Medical Science

pISSN 2321–7359; eISSN 2321–7367

Prevalence, knowledge, attitude and practice of using topical retinoids among Saudi population, Saudi Arabia

Sahar Hasan Alsharif[1], **Ashwaq Alosaimi**[2], **Raghad Aldoobi**[2], **Yousra Alturki**[2], **Rawan Aldhahwani**[2], **Suha Alsayed**[2], **Shahad Bukhari**[2]

To Cite:
Alsharif SH, Alosaimi A, Aldoobi R, Alturki Y, Aldhahwani R, Alsayed S, Bukhari S. Prevalence, knowledge, attitude and practice of using topical retinoids among Saudi population, Saudi Arabia. Medical Science, 2022, 26, ms5e2023.
doi: https://doi.org/10.54905/disssi/v26i119/ms5e2023

Author Affiliation:
[1]Department of Dermatology, Alnoor Specialist Hospital Makkah, Kingdom of Saudi Arabia
[2]Medical student, College of medicine, Umm Al-Qura University, Makkah, Kingdom of Saudi Arabia

Peer-Review History
Received: 05 December 2021
Reviewed & Revised: 08/December/2021 to 26/December/2021
Accepted: 28 December 2021
Published: 5 January 2022

Peer-review Method
External peer-review was done through double-blind method.

URL: https://www.discoveryjournals.org/medicalscience

ABSTRACT

Background: Vitamin A (all-trans-retinol) derivatives are collectively referred to as retinoids. It is FDA approved to treat acne. We aimed to assess the prevalence, knowledge, attitude, and practice of using topical retinoids among all the region's populations. *Methods:* A cross-sectional study was carried out in all Saudi Arabian regions from October 2021 to November 2021 through a verified electronic-based self-administered questionnaire. *Results:* The survey questionnaire was completed by a total of 1,139 people. In Saudi Arabia, the frequency of acne among males and females is approximately 73.2 percent. The subject's knowledge of topical retinoids contraindicates is spread out between 44.6 percent and 77.5 percent. Approximately half of the study participants took topical retinoids without a prescription. *Conclusion:* In this study, the most commonly reported effect after using topical retinoids was a reduction in acne formation. This indicates that topical retinoids have a very good effect in the treatment of acne. The other preferable outcomes to use retinoids include preventing wrinkles and facial lines, as well as enhancing skin brightness. The majority did not seek a medical prescription for topical retinoids and did not utilize them properly, which lowered their satisfaction with the benefits of topical retinoids.

Keywords: Prevalence, Saudi Arabia, Vitamin A, Topical retinoids, Isotretinoin, Roaccutane, Side effects, Acne, large pores, Knowledge, Satisfaction.

1. INTRODUCTION

Isotretinoin (13-cis-retinoic acid), also known as Accutane or Roaccutaneis an orally active retinoic acid derivative for the treatment of severe refractory nodulocystic acne (National Library of Medicine (US), National Center for Biotechnology Information, Ward et al., 1984). Isotretinoin was first approved by the United States Food and Drug Administration (FDA) in 1982 (Layton, 2009). It affects the skin, mainly by reducing sebaceous gland size and sebum

production. Bacterial skin microflora is reduced as well as a result of altered sebaceous factors (Ward et al., 1984). It achieves this remarkable efficacy by affecting cell proliferation, cell cycle, and apoptosis (Nelson et al., 2006).

According to a recently published article based on a study conducted in Riyadh showed that 78% of respondents had acne (Alanazi et al., 2020). This is contrasted with the previously reported prevalence in Saudi Arabia, at 64.5% and 55.5% (Al Mashat et al., 2013; Alajlan et al., 2017). In general, acne is a common inflammatory skin disorder, and hence understanding the pathogenesis is of utmost importance. There are four main pathogenic factors for acne: sebaceous gland secretion stimulated by androgens, hyperkeratinization process and obstruction of sebaceous follicles, proliferation of *Propionibacterium acnes*, and inflammation (Toyoda & Morohashi, 2001). There are many side effects associated with taking isotretinoin, the most common of which is the dryness of the face, lips, and skin, in addition to constipation and joint pain (Al-Harbi, 2010). Other side effects in some patients include hypertriglyceridemia, hypercholesterolemia, and elevation of liver enzymes. The American Academy of Dermatology (AAD) recommends doing some laboratory tests at baseline for monitoring, which include liver function, serum cholesterol, and triglycerides tests (Zaenglein et al., 2020). Because of its teratogenic qualities, isotretinoin is contraindicated in all women of childbearing potential (Ward et al., 1984).

