

Section **Dermatology**

Original Article

Trends and Opinion of Isotretinoin Use for Acne Treatment by Dermatologists in Western Area of Saudi Arabia: A Cross-Sectional Survey

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ABSTRACT

Background: Acne is a common disease. Variety of treatment methods are available. Oral isotretinoin is an effective treatment but has some precautions. **Methods:** In this study, the attitude of dermatologists in western area of Saudi Arabia toward isotretinoin and their practice are being studied through online questionnaire survey. **Results:** More than half of responding dermatologists used the dose of 0.5mg per kg per day. Variable dosing, length of therapy, and laboratory investigations were reported. All responding dermatologists did laboratory investigations before commencing therapy and most did it as well after one month. Most of responding dermatologists thought it was safe to perform laser hair removal during or shortly (1-2 months) post isotretinoin therapy, but laser resurfacing was not thought to be safe to do while on therapy. The most common side effects encountered with oral isotretinoin were skin and lip dryness and cheilitis. All dermatologists counselled females for teratogenicity and pregnancy prevention.

There were variable responses to depression, blood donation abstinence and irritable bowel syndrome.

Conclusions: In conclusion, isotretinoin is an effective therapy for acne. There is a controversy among physicians on the dose, length of therapy and laboratory follow up. Controversies for depression, irritable bowel syndrome still exist.

Key words: Isotretinoin; dermatologists

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INTRODUCTION

Acne is a chronic disease affecting majority of adolescents. Depending on its severity and other factors different modalities of treatment are being used. Isotretinoin is the most effective oral therapy for acne treatment.^[1] Since its FDA approval on 1982, Isotretinoin is becoming widely prescribed to treat acne. With the wide availability and more knowledge of side effects, dermatologists nowadays use isotretinoin more widely and with varying doses to tailor for their patient's needs. Earlier guidelines were published to guide the usage of this medication.^[2] Few changes were made to these guidelines later such as

European Evidence-based (S3) Guidelines for the Treatment of Acne.^[3] Teratogenicity is a major issue. Additionally, biochemical monitoring is needed (namely lipids and liver enzymes). Although there are some recent publications warranting a less cautious approach and less frequent assessment,^[4] still this medication must be given and monitored by dermatologists. Several other issues such as the optimum dosage, length of therapy, laser treatment with the use of isotretinoin are still debatable. A previous questionnaire study to practicing dermatologists in USA showed variation in the prescription pattern.^[5]

In this study, the attitude of dermatologists in western area of Saudi Arabia toward isotretinoin and their practice are being studied.

METHODS

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<p>Website: www.iabcr.org</p> <p>DOI: 10.21276/iabcr.2017.3.3.4</p>	<p style="text-align: center;">Quick Response code</p> <div style="text-align: center;">  </div>

An electronic invitation to participate in the study was sent by e mails and social media (what's up application) to groups of dermatologists in western area of Saudi Arabia. The invitation contained a link to the survey questionnaire. It was administered through Survey Monkey survey tool and it was anonymous. No identifying information was collected as IP or email addresses. The questionnaire included demographic questions about the dermatologist (gender, age, position, and years of experience in dermatology, workplace and approximate number of acne cases usually seen per week). For dermatologists prescribing isotretinoin were asked to complete the questionnaire. Questions were related to the attitude and practice of isotretinoin. The study protocol was approved by the unit of biomedical ethics research committee at King Abdul-Aziz University Hospital (Reference No 249-15).

All data were exported from the questionnaire program to EXCEL 2013 for the statistical calculations.

RESULTS

In total 42 dermatologists have responded to the questionnaire. Twenty-eight were female (66.67), 12 male (28.57%) and 2 (4.76%) did not define with variable levels of experiences (from less than 5 years to more than 30 years of experience). More than 60% were in the age group of 31 to 50. Most of the study sample were specialist or consultant dermatologists with experience of 5 years or more in dermatology.

