

Knowledge and Use of Isotretinoin in Saudi Female College Students: Cross-Sectional Study

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Abstract

Background: The most effective treatment for severe acne is isotretinoin. However, it carries major side effects, such as teratogenicity, depression, and increased lipid profiles. It is advised to monitor the lipid profile and to use two forms of contraception during isotretinoin use. Although it is commonly prescribed, little data are available regarding patients' understanding of isotretinoin. **Objectives:** The aim of this study is to assess Saudi female college students' knowledge about isotretinoin use and side effects. **Methods:** Data were collected by a validated online questionnaire disseminated through social media, allowing the collection of information from students from different regions of the country. **Results:** The total number of responses was 622. The majority of respondents were 18–24 years old, single, and college students; all were female. About 48.6% (282) of the sample used isotretinoin. Most had good knowledge of isotretinoin side effects. Medical students were more knowledgeable than students of other majors, and users were more knowledgeable than nonusers. The most common side effect was dryness. Use among married females was 2.8%, the majority of whom were instructed by their physicians to use only one method of contraception. One respondent got pregnant while using the drug. **Conclusion:** College-aged females generally have good knowledge of isotretinoin and its side effects. However, awareness about proper contraceptive use while on the drug is lacking.

Keywords: College-age, female of childbearing age, isotretinoin, Saudi Arabia

INTRODUCTION

Acne vulgaris is the most commonly treated dermatological disorder.^[1] In Saudi Arabia, it constitutes one-fifth of all dermatology clinic visits.^[2] Furthermore, its prevalence is as high as 80% in adolescents, with females more commonly seeking medical guidance than males.^[2,3] The treatment guidelines of moderate-to-severe acne include the use of oral antibiotics with a topical retinoid, and in severe or resistant cases, oral isotretinoin.^[4] Isotretinoin side effects include liver dysfunction, increased blood cholesterol levels, depression, and teratogenicity.^[5] Females of childbearing potential are expected to use at least two methods of contraception while using isotretinoin.^[6]

Awareness of isotretinoin teratogenicity and side effects among females of childbearing age is important. In a university hospital clinic in Riyadh, Saudi Arabia, most isotretinoin patients were women (69.9%), and 99% of the users of isotretinoin experienced one or more side effects.^[7] In a 2018 study in Al-Ahsa, Saudi Arabia sampling the general public

88.9%, 58.7%, 44.1%, and 53.3% of participants correctly identified teratogenicity, lipid profile disturbance, liver dysfunction, and depression as side effects, respectively.^[8] In a 2011 study in Qassim, 63% of acne patients of both genders on isotretinoin claimed to know its risk factors, with the most common being dryness.^[9] However, females of childbearing potential were not examined specifically, and the use of double contraception was not investigated.

Until recently, isotretinoin has been widely sold in pharmacies throughout the Kingdom, and often without a prescription.^[10] In a 2012 study, the majority of community pharmacists did not adequately understand the teratogenicity of the drug.^[10] The Ministry of Health recently withheld selling of isotretinoin in independent pharmacies.

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Despite the teratogenicity of the drug, only 62% of dermatologists in Saudi recommend two methods of contraception to females of childbearing potential, and only 16% perform monthly pregnancy tests.^[6] Since Saudi Arabia has strict restrictions on abortion, isotretinoin users of childbearing potential must fully understand and comply with required contraceptive measures. Furthermore, in a Dutch cohort, 60% of women using isotretinoin while pregnant started using it after they were already pregnant.^[11]

In the West, several programs and guidelines have been implemented to promote isotretinoin awareness among users. In a 2015 study, the vast majority overestimated the effectiveness of common contraceptive methods, with the participant knowledge markedly improving after revising a contraception information sheet.^[9] The most prominent program used currently in the United States is iPLEDGE, which is a monthly quiz isotretinoin users must take to fulfill their month's prescription. However, at least 150 U. S. women got pregnant on isotretinoin despite the iPLEDGE program.^[12] Furthermore, although isotretinoin users clearly understand its teratogenicity, many first learned of correct contraceptive methods through iPLEDGE.^[13] Reading isotretinoin medication guides and mandatory patient package inserts alone yielded similar answers to guessing.^[14]

Our objectives include obtaining demographic data on isotretinoin usage among Saudi female college students and measuring knowledge of isotretinoin uses, side effects, need for contraception.