A study was conducted in 2018 to explore the public understanding and awareness of isotretinoin use in Al-Ahsa Governorate, showing a lack of satisfactory awareness of the safe use of isotretinoin among the study population (Younis et al., 2018). Another study conducted in 2010 in the Qassim Region showed that 85.9% of the study sample was well acquainted with the dryness and teratogenic side effects of the drug (Al-Harbi, 2010). The last study was conducted in 2020 to assess females' knowledge and use of isotretinoin in Saudi Arabia's western region, where 93% of the sample obtained isotretinoin by a doctor's prescription. Some 84.6% of users were informed of the drug's side effects. However, this study included females only, and 82.7% of the population were from Jeddah (Bakheet et al., 2020). However, no study was done about the use of topical retinoids in Saudi population. Our objective was to assess the prevalence, knowledge, attitude, and practice of using topical retinoids in Saudi Arabia.

2. METHODS

Study design

A cross-sectional study was conducted from October 2021 to November 2021 in all of Saudi Arabia's regions using self-administered electronic-based validated questionnaires in the Arabic language. After conducting a thorough assessment of the literature, the questionnaire was developed, and validity and reliability assessments were done

Validity assessment

A panel of three experts reviewed the questionnaire items in context to study objectives to assess its content validity. Assessment was firstly done independently, and then items with debates were discussed in details until having consensus. All suggested modifications were applied to improve the questionnaire validity till the final format used in the current study was obtained.

Reliability

The questionnaire showed acceptable level of reliability with Cronbach's Alpha of 0.73. The reliability of the questionnaire will not be improved by removing any of the items; hence all of them were preserved.

Inclusion and Exclusion criteria

All males and females aged 13 years or older, agreed on participating in this study, residing in Saudi Arabia were included. Participants aged less than 13 years old or residing outside of the Kingdom of Saudi Arabia were excluded.

Data collection

The self-administered electronic-based validated questionnaire was composed of 22 questions distributed across five sections according to the current AAD Guidelines regarding the following: participant prevalence, demographics data section, side effects, physician practice, and contraindications. Ethical approval for this study was obtained from the Institutional Review Board, Ministry of Health—Health Affairs, Makkah, Saudi Arabia, with approval number: H-02-K-076-0921-572.

Statistical analysis

Data were collected and analyzed using the statistical software IBM SPSS version 22 (SPSS Inc., Chicago, IL, USA).

Data analysis

After the data were extracted, it was revised, coded, and fed to statistical software IBM SPSS version 22 (SPSS Inc.). All statistical analysis was done using two-tailed tests. P-value less than 0.05 were statistically significant. Descriptive analysis based on frequency and percent distribution was done for all variables, including participants' bio-demographic data, topical retinoid uses and practice, indications, knowledge about topical retinoids, side effects, and level of users' satisfaction with topical retinoids. Cross tabulation was used to assess the distribution of topical retinoid uses among participants by their personal data. Relations were tested using the Pearson chi-square test and exact probability test for small frequency distributions to assess their significance.

3. RESULTS

A total of 1,139 participants fulfilled the inclusion criteria and completed the study questionnaire. Participants were aged 13–80 years with a mean age of 24.6 ± 7.7 years old. A total of 974 (85.5%) participants were females. An exact number of 643 (73.2%) had acne. Acne was noninflammatory (only facial pores) among 27.4% of them, mild (blackheads and whiteheads with a few erythematous papules and pigmentation) among 58.6%, moderate (blackheads and whiteheads with more erythematous papules and pigmentation) among 9.7%, and severe (erythematous papules, pustules, cyst, scar, and pigmentation) among 4.3% (Table 1).