Respondents reported different numbers of acne cases seen per week: 11 (26.19%) see less than 10 patients, 20 (47.62%) see 11-25 acne patients, 4 (9.52%) 26-50 acne patients and 2 (4.76%) see 51-100 or more than 100 acne patients per week. Number of acne patients on isotretinoin currently varied as well with 9 (21.43%) of less than 5 patients currently under their care and using isotretinoin, 14 (33.33%) of 6-10 patients, 8 (19.05%) of 11-25 patients (Table 1).

Dermatologists responded variably to the question about the dose of isotretinoin with highest responses of 0.5 mg per Kg body weight 25 (62.5%). The length of therapy was reported mostly to be of 3-6 months and by calculating the cumulative dose by 11 dermatologists (36.67%) for each category (Figure 1). Two thirds of dermatologists 20 (66.67%) confirmed calculation of isotretinoin cumulative dose and 10 (33.33%) do not calculate the cumulative dose. The cumulative dose they aimed for included 1 mg/kg, 100 mg/kg, 120-150 mg/kg and 150 mg/kg.

Indications to use isotretinoin for acne was mostly to treat severe nodular acne by 25 (83.3%) responding dermatologists, followed by when systemic antibiotics and topical retinoid does not provide good control by 21 (70 %) dermatologists, when the patient suffers great psychological impact from his/her acne by 20 (66.67%) dermatologists, scarring acne by 19 (63.3 %) dermatologists, extensive back lesions by 17 (56.67 %) dermatologists, facial acne when it causes social or work disability by 16 (53.3%) dermatologists and extensive lesions area such as large area of back by 15 (50 %) dermatologists. Additionally, 2 (6.67

%) dermatologists can give it for all patients or if patient asks for it (Fig 2).

Table 1: Demographics of responding dermatologists:

Variables	Number (%)
Gender:	
male	12 (28.57%)
female	28 (66.67%)
did not define	2 (4.76%)
Age:	
less than 30years old	7 (16.67%)
31-40 years old	13 (30.95%)
41-50 years old	13 (30.95%)
more than 50 years old	8 (19.05%)
did not define	1 (2.38%)
Position:	
Resident	1 (2.38%)
Specialist	24 (57.14%)
Consultant	15 (35.71%)
Others	0
did not define	2 (4.76%)
Years of experience in dermatology:	
less than 5 years	1 (2.38 %)
5-10 years	16 (38.1 %)
11-20 years	8 (19.05%)
21-30 years	11 (26.19%)
more than 30 years	5 (11.90%)
did not define	1 (2.38%)
Work place:	
hospital based (government)	19 (45.24%)
hospital based (private)	11 (26.19%)
Clinic based	16 (38.1%)
Other (please specify)	3 (7.14%)
did not define	1 (2.38%)
Approximate number of acne cases seen per week:	
less than 10 patients	11 (26.19%)
11-25 patients	20 (47.62%)
26-50 patients	4 (9.52%)
51-100 patients	2 (4.76%)
more than 100 patients	2 (4.76%)
I do not know	0
did not define	3 (7.14%)
Currently how many patients approximately on isotretinoin:	
Less than 5 patients	9 (21.43%)
6-10 patients	14 (33.33%)
11-25 patients	8 (19.05%)
26-50 patients	2 (4.76 %)
More than 50 patients	3 (7.14%)
I do not know	2 (4.76 %)
did not define	4 (9.52%)

On questioning whether they consent female patients about contraception and risk of pregnancy, 10 (25.64%) responding dermatologists only verbally did, 18 (46.15%) always by written consent, 6 (15.38%) usually did by written consent and 5 (12.82%) only if married and there is a possibility of pregnancy. No one never consented female patients (Fig2).

On questioning about laboratory investigations of liver enzymes and lipid profile, all responding dermatologists to this question 29 (100%) did it before starting therapy, 21 (72.4%) did at 1 month after starting therapy as well, 8 (27.59%) after 1 month of changing the dose, 10 (34.48%) every 3-4 months and 2 (6.9%) if there is any complaint. Some dermatologists 4 (13.79%) added other times of 6 or

6-8 weeks and before finishing (figure 3a). On questioning how they manage elevations in cholesterol or triglycerides, 5 (17.86 %) thought that If mild give verbal advice about diet, 15 (53.57 %) thought that If mild give verbal advice about diet and repeat blood tests after one month, 11 (39.29%) Lower the dose of isotretinoin and repeat blood tests after one month, 6 (21.43 %) if mild give written advice about diet and repeat blood tests after one month, 2 (7.14 %) would lower the dose of isotretinoin, 8 (28.57%) would stop isotretinoin immediately and 6 (21.43%) would give lipid lowering agents. Some added that they would refer to medical doctor if persistent (Fig 3b).

