception. Both, the physicians’ and females’ compliance with the PPP rules was evaluated from the women’s perspective. Statistical calculations were performed using STATISTICA version 9.0. Results are presented as mean ± standard deviation or the number/percentage of patients. The analysis of the association between baseline variables and outcomes were determined using Chi-squared test. A p value<0.05 was considered statistically significant.

Results

412 women completed the questionnaire. Mean age was 23.4 ± 4.8 years (range: 15-45 years). Among them-229 (55.6%) gained information about possibility of isotretinoin treatment from dermatologists, 75 (18.2%) from the Internet and 62 (15%) from friends. Less common sources were: family-25 (6%), newspapers-7 (1.7%), other physicians-5 (1.2%), medical literature-1 (0.2%) and other-8 (1.9%). 387 (93.9%) participants had other acne treatment administered before isotretinoin.

On average, 324 (78.6%) of isotretinoin cured patients believed to be clearly informed by their physician about possible side-effects during the therapy. 326 (77%) used Internet to gain more information, of whom 248 (76%) found this knowledge very useful. Patients’ concern before isotretinoin treatment is shown in Table 1.

There was a statistically significant relationship between awareness of possible side-effects and compliance with the therapy (p<0.05). Patients insufficiently informed about possible side-effects before initiation of the therapy (n=88; 21.4%) were twice more likely to withdraw treatment than those well-informed. Among insufficiently informed females, 37 (42%) considered quitting isotretinoin, compared to 64 (19.8%) of well-informed group. 44 (10.7%) participants finished treatment before the scheduled time.

Table 1. Patients’ concerns before isotretinoin treatment.

<table>
<thead>
<tr>
<th>Patients’ Concerns</th>
<th>Percent of patients [%]</th>
<th>Number of patients (n=412)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Side-effects</td>
<td>56.8</td>
<td>234</td>
</tr>
<tr>
<td>Relapse of acne</td>
<td>14</td>
<td>58</td>
</tr>
<tr>
<td>Price of the drug</td>
<td>13.8</td>
<td>57</td>
</tr>
<tr>
<td>Duration of treatment</td>
<td>7.8</td>
<td>32</td>
</tr>
<tr>
<td>Teratogenicity</td>
<td>7.5</td>
<td>31</td>
</tr>
</tbody>
</table>

Table 2: Physicians’ actions regarding PPP before isotretinoin administration reported by patients.

Regarding contraception, 234 (56.8%) obtained detailed information and materials from their physician, 134 (32.5%) were insufficiently instructed and 44 (10.7%) were not informed about it. During the treatment, 202 (49%) women claimed not to be sexually active and 210 (51%) women declared themselves sexually active. Among this group 72 (34.3%) used two methods of effective contraception, 119 (56.7%) used one method, and 19 (9%) used no contraception during the treatment (Figure 1). There was a significant relationship between the use of effective contraception by the patients and awareness of possible isotretinoin teratogenicity discussed with their physician (p<0.05). Among insufficiently informed females 60 (50%) did not use any method of contraception, compared to 13 (3.4%) of those who were well-informed. Among sexually active women 60 (29.1%) performed pregnancy test every month. The majority of women - 330 (80.1%) would be afraid of getting pregnant after a period of one year after finishing the treatment.

When asked about repeated isotretinoin treatment 163 (39.6%) would definitely and 154 (37.4%) would rather start this treatment again. Sixty-one (14.8%) would rather and 34 (8.3%) would definitely not undergo therapy again.
Discussion

This survey performed from patient’s viewpoint aimed to evaluate their awareness and what they recall from their doctor’s practice during the course of isotretinoin therapy. To our knowledge this is the first study in Poland that assessed compliance of females of childbearing potential with the requirements indispensable during isotretinoin acne treatment. The main findings from our study are that most of women gained some information about side-effects, teratogenicity and safety rules before isotretinoin treatment initiation. However, nearly in half of them (48%) pregnancy was not excluded prior to retinoid administration, and only 34.3% of sexually active females used double contraception during therapy. The strength of our findings relies on perception of the large population questioned women. The main drawback of the study is its subjective character and, in consequence, response accuracy.