Table 1 Bio-demographic data of the sampled Saudi population

Bio-demographic data	No	%
Age in years		
<20	196	17.2
20–29	757	66.5
30–39	90	7.9
40+	96	8.4
Gender		
Male	165	14.5
Female	974	85.5
Have acne?		
Yes	643	73.2
No	235	26.8
Severity of acne (n=643)		
Light: only facial pores	178	27.4
Mild: blackheads and whiteheads with few erythematous papules and pigmentation	381	58.6
Moderate: blackheads and whiteheads with more erythematous papules and pigmentation	63	9.7
Severe: erythematous papules, pustules, cyst, scar,and pigmentation	28	4.3

Table 2 (a and b) shows the prevalence, frequency, and causes of topical retinoids among the study participants. An exact number of 799 (70.1%) of the study respondents reported using topical retinoids. The most used types were Differin gel (49.9%), followed by Acretin cream at 0.05% (45.8%), Differin cream (35.8%), Acretin cream at 0.025% (21.2%), serum retinol (8.1%), and Pigmanorm (6.5%). Regarding reasons for the use of topical retinoids, the most reported cause by 69.6% of respondents was acne treatment, followed by the treatment of large pores (37.7%), black heads and white heads (37.3%), hyperpigmentation (35.7%), and wrinkles and fine lines (15.1%). Physicians prescribed topical retinoids for 36.1% of users and pharmacists for 16.4%. Meanwhile, 51.7% of participants used the topical retinoids by themselves, 26.9% of them used them once daily, 34.2% 3–4 times/week, and 38.9% 1–2 times/week. As for the duration of use, 47.3% used topical retinoids for less than 1 month, 31.8% for 2–3 months, and 11.9 percent for a period of more than six months. Furthermore, 36% of topical retinoids users had it regularly. An exact percentage of

83.1% use moisturizing creams while using topical retinoids and 60.5% use sunscreen while using topical retinoids. The most reported source of information regarding topical retinoids was social media (54.2%), followed by physicians (45.8%), family and friends (24.9%), pharmacists (17.6%), and study (1.4%).

Table 2a Prevalence, frequency, and causes of using topical retinoids among study participants

Use of topical retinoids	No	%
Have you ever used topical retinoids?		
Yes	799	70.1
No	340	29.9
Type of used topical retinoids		
Differin gel	399	49.9
Acretin cream 0.05%	366	45.8
Differin cream	286	35.8
Acretin cream 0.025%	169	21.2
Serum retinol	65	8.1
Pigmanorm	52	6.5
Triluma cream	24	3.0
Melano free cream	17	2.1
Other	8	1.0
Reasons for using topical retinoids		
To treat acne	556	69.6
To treat large pores	301	37.7
To treat blackheads and whiteheads	298	37.3
To treat hyperpigmentation	285	35.7
To prevent wrinkles and fine lines	121	15.1
Other	15	1.9
Who prescribed it for you?		
Physician	288	36.1
Pharmacist	131	16.4
Yourself	412	51.7
Friend/family	180	22.6
Frequency of using topical retinoids		
Once daily	215	26.9
3–4 times/week	273	34.2
1–2 times/week	311	38.9
How long have you continued using topical retinoids?		
<1 month	378	47.3
2–3 months	254	31.8
4–6 months	72	9.0
>6 months	95	11.9
Do you use topical retinoids regularly?		
Yes	288	36.0
No	511	64.0

Table 2b Prevalence, frequency, and causes of using topical retinoids among study participants

Use of topical retinoids, continued	No	%
Do you use moisturizing creams while using topical retinoids?		
Yes	664	83.1
No	135	16.9
Do you use sunscreen while using topical retinoids?		
Yes	483	60.5
No	316	39.5
Source of information regarding topical retinoids		
Social media	433	54.2
Physician	366	45.8
Friend/family	199	24.9
Pharmacist	141	17.6
Study	11	1.4

The distribution of knowledge about topical retinoids among the study participants is presented in Table 3. An exact percentage of 58.1% of participants are aware that topical retinoids are contraindicated in pregnancy. Some 52.2% know that topical retinoids are not recommended for use by lactating women, and 56.7% know that topical retinoids are contraindicated for use on the skin after sunburn. Approximately 42.7% are aware that topical retinoids are not recommended for use by people with eczema, 44.6% agree that topical retinoids cause an increase of acne initially, and 77.5% know that they should avoid sun exposure while using topical retinoids.