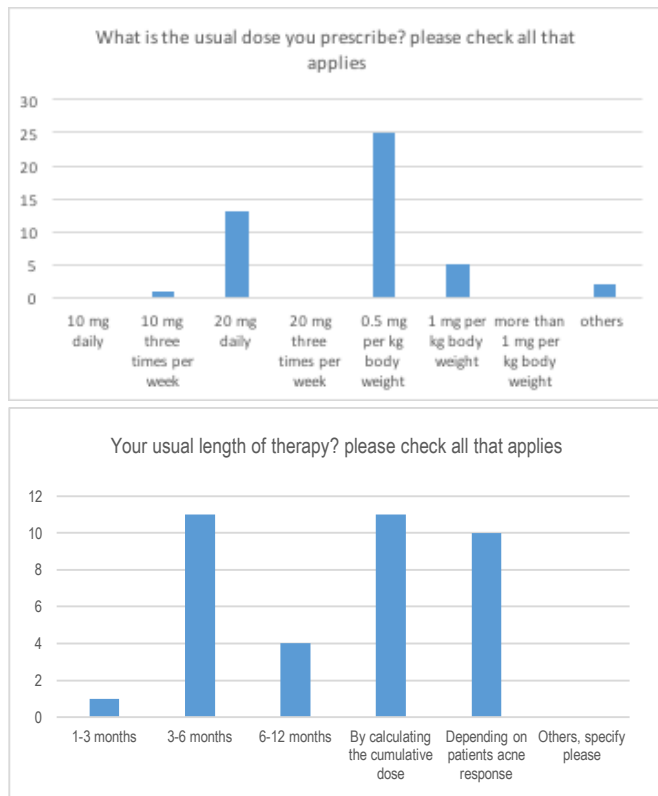


Fig 1: Responses to the question of the dose of isotretinoin and length of therapy used by responding dermatologists

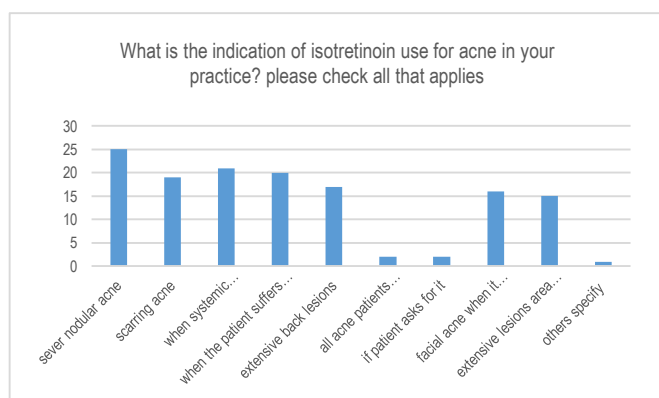
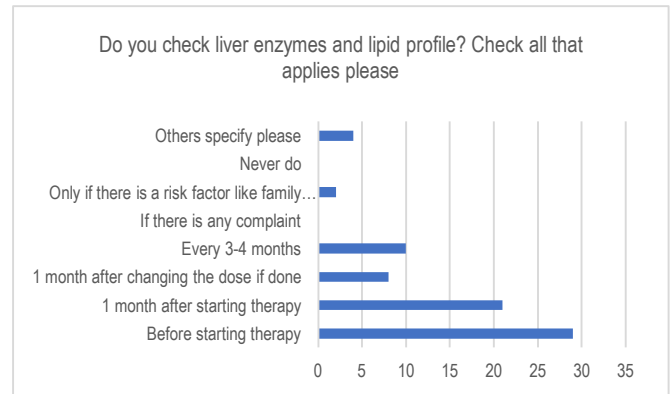