Although isotretinoin remains the most effective acne medication, 10.7% of respondents decided to finish the therapy prematurely. Thus, some patients found adherence with treatment regimen troublesome. Therapy can be abandoned before scheduled time when unexpected side-effects appear. Understanding dangers connected with the therapy increases the likelihood that the patient will obey dosing and monitoring requirements and accomplish successful outcome safely. Our results showed that females with worse preparation for possible side-effects, got discouraged easier and considered to quit therapy more often. In general, 79% females reported to be clearly informed by the physician about the teratogenic effect of isotretinoin. This proportion is nearly 16% greater than in Saudi Arabia survey [11]. Nevertheless, in our study many females (77%) searched for additional information in the Internet, which may suggest that medical explanations were insufficient. Side-effects were the most bothersome of all concerns that patients recall from the therapy, thus physicians must explain this issue wider. More attention should be also paid to actions contraindicated during isotretinoin treatment. Respondents were best informed about the need of the sunlight avoidance. Surprisingly, only 67.7% of patients knew that cosmetic procedures are not to be performed during isotretinoin treatment and this issue should be discussed in details with females to obtain the most beneficial effect of the therapy.

Isotretinoin treatment requires careful patient monitoring and medical appointments should be arranged in monthly intervals. As only 62.6% females followed control visits as recommended it may suggest that patients found it difficult to incorporate long therapy into their daily activities. To exclude abnormalities of liver function and lipid metabolism, liver enzymes and serum lipids levels should be checked before the treatment, one month after its initiation and every three months during isotretinoin therapy. In our study 78% of patients attending follow-ups in monthly intervals reported to have blood tests regularly, which indicates that most of physicians conducted monitoring requirements according to the guidelines, not only provided prescriptions monthly.

In the present study the majority of females (94.2%) claimed to be clearly informed by the physician about the teratogenic effect of isotretinoin. This proportion is comparable to findings from the Canadian study [9]. Nevertheless, like in the meta-analysis on studies performed among dermatologists from different European countries [12], our survey reported poor compliance with the Pregnancy Prevention Program (PPP). Neither patients, nor physicians followed the safety instructions obligatory for women of childbearing potential. Whereas before the treatment only 7.5% found fear of eventual conception the most bothersome of all concerns, surprisingly large number of participants (80.1%) would be afraid of getting pregnant one year after the course of isotretinoin. According to summary of product characteristic, it is safe just one month after finishing isotretinoin administration. Our results may indicate that information given by physicians is not well understood and females too often rely their actions on myths. In consequence some of necessary precautions are underestimated while other are exaggerated.

According to the PPP women of childbearing potential should use at least one method of effective contraception, preferably two forms, starting one month before and finishing one month after the course of isotretinoin treatment. In our study only 34.3% of sexually active females used double contraception. Unfortunately, as long as women disregard the need of two contraceptives, fetal exposure to isotretinoin may happen [13]. What is the most worrisome, 9% of females did not use any contraception during the treatment, and this is similar to findings from another study [9]. Our results show that patients’ use of effective contraception depends truly on their understanding how isotretinoin influences developing fetus. Women who discussed with their doctors teratogenic impact of isotretinoin, understood better the importance of effective contraception and strictly obeyed recommendations. Our results suggest that safety of the therapy depends mainly on dermatologist’s practice and that is why doctors should take every action to make sure that patients understand risks of the treatment, as well as contraception requirements. Before starting
the therapy females should be properly advised on pregnancy prevention methods. Educational brochures about contraception measures can be helpful. Unfortunately, in our group not all women were properly counseled or provided with such materials.

The most disturbing fact is that nearly half of females (48%) did not have pregnancy excluded prior to starting the treatment, whereas even a single dose of isotretinoin can lead to congenital malformations [14]. According to the guidelines, physician should always perform medically supervised test or recommend gynecological consultation to women of childbearing potential before isotretinoin administration. The history of sexual activity should be taken from all women. Questionnaire survey performed among Scottish dermatologists revealed that girls at age below 16 years were asked of chance of being pregnant less frequently than those older [15]. As nowadays some of women start sexual intercourse very early, pregnancy should be excluded regardless of the female’s age and circumstances. Cross-sectional study showed that incidence of pregnancy is the highest during the course of treatment (43%), followed by the beginning (32%), and then within one month of its discontinuation (25%) [16]. In all sexually active women pregnancy testing should be repeated every month during the therapy and five weeks after finishing it. Among our participants only 29.1% ruled out being pregnant every month. Our data and findings from other studies [15,16] indicate that physicians neglect the possibility of pregnancy too often, perhaps because of making assumptions on female’s sexual activity.

It should be emphasized that this survey was performed from women’s perspective and it reflects how they perceive physician’s advises. Due to various time of undergoing Isotretinoin treatment over past few years, some percentage of patients may not remember details connected with doctor’s recommendations. Therefore, the potential of recall bias may affect the obtained results and the exact assessment of dermatologists’ practice cannot be provided. However, we found results from our survey important to improve the patient – doctor cooperation and the treatment outcome.

References