Table 3 Distribution of awareness of topical retinoids among study participants, Saudi Arabia

Knowledge regarding topical retinoids	Yes		No		Don't know	
	No	%	No	%	No	%
Do you know that topical retinoids are contraindicated in pregnancy?	464	58.1	106	13.3	229	28.7
Do you know that topical retinoids are not recommended for use by lactating women?	417	52.2	123	15.4	259	32.4
Do you know that topical retinoids are contraindicated for use on skin after sunburn?	453	56.7	122	15.3	224	28.0
Do you know that topical retinoids are not recommended for use by a person with eczema?	341	42.7	180	22.5	278	34.8
Do topical retinoids cause an increase of acne initially?	356	44.6	229	28.7	214	26.8
Do you have to avoid sun exposure while using topical retinoids?	619	77.5	109	13.6	71	8.9

Table 4 summarizes the side effects reported by participants taking topical retinoids. Specifically, 44.6% of users reported that topical retinoids cause an initial increase in acne, whereas 64.5% know that topical retinoids sometimes cause skin dryness, itchiness, redness, and scaling. When asked "when should you visit the doctor while using topical retinoids?," 66.6% of participants said when symptoms cause an allergic reaction, 50.4% said when blisters or vesicles form, 50.1% said in cases of eyelid swelling or red eye, and 38.9% said when light or dark patches on the skin appear. Answering the question what side effects did you experience while using topical retinoids?," 55.1% had scaling, 46.7% had skin dryness, 35.7% had redness, 29.5% had itching, 16% had increased acne, and 8.5% had photosensitivity. At the same time, 16% had no side effects.

Table 4 Side effects reported by topical retinoid users, Saudi Arabia

Side effects	No	%
Do topical retinoids cause an increase of acne initially?		
Yes	356	44.6
No	229	28.7
Don't know	214	26.8
Topical retinoids cause skin dryness, itchiness, redness, and scaling		
Never	132	16.5
Sometimes	515	64.5
Always	152	19.0
When should you visit the doctor while using topical retinoids?		
Symptoms of an allergic reaction	532	66.6
Formation of blisters or vesicles	403	50.4
Eyelid swelling or red eye	400	50.1
New onset of light or dark patches on the skin	311	38.9
Don't know	125	15.6
Side effects you experienced while using topical retinoids?		
None	128	16.0
Scaling	440	55.1
Skin dryness	373	46.7
Redness	285	35.7
Itchiness	236	29.5
Increase of acne	128	16.0
Photosensitivity	68	8.5
New onset of light or dark patches on the skin	55	6.9
Symptoms of an allergic reaction	14	1.8
Formation of blisters or vesicles	9	1.1

The level of satisfaction with the use of topical retinoids among the study participants is shown in Table 5. An exact percentage of 22.5% of topical retinoid users had less than 25% satisfaction level regarding its benefit, 41.3% had a satisfaction level of 25%–50%, 26% had a satisfaction level of 50%–80%, and only 10.1% had a satisfaction level exceeding 80%. As for the preferable outcome after using topical retinoids, decreased acne formation was the most reported (61%), followed by reduced large pores (38.5%), decreased blackheads and whiteheads (33.1%), improved and prevented wrinkles and fine lines (17.4%), and improved skin brightness (2.6%), whereas 2% had no benefits to report.

Table 5 Level of satisfaction for used topical retinoids among study participants, Saudi Arabia

Satisfaction	No	%
Level of satisfaction after using topical retinoids		
<25%	180	22.5
25%–50%	330	41.3
50%–80%	208	26.0
>80%	81	10.1
The most preferable outcome after using topical retinoids		
Decreases acne formation	484	61.0

Decreases large pores	306	38.5
Decreases blackheads and whiteheads	263	33.1
Improves and prevents wrinkles and fine lines	138	17.4
Improves skin brightness	21	2.6
None	16	2.0
Other	12	1.5

Table 6 demonstrates the distribution of used topical retinoids by participants' demographic data. The highest topical retinoid use was reported among participants aged 20–29 years (71.6%) compared to 65.6% of those aged 40 years or more, with no statistical significance (P=0.472). However, most of the participants who used topical retinoids were females (72.8%), whereas 54.5% were males, with a recorded statistical significance (P=0.001).