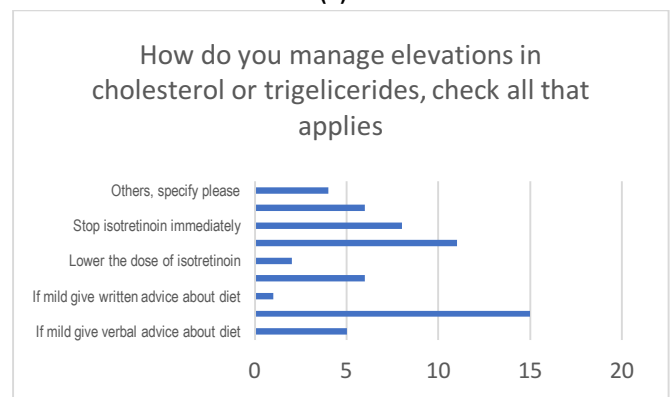
Fig 2: Responses to the question of the indications for isotretinoin use for acne:

Regarding laser hair removal advice with the usage of isotretinoin, most responding dermatologists thought that it is safe to do it during therapy, or immediately or 1-2 months after stopping treatment. No one thought that it should be delayed more than 1-2 months post treatment (Fig 4a). On

the other hand, for laser resurfacing, only one (5.56%) of responding dermatologists thought that it can be done during therapy or immediately after stopping therapy. Mostly they would wait for 1-2 months by 6 (33.33%), or 3-5 months by 2 (11.11%), or 6 months post treatment by 6 (33.33%). One (5.56%) thought that it should be after 1 year of stopping therapy (Fig 4b).



(a)

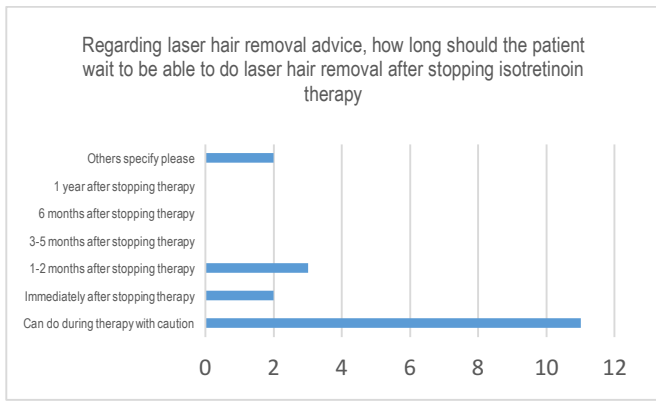


(b)

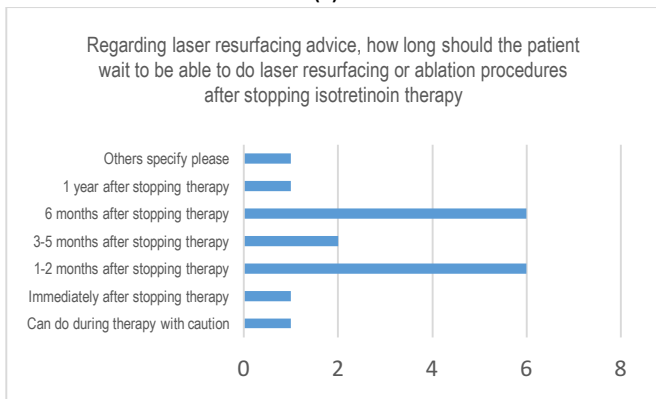
Fig 3: Responses to the question of the checking liver enzymes and lipids with isotretinoin therapy and management of elevations of cholesterol or triglycerides

On questioning about the recurrence rate of acne 3 years after stopping isotretinoin 1 (4.35%) of responding dermatologists thought it is <1%, 4 (17.39%) thought is 1-5%, 5 (21.74%) thought it is 6-10%, 10 (43.48%) thought it is 11-50% and 3 (13.04%) it was >50%.