METHODS

This is a cross-sectional study of Saudi students, using an Arabic questionnaire. The questionnaire was disseminated through social media (Twitter and Whatsapp) to increase the response rate from all regions of Saudi Arabia. A question asking to choose all known side effects of isotretinoin was included, with four correct answers (liver injury, fetal abnormalities, increased blood cholesterol, and depression) and four incorrect answers (kidney injury, abortion, increased blood glucose, and sleep disturbance). Isotretinoin users were asked to report the side effects they experienced while using the drug; the answers were grouped into broader categories to ease analysis.

Data were entered into Excel (Microsoft Corporation, Redmond, Washington, USA) worksheets and then transferred to SPSS (version 21, IBM Corporation, Armonk, New York, USA) for statistical analyses. Categorical analyses of frequencies and cross tabulations were done using the Chi-square and standardized residual analysis in SPSS. IRB approval was approved from the Alfaisal University IRB vide IRB-66-18.

RESULTS

This study was carried out from April to August 2018. The sample comprised 622 participants, repetitive sentence. Of the total sample size, 42 participants were excluded for various reasons, such as duplication or discrepancy in responses, or not being a college student or recent graduate. Further analysis was

performed on the remaining 580 responses. All the respondents were female Saudi college students or recent graduates.

Demographics

The majority of respondents were between the ages of 18–24 (81%), single (87%), and current college students (78%). Most of the respondents were business and finance students, followed by students of humanities, then medicine. About 72% of respondents attended public universities [Table 1].

Prevalence of acne

About 22.6% of respondents reported that they currently have acne, whereas 43.4% only suffer from acne occasionally. About 76.9% had acne in the past, regardless of their current acne status. 92.4% of those who currently have acne have also had acne in the past. 38% do not have acne and never did.

Table 1: Demographics

Demographics	n (%)
Age (years)	
<18	22 (4)
18-24	469 (81)
>24	89 (15)
Marital status	
Single	503 (87)
Married	70 (12)
Widowed/divorced	7 (1)
Student status	
Current student	451 (78)
Recently graduated	129 (22)
University	
Imam Muhammad bin Saud Islamic University	75 (13)
King Saud University	123 (21)
Princess Nora bint Abdul Rahman University	96 (17)
Prince Sultan University	72 (12)
Alfaisal University	56 (10)
Other (public)	158 (27)
Other (private)	56 (10)
Year of study	
1	123 (21)
2	66 (11.4)
3	88 (15.2)
4	66 (11.4)
5	88 (15.2)
6	64 (11.4)
Recent graduate	79 (13.6)
Major	
Medicine	129 (22.2)
Business and finance	66 (11.4)
Health sciences except medicine	114 (19.7)
Engineering	155 (26.7)
Information technology	54 (9.3)
Humanities	38 (6.5)
Miscellaneous	50 (8.6)
	8.6)
	148 (25.5)
	21 (3.6)

Knowledge of side effects among college students in general

The study participants had good knowledge about the side effects. Participants were more likely to answer correctly to the correct side effects than not for each of the questions [Figure 1]. Similarly, they were less likely to claim that the incorrect side effects were true [Figure 2].

Lack of knowledge of side effects was assumed when participants did not choose the correct side effects as true in the multiple choice question. Those receiving isotretinoin were less likely to say that each of liver injury (standardized residual = -2.1), depression (SR = -3.0), fetal abnormalities (SR = -3.0), and increased blood cholesterol (SR = -3.0) is not a side effect. Those who have never used isotretinoin were more likely to say the liver injury is not a side effect of the drug (SR = 2.0), as well as fetal abnormalities (SR = 3.0), increased blood cholesterol (SR = 3.0), and depression (SR = 2.9). Users and nonusers had exact opposite views on depression and increased blood cholesterol as side effects.