Table 6 Distribution of topical retinoid use by participants' demographic data

Personal data	Have you ever used topical retinoids?				P-value
	Yes		No		
	No	%	No	%	
Age in years					
<20	134	68.4	62	31.6	
20–29	542	71.6	215	28.4	0.472
30–39	60	66.7	30	33.3	
40+	63	65.6	33	34.4	
Gender					
Male	90	54.5	75	45.5	0.001*
Female	709	72.8	265	27.2	

P: Pearson X^2 test ** P < 0.05 (significant)*

4. DISCUSSION

The focus of this research was to determine the prevalence, knowledge, attitude, and practice of using topical retinoids in all regions of Saudi Arabia. A percentage of 73.2% represents the level of prevalence of acne among males and females in the Saudi population, with a mean age of 24.6 ± 7.7 years old, which is similar to a systematic review done in 2020 that the peak incidence of acne is in late adolescence and young adulthood (Ibrahim et al., 2021). Of 974 participants, 85.5% were females (Table 1), higher than reported in the previous cross-sectional study conducted in Jeddah, Saudi Arabia, which showed a prevalence level of 64.5% (Al Mashat et al., 2013). Similarly, a prevalence level of 78% was shown in the recently published cross-sectional study in Riyadh, Saudi Arabia (Alanazi et al., 2020).

Our study shows that the prevalence of topical retinoid use is higher in females (72.8%) aged 20–29 years old, as shown in Table 6, in comparison to (Alanazi et al., 2020) recently published cross-sectional study in Riyadh, Saudi Arabia, which showed a rate of 17.6% (Alanazi et al., 2020). A total of 799 (70.1%) of the study respondents reported using topical retinoids. The most used types were Differin gel (49.9%), followed by Acretin cream 0.05% (45.8%), Differin cream (35.8%), Acretin cream 0.025% (21.2%), serum retinol (8.1%), and Pigmanorm (6.5%). A systematic review in 2019 showed that Differin has superior tolerability among topical retinoids, which may explain why it is the most frequently used (Al-Mekhlafi et al., 2021). Regarding the reasons for topical retinoid use, the most reported cause that the respondents cited was treating acne (69.6%), followed by treating large pores (37.7%), treating blackheads and whiteheads (37.3%), treating hyperpigmentation (35.7%), and preventing wrinkles and fine lines (15.1%). Topical retinoids demonstrate a major role in inhibiting the formation of new lesions and microcomedones and treating active acne lesions; therefore, topical retinoids are a cornerstone in treating acne (See et al., 2018).

An exact percentage of 36.1% of all participants used topical retinoids prescribed by a physician, 16.4% by a pharmacist, and 51.7% by themselves. Regarding the frequency, 26.9% of users took topical retinoids once daily, 34.2% 3–4 times/week, and 38.9% 1–2 times/week. As for the duration of use, 47.3% used them for less than 1 month, 31.8% for 2–3 months, and 11.9 percent for a period of more than six months. Moreover, 36% of topical retinoid users took topical retinoids regularly. According to the responses, 83.1% of participants used moisturizing creams while using topical retinoids. However, 39.5% of participants did not use sunscreen while

using topical retinoids and this might be because half of the participants used topical retinoids by themselves, which reveals the importance of increasing the awareness to avoid direct sun lighting and wearing sunscreen while using topical retinoids. The most reported source of information regarding topical retinoids was social media (54.2%), followed by physicians (45.8%). Utilizing this source for correcting misconceptions and raising the population's level of awareness regarding the use of topical retinoids will hold promise for improving satisfaction and reducing the risk of skin irritation and other side effects.

In this study, 58.1% of participants knew that topical retinoids are contraindicated in pregnancy. As we mentioned previously, there is dearth of evidence about public awareness of topical retinoids' side effects in Saudi Arabia. A few studies have been undertaken in various parts of the country to measure community understanding of the usage of isotretinoin. These studies have shown that approximately 84%–94% of patients knew that isotretinoin is not recommended during pregnancy (Younis and Al-Harbi, 2019; Bakheet et al., 2020; Ibrahim et al., 2021; Al-Mekhlafi et al., 2021). As shown in this study, public awareness of topical retinoid contraindications was inadequate; this is linked to the importance of taking topical retinoids only after consulting a doctor or pharmacist to avoid teratogenicity and other side effects.

Furthermore, educate the public about it. Our findings showed that approximately 50% of participants would seek medical advice if they had eyelid swelling or redeye, symptoms of allergy, or formation of blisters and vesicles. Our data determined that the most reported side effect among participants was scaling (55.1%). Other side effects were skin dryness (46.7%), redness (35.7%), itchiness (29.5%), and initial increased acne (44.6%). These results may negatively affect the level of satisfaction after the use of topical retinoids. It is important to note that more education is needed for topical retinoid users, especially regarding serious side effects, such as anaphylaxis shock or severe allergies. A previous study reported better satisfaction levels and adherence with the implementation of individual education intervention (Myhill et al., 2017).