The most commonly encountered side effects during oral isotretinoin therapy is skin dryness and lip dryness or chelitis. On questioning about the discussion of specific side effects planning to start on isotretinoin, all of responding dermatologists did for pregnancy control methods, dry skin, chelitis and photosensitivity and sun protection. For the other side effects, variable responses obtained. The least side effects encountered were pancreatitis, corneal ulcers, intracranial hypertension and menstrual disturbances (Fig 5). There were dermatologists who never discussed blood donation abstinence during therapy (6 out of 21 responding dermatologists to this question, 28.57%), intracranial hypertension symptoms (10 out of 22, 45.45%), possible association with depression (7 out of 22, 31.82%) and possible association with irritable bowel syndrome (7 out of 21, 33.33%) (Fig 6).



(a)



(b)

Fig 4: Responses to the question of laser use with isotretinoin therapy:

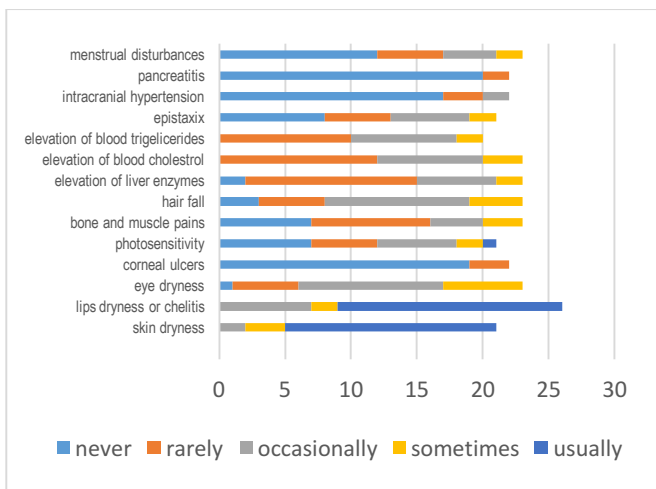


Fig 5: Responses to the question of the Side effects encountered during isotretinoin therapy for acne treatment

DISCUSSION

Oral isotretinoin is very effective treatment of acne vulgaris. Its use is limited to more severe cases or resistant cases owing to its side effects and monitoring recommendations. In this small study, dermatologists’ opinion about prescription of this medication and other issues were studied. More than half of dermatologists in our study used isotretinoin dose of 0.5 mg per kg body weight per day. Some have used the 20 mg per day fixed dose. Length of therapy mostly was of 3-6 months or by calculating the cumulative dose. There is controversy regarding the optimum dosing and the length of treatment.^[5] The usual dose is 0.3-1 mg/kg body weight.^[6,7] Low doses now being

investigated for their efficacy.^[8,9] On the other hand, higher doses is being advocated for less recurrence rate for acne.^[10] On the other hand, a recent study concluded that neither daily nor cumulative dosages influenced relapse of acne vulgaris in patients treated with different doses as long as treatment was continued for ≥ 2 months after the acne lesions had completely resolved.^[11]

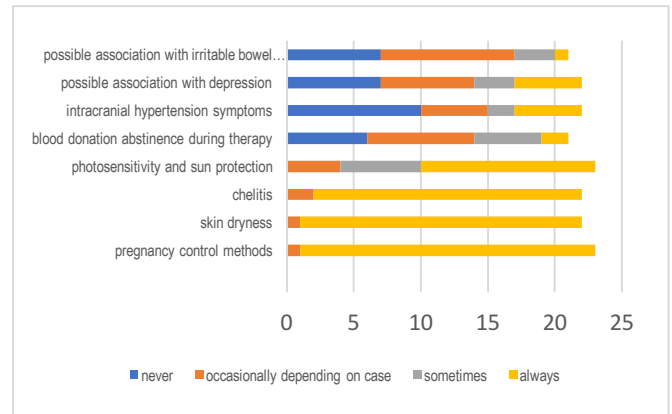


Fig 6: Responses to the question of : “Do you discuss side effects with patients planning to receive oral isotretinoin”:

Isotretinoin is indicated for the treatment of severe nodular acne, and appropriate for treatment of moderate acne that is resistant to management, producing physical scarring or psychological distress.^[12] This is reflected in our study group as most of responding dermatologists would prescribe oral isotretinoin to these indications. Interestingly, 2 dermatologists would do if the patient asks for it.