There was no association between taking isotretinoin and the mistaking each of increased blood sugar, kidney failure, and sleep disturbance as a side effect of isotretinoin. However, users were more likely to say that abortion is not a side effect compared to nonusers ($P = 0.002$).

A variation in knowledge of correct side effects according to college major was noted [Figure 3]. There was a strong overall association between major and knowledge of liver injury as a side effect. Medical students were less likely to say that liver injury is not a side effect (standardized residual = -2.2) and humanity students were more likely to say it was (SR = 2.7). An overall strong association between major and knowledge of fetal abnormalities as a side effect was also noted. Medical students were less likely to say that fetal abnormalities are not a side effect (standardized residual = -3.0). There was no obvious association between major and knowledge of increased blood cholesterol as a side effect. Humanity students were more likely to say that depression is not a side effect (SR = 2.1)

In regard to knowledge of incorrect side effects, there was less variation among answers from students of different majors [Figure 4]. Medical students were more likely to say kidney failure is not a side effect (SR = 2.2). However, there was no obvious association between major and misconception of each of increased blood sugar, abortion, and sleep disturbance as side effects.

Isotretinoin use

Of the total sample (580), 48.6% (282) used isotretinoin. From this point onward, this sample number (282) will be considered 100% [Table 2].

Relationship between who prescribed isotretinoin and who informed the patient about the side effects

The vast majority (96.8%) of respondents who had used isotretinoin had been prescribed it by a physician or pharmacist.

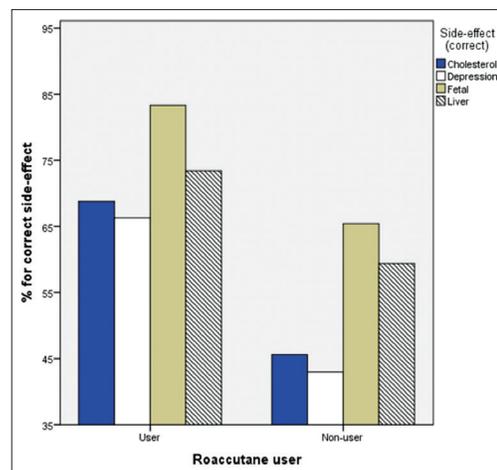


Figure 1: Comparison of knowledge of correct side effects between isotretinoin users and nonusers

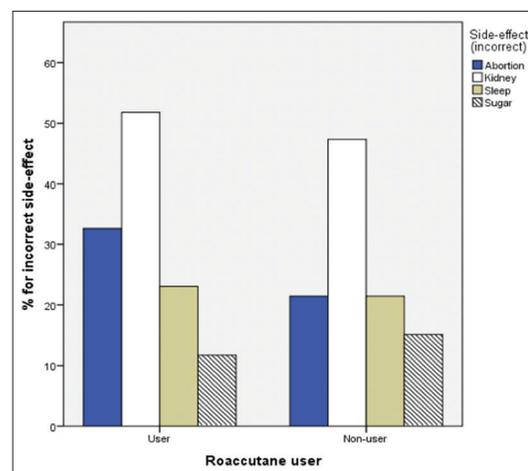


Figure 2: Comparison of knowledge of incorrect side effects between isotretinoin users and nonusers

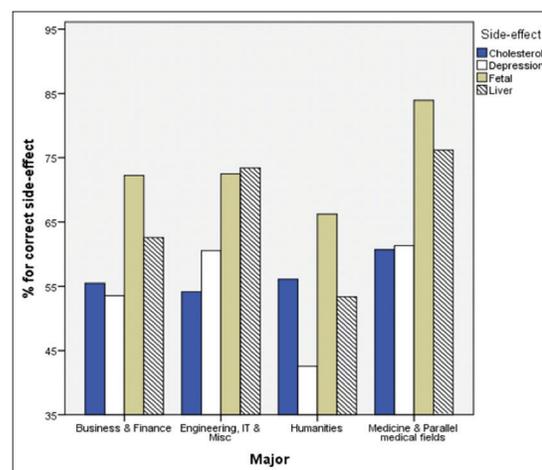


Figure 3: Knowledge of correct isotretinoin side effects according to college major