As previously reported, one of the challenges for this specific population is increased susceptibility to skin irritation. After the initiation of topical retinoid therapy, this controversy about racial differences still exists (See et al., 2018). More strategies considering skin irritation might be used, such as moisturizers, to enhance patients' satisfaction (See et al., 2018). The most reported outcome after using topical retinoids in this study was a decrease in acne formation (61%); this indicates an excellent effect for topical retinoids in acne treatment. The other preferable outcomes to using topical retinoids include preventing wrinkles and fine lines (17.4%) and improving skin brightness (2.6%).

The study's limitation was that the side effects and the outcomes of administering topical retinoids were all self-reported, although clinical evaluation and follow-up would provide more reliable information. In addition, there are no data about public awareness of topical retinoids used in Saudi Arabia to compare it with our results.

5. CONCLUSION

This study explored the prevalence, knowledge, attitude, and practice of using topical retinoids among the Saudi population. Around half of this study subjects used topical retinoids by themselves without medical prescription. Therefore, the vast majority of this study subjects had an unsatisfactory level regarding topical retinoids benefits. For future studies, the satisfaction level among users of topical retinoids with a medical prescription might be measured. As a result, more attention should be paid to educating this specific segment of the population regarding the safe use of topical retinoids based on proper medical advice.

Author's contributions

Sahar Alsharif: Supervised and Final Review of the data and final editing.

AshwaqAlosaimi: Literature review of previous studies, Data collection, Analysis of the collected data, Statistical analysis and calculation of the results, Writing an introduction, methodology and discussion.

Raghad Aldoobi: Literature review of previous studies, Data collection Analysis of the collected data, Statistical analysis and calculation of the results, Writing an introduction, methodology and discussion.

YousraAlturki: Literature review of previous studies, Data collection Analysis of the collected data, Calculation of the results, Writing an introduction, methodology and discussion.

Rawan Aldhahwani: Literature review of previous studies, Data collection, Analysis of the collected data, Statistical analysis and calculation of the results, Writing an introduction, methodology and discussion.

SuhaAlsayed: Literature review of previous studies, Data collection, Analysis of the collected data, Statistical analysis and calculation of the results, Writing an introduction, methodology and discussion.

Shahad Bukhari: Literature review of previous studies, Data collection, Analysis of the collected data, Statistical analysis and calculation of the results, Writing an introduction, methodology and discussion.

Ethical approval

This study was approved by Institutional Review Board, Ministry of Health - Health Affairs, Makkah, Saudi Arabia before starting the study (H-02-K-076-0921-572).

Acknowledgement

This study completion and aims could not have been achieved without the guidance, help and contribution of many colleagues. Their names may not all be listed, but their contribution is much appreciated and acknowledged.

Conflicts of interest

The authors declare that they have no conflict of interest

Funding

This study has not received any external funding.

Data and materials availability

All data associated with this study are present in the paper.