No dermatologist in our study has never consented a female patient about pregnancy and teratogenicity risk before starting isotretinoin. Nearly half of the responding dermatologists did it in written form. Some only did it only verbally or if there is possibility of pregnancy only (married females). Prior survey among dermatologists in Saudi showed that not all dermatologists would take a written consent and discuss the teratogenicity of isotretinoin.^[13]

In this study, all responding dermatologists did laboratory investigations before starting therapy with isotretinoin, and the majority (more than 70%) did it after 1 month as well. More frequent testing was not thought to be important as those before and 1 month after starting therapy. A very recent meta-analysis^[4] of the effect of isotretinoin on the laboratory changes suggest that monthly laboratory monitoring is not needed. Although there were significant changes of the lipids, these were not in the dangerous level. In this analysis only studies of 40 mg/day or more of isotretinoin users were included. For management of lipid abnormalities with isotretinoin therapy, there were different responses in our group of respondents. Half of dermatologists would have thought they would give verbal advice about diet if mild and repeat blood test after 1 month and very few (only 2) would give lipid lowering agents. Previous studies suggested using lipid lowering agents if lipid elevation were extremely high and to check lipids one month after stopping isotretinoin.^[14]

In regard to laser treatment with isotretinoin in this study, most dermatologists thought it was safe to perform laser hair removal while on treatment or immediately after stopping therapy by 1-2 months, while only one dermatologist thought it was safe to do laser resurfacing procedure during therapy. Mostly will wait for 1-6 months post-treatment. Safety of oral isotretinoin was assessed in 55 patients who had invasive acne scar treatment and laser hair removal was performed without any untoward effects^[15]. A recent survey of experts in cutaneous laser surgery at US concluded that “it would seem that the risk of performing laser procedures on patients receiving isotretinoin or having recently completed a course, as estimated and observed by cutaneous laser experts, is lower than the currently perceived risk among the general medical community”^[16].

In our study, most dermatologists from their experiences thought that recurrence rate of acne after stopping isotretinoin is more than 5 %. The rate of relapse of acne after isotretinoin therapy still debatable^[17]. In this study, a high relapse rate was noted (47.4%) after 12 months of stopping therapy in the group who received a cumulative dose of less than 220mg/kg. Lower relapse rate was noted in the group who received more than 220mg/kg (26.9%). Though, this is a high dose and is not usually aimed for.

The most common side effect encountered by dermatologists in this study were skin dryness, lip dryness and cheilitis as previous studies reported.^[18] The least side effects encountered were pancreatitis, corneal ulcers, intracranial hypertension and menstrual disturbances.

Several studies have been conducted to study the effect of the psychological impact of isotretinoin, mainly depression.^[19] Incidences from 1-11% of depression among isotretinoin users were reported.^[20] On the other hand, several studies demonstrated improvement in anxiety and depression scales with the use of isotretinoin^[21]. In two recent meta-analysis,^[22,23] concluded that Isotretinoin use is not associated with an increased risk of developing both ulcerative colitis and Crohn's disease. In our study, there were dermatologists who never discussed blood donation during therapy, intracranial hypertension symptoms, possible association with depression and possible association with irritable bowel syndrome. These could be due to the fact of they do not pay attention to these side effects or to the time limitation usually encountered during patient consultations at clinics. A recent guideline recommends monitoring symptoms and education about depression and inflammatory bowel disease.^[12]

This study explored the beliefs, opinions and practices of dermatologists in Saudi about issues related to isotretinoin therapy for acne treatment. The limitation of this study is its small size of participants. This is related to the response rate which could not be determined and the reluctance of some to answer possibly because they do not prescribe it or have some negative thoughts about the medication.

CONCLUSION

In conclusion, isotretinoin is an effective therapy for acne. There is still controversy on the dose, length of therapy and laboratory follow up and modalities of management of side effects namely the hyperlipidemia. Controversies for depression, irritable bowel syndrome still exist.

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