About 72.9% of those who were prescribed the drug by a physician were also informed about the side effects by a

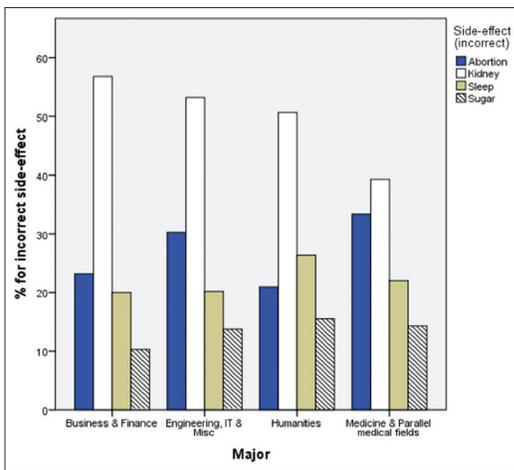


Figure 4: Knowledge of incorrect isotretinoin side effects according to college major

Isotretinoin user questions	Answer	n (%)
Who prescribed isotretinoin?	Physician/pharmacist	273 (96.8)
	Self-medicated	9 (3.2)
Dose prescribed for most of the treatment (mg)	10	15 (5.3)
	20	117 (41.5)
	30	42 (14.9)
	40	65 (23)
	50	1 (0.35)
	>50	5 (1.7)
	I can't remember	37 (13.12)
Duration of treatment (months)	<6	90 (31.9)
	6-12	174 (61.7)
	>6	18 (6.38)
Side effects experienced*	No side effects	104 (36.9)
	Dryness	137 (48.6)
	Depression and suicidal thoughts	30 (10.6)
	Cholesterol and triglycerides	19 (6.7)
	MSK pain	60 (21.3)
	Hair loss	19 (6.7)
	Miscellaneous	60 (21.3)
Were you informed about the side effects of isotretinoin?	Yes	245 (86.8)
	No	36 (12.7)
Who informed you about the side effects of isotretinoin?*	Physician/pharmacist	204 (72.3)
	Friends/family	16 (5.7)
	Nobody informed me	6 (2.1)
	I read about them myself	58 (20.6)
If you have been informed by a physician or a pharmacist, how did that happen?	Oral	148 (52.5)
	Written	8 (2.8)
	Both	40 (14.2)

*Respondent may choose more than one answer to this question. MSK: Musculoskeletal

physician. About 18.3% of those who were prescribed the drug by a physician learned about the side effects by reading about them, whereas 5.5% were educated by friends or family. Only

1.8% of those who were prescribed the drug by a physician were not educated about the side effects at all.

Of the nine respondents who were self-medicated, 5 read about the side effects themselves and 2 were educated by a physician or pharmacist. One respondent learned about the side effects from family or friends, and one was not educated about the side effects at all.

Side effects experienced by isotretinoin users

Side effects were grouped into the following broad categories: Dryness, depression and suicidal thoughts, cholesterol and triglycerides, musculoskeletal pain, hair loss, and miscellaneous. Miscellaneous included the following reported symptoms: eye pain, blurry vision, eyelid swelling, forgetfulness, vitamin D instability, new skin hypersensitivity, thin skin, nosebleeds, anxiety, GI upset, weight changes, sleep disturbance, menstrual cycle disturbances, increased acne, appetite changes, headache, and lumbar pain.

There was a weak nonstatistically significant positive correlation between dose given (10 mg– over 50 mg) and number of side effects, $R = 0.096$, $P = 0.134$ ($n = 245$), as well as a very weak nonstatistically significant positive correlation, $R = 0.022$, $P = 0.713$, ($n = 282$) between duration and number of side effects.