REFERENCES AND NOTES

1. Al Mashat S, Al Sharif N, Zimmo S. Acne awareness and perception among population in Jeddah, Saudi Arabia. J Saudi Soc Dermatol Dermatol Sur 2013; 17(2):47–9. doi: 10.1016/j.jssdds.2013.05.003
2. Alajlan A, Al Turki YA, AlHazzani Y, Alhowaish N, AlEid N, Alhozaimi Z, et al. Prevalence, level of knowledge and lifestyle association with acne vulgaris among medical students. J Dermatol Dermatol Surg 2017; 21(2):58–61. doi: 10.1016/j.jdds.2017.01.001
3. Alanazi TM, Alajroush W, Alharthi RM, Alshalhoub MZ, Alshehri MA. Prevalence of acne vulgaris, its contributing factors, and treatment satisfaction among the Saudi population in Riyadh, Saudi Arabia: A cross-sectional study. J Dermatol Dermatol Surg 2020; 24(1):33. doi: 10.4103/jdds.jdds_71_19
4. Al-Harbi M. Concerns and awareness of acne patients about isotretinoin in qassim region of saudiarabia. Int J Health Sci (Qassim). 2010; 4(1):47-51. PMID: 21475525; PMCID: PMC3068800.
5. Al-Mekhlafi R, Attiyah RE, Haddad YR, Salah LA. Awareness on Teratogenic Effects of Isotretinoin and Compliance with Precautionary Measures among Women of Childbearing Age in Makkah Province, Saudi Arabia. Obstet Gynecol Int 2021; 2021:9966300. doi: 10.1155/2021/9966300. PMID: 33936210; PMCID: PMC8055435.
6. Bakheet KMA, Alghanemi RG, Alsiyoufi AM, Abduljabbar M, Hariri J. Females' Knowledge and Use of Isotretinoin (Roaccutane) in the Western Region of Saudi Arabia. Cureus 2020; 12(12):e12148. doi: 10.7759/cureus.12148. PMID: 33489560; PMCID: PMC7813519.
7. Ibrahim AAM, Alshatri AA, Alsuwaidan S, Almutairi L, Aljasser N, Mahmoud MA, Alaseeri A, Almonysir A, Alotaibi B, Alrasheed B, Alfawaz M. Awareness of isotretinoin use and Saudi FDA pregnancy prevention program in Riyadh, Saudi Arabia: A cross-sectional study among female patients. Saudi Pharm J 2021; 29(6):527-532. doi: 10.1016/j.jsps.2021.04.013. Epub 2021 Apr 23. PMID: 34194259; PMCID: PMC8233528.
8. Layton A. The use of isotretinoin in acne. Dermato endocrinol 2009; 1(3):162-9. doi: 10.4161/derm.1.3.9364. PMID: 20436884; PMCID: PMC2835909.
9. Myhill T, Coulson W, Nixon P, Royal S, McCormack T, Kerrouche N. Use of Supplementary Patient Education Material Increases Treatment Adherence and Satisfaction Among Acne Patients Receiving Adapalene 0.1% Benzoyl Peroxide 2.5% Gel in Primary Care Clinics: A Multicenter, Randomized, Controlled Clinical Study. Dermatol Ther (Heidelb) 2017; 7(4):515-524. doi: 10.1007/s13555-017-0203-4. PMID: 29027127; PMCID: PMC5698202.
10. Nelson AM, Gilliland KL, Cong Z, Thiboutot DM. 13-cis Retinoic acid induces apoptosis and cell cycle arrest in human SEB-1 sebocytes. J Invest Dermatol 2006; 126(10):2178-89. doi: 10.1038/sj.jid.5700289. PMID: 16575387.
11. PubChem [Internet]. Bethesda (MD): National Library of Medicine (US), National Center for Biotechnology Information; 2004-. PubChem Compound Summary for CID 5282379, Isotretinoin; [cited 2021 Dec. 24]. Available from: https://pubchem.ncbi.nlm.nih.gov/compound/Isotretinoin
12. See JA, Goh CL, Hayashi N, Suh DH, Casintahan FA. Optimizing the use of topical retinoids in Asian acne patients. J Dermatol 2018; 45(5):522-528. doi: 10.1111/1346-8138.14314. PMID: 29611225; PMCID: PMC5969268.
13. Toyoda M, Morohashi M. Pathogenesis of acne. Med Electron Microsc 2001; 34(1):29-40. doi: 10.1007/s007950100002. PMID: 11479771.
14. Ward A, Brogden RN, Heel RC, Speight TM, Avery GS. Isotretinoin. A review of its pharmacological properties and

therapeutic efficacy in acne and other skin disorders. Drugs 1984; 28(1):6-37. doi: 10.2165/00003495-198428010-00002. PMID: 6235105.

15. Younis NS, Al-Harbi NY. Public Understanding and Awareness of Isotretinoin Use and Safety in Al Ahsa, Eastern Saudi Arabia. Ther Innov Regul Sci 2019; 53(5):618-622. doi: 10.1177/2168479018807677. PMID: 30380941.
16. Zaenglein AL, Pathy AL, Schlosser BJ, Alikhan A, Baldwin HE, Berson DS, Bowe WP, Graber EM, Harper JC, Kang S, Keri JE, Leyden JJ, Reynolds RV, Silverberg NB, Stein Gold LF, Tollefson MM, Weiss JS, Dolan NC, Sagan AA, Stern M, Boyer KM, Bhushan R. Guidelines of care for the management of acne vulgaris. J Am Acad Dermatol 2016; 74(5):945-73.e33. doi: 10.1016/j.jaad.2015.12.037. Erratum in: J Am Acad Dermatol 2020; 82(6):1576. PMID: 26897386.