Knowledge and experience of married students

Among those who used isotretinoin, 2.8% (8) used it while married. All were advised to use contraceptives during the treatment period, and all by a physician. However, the majority were advised to use only one method of contraception, and only 2 of them were advised to use two methods. The method of physician delivering prescription and drug information to patients was most commonly by oral instructions (5), then by combined oral and written (2). All were informed about the teratogenicity of the drug, all by a physician except for one respondent who read about the side effect herself. Seven of the participants did a pregnancy test before starting the drug, and none reported performing one during the duration of treatment. One participant got pregnant while using isotretinoin.

The number of women using isotretinoin while married among our sample was too small to perform the Chi-square test. Therefore, we focused on one participant who got pregnant while on the drug. In that case, she was prescribed isotretinoin as well as one contraceptive only by a physician before taking the drug. Both the contraceptive prescription and education about teratogenicity was done orally without written instructions. Furthermore, she only took a pregnancy test before starting the drug and not while using it.

DISCUSSION

Acne was widely prevalent (76.9%) among the population sampled. The participants generally had good knowledge of the side effects of isotretinoin. They were more likely to choose the correct side effects as true (64.2%–81.9%) rather than not for each of the questions. Similarly, they were less likely to claim that the incorrect side effects were true (14.2%–34.4%).

In this study, a discrepancy in the knowledge of side effects according to college major was noted. For example, medical students were generally more knowledgeable of the side effects, with humanity students being the least aware among the sample. However, there was no association between major and misconception of the rest of the incorrect side effects asked being true. There is a lack of studies comparable to this in the region as well as in other countries worldwide.

Almost half (48.6%) of our sample used isotretinoin, with the vast majority being prescribed by a physician or pharmacist, which is comparable to other studies in the region.^[8,15] Only 3.2% of the sample were self-medicated. The most common side effect reported was dryness, followed by musculoskeletal pain, which is similar to regional study findings.^[7,8,16] Depression and suicidal thoughts were reported in 10% of the respondents. Adequate knowledge of the side effects of isotretinoin was demonstrated in our sample. Increased cholesterol level was the most common side effect users did not acknowledge. Furthermore, kidney injury was the most common incorrect side effect chosen as true by the users in our sample.

Isotretinoin use among married female college students

In the conservative society of Saudi Arabia, it is assumed that women become sexually active only after marriage. Therefore, it is most common for clinicians in the country to ask about marital status, as opposed to sexual activity, when prescribing teratogenic drugs. For the purpose of our study, we assumed potential pregnancy among those who were married during the use of the drug. Although the number of participants who used isotretinoin while married was small, there was one respondent who got pregnant while on the drug. She was only instructed to use one method of contraception, while the guidelines require at least two.^[6,12,13,17] The majority of married isotretinoin users in our sample were instructed to use only one method of contraception. To the extent of our knowledge, this is the only study in the country measuring the use of contraceptives among married isotretinoin users, and the results show a need for increased awareness about contraceptives among this population. However, further studies need to be done with a larger sample size of married isotretinoin users to accurately capture the issue.

Study limitations

The weaknesses of this study include it being cross-sectional and the response rate being unknown due to dispersing the questionnaire through social media. Mean age was not calculated as the age was grouped in the questionnaire.

CONCLUSION

The majority (up to 81.9%) of isotretinoin users among our sample correctly identified side effects of the drug. All married users among our sample were educated to use contraceptives during drug use, although number of contraceptives varied. One participant got pregnant while using isotretinoin. To the extent of our knowledge, this is the first study to relate college major to the knowledge of side effects of isotretinoin, as well as the use of isotretinoin and contraceptives among

married women in Saudi Arabia. The study has shown a need to further educate married patients about using at least two contraceptive methods while using isotretinoin. We encourage implementation of national programs such as iPLEDGE for educating patients about isotretinoin and proper contraceptive use.^[13] Furthermore, it is necessary to establish clear guidelines for pregnancy testing before, during and within 1 month of discontinuing isotretinoin for physicians in the country. Monthly prescriptions for married women should be monitored to ensure strict compliance with pregnancy testing.

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Conflicts of interest

There are no conflicts of interest.

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