Community pharmacists' knowledge of isotretinoin safety

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ABSTRACT

الأهداف: استقصاء ممارسة ومعرفة الصيادلة العاملين في قطاع الصيدليات الأهلية في المملكة العربية السعودية فيما يخص صرف المستحضرات المحتوية على عقار آيزوتريتينوين (Isotretinoin) والتي تستخدم عن طريق الفم.

الطريقة: في عام 2012م تم إجراء دراسة مقطعية شملت الصيادلة العاملين في الصيدليات الأهلية في ثلاثة مدن في المملكة العربية السعودية. تم إعداد استبيان لجمع معلومات عن البيانات الديموغرافية ومدى معرفة الصيادلة المشاركين في الدراسة فيما يخص الاحتياطات ومحاذير الاستخدام المتعلقة بعقار آيزوتريتينوين وصرفه والإرشادات التي تقدم للمرضى.

النتائج: تم جمع 116 استبيان وذلك بمعدل استجابة يعادل (72.5%). وجد أن نصف المشاركين تقريبا (56%) على علم بتصنيف الخطورة لاستخدام العقار أثناء الحمل. ميز أغلب المشاركين (78%) وبشكل صحيح أن أخطر المضاعفات التي قد تحدث من استخدام العقار تتمثل في حدوث تشوهات في الأجنة بينما أوصى 6.2% من الصيادلة فقط بضرورة استخدام وسيلتين لمنع الحمل. ما يقارب خُمس الصيادلة قاموا بصرف المستحضر دون وصفة طبية. 11% من الصيادلة لم يقوموا بالاستفسار عن قيام النساء اللاتي سوف يستخدمن المستحضر عن قيامهن بفحص الحمل قبل صرف الدواء.

خاتمة: الصيادلة العاملين في الصيدليات الأهلية ليست لديهم المعرفة الكافية بمحاذير ومخاطر استخدام عقار آيزوتريتينوين. إضافة إلى ذلك، هناك نسبة عالية من الصيادلة يقومون بصرف العقار بدون وصفة طبية. من الضرورة وضع خطط لتقليل خطورة الأدوية وذلك لتقليل فرصة حدوث بعض الأعراض الجانبية.

Objective: To explore the practice and knowledge of community pharmacists in Saudi Arabia regarding dispensing isotretinoin-containing products.

Methods: This was a cross-sectional study conducted in 2012 that included community pharmacists from 3 cities in Saudi Arabia. A validated and piloted self-administered survey collected demographics and information on the pharmacist's knowledge regarding isotretinoin precautions, as well as his dispensing, and counseling practices.

Results: One hundred and sixteen questionnaires were returned with a 72.5% response rate. Only around half of the participants (56%) knew the correct pregnancy risk classification category for oral isotretinoin. Most participants (78%) correctly identified teratogenicity as the most serious risk associated with the use of oral isotretinoin. However, only 6.2% of the pharmacists recommended using 2 methods of contraception. Almost one-fifth of the pharmacists dispensed isotretinoin without a prescription. Finally, 11% of the pharmacists did not ask whether the patient performed a pregnancy test prior to dispensing oral isotretinoin.

Conclusions: Pharmacists at community pharmacies are not adequately aware of the risks for female patients using isotretinoin. Additionally, an alarming proportion of pharmacists dispense isotretinoin without a prescription. It is essential to implement risk minimization plans for certain medications to limit and prevent adverse drug reactions.

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Risk minimization plans (RMPs) are tools implemented to improve the safe use of medicines. They vary from communication with healthcare professionals and patients to restrictive access programs where specific requirements must be fulfilled to prescribe and/or dispense medication.[1] The efficacy of such programs is dependent on the cooperation and compliance of healthcare professionals with the directions and information provided by either the regulators or the marketing authorization holders. Oral isotretinoin, a vitamin A derivative, was first approved in the United States in 1982 for the treatment of acne vulgaris that is not responsive to other treatment options, such as topical preparations, and antibiotics.[2] Three years later, a study[3] showed that exposure to oral isotretinoin during pregnancy was associated with an increased risk of fetal malformation (relative risk=25.6), including cardiac, craniofacial, and neural malformations. From 1982 until 2002, more than 2000 reports of isotretinoin exposure during pregnancy were submitted to the United States Food and Drug Administration (U.S. FDA), with a total of 172 reporting congenital defects or anomalies.[4] Thus, several programs have been developed and implemented in the U.S. to reduce the risk of exposure to isotretinoin during pregnancy by providing educational materials and specific measures that should be applied before, during, and after oral isotretinoin treatment. The success of such programs likely depends on the awareness of the healthcare professionals, such as physicians, and pharmacists, as well as the patients. In Saudi Arabia, more than 240,000 packages of oral isotretinoin were sold in 2010.[5] However, at the time of writing this manuscript, there were no specific risk minimization requirements in place other than the warnings and precautions in the product leaflet. This may lead to an increase in the chance of exposure to oral isotretinoin during pregnancy. More worryingly, a recent study showed that dermatologists have a lower level of compliance with providing adequate counseling to women of childbearing age on the teratogenic effects of oral isotretinoin.[6] Indeed, the role of pharmacists in counseling patients is vital to ensure they understand the risks of their prescriptions. Therefore, the aim of this study was to investigate the knowledge and practice of pharmacists at community pharmacies when dispensing oral isotretinoin-containing products to women of childbearing age in Saudi Arabia.

Methods. The cross-sectional study was conducted in 3 different Saudi Arabian cities, Riyadh, Buraydah, and Ha'il, where the estimated number of private community pharmacies was 1200 (Riyadh), 150 (Buraydah), and 80 (Ha'il). To avoid the possible influence of a chain's policies on the pharmacists' practice and knowledge, the surveyors were instructed not to distribute the questionnaires to pharmacy branches within the same chain. The questionnaire comprised 13 questions, in addition to those relating to the demographics of the participants. The questions asked were on general knowledge of isotretinoin precautions, the patient's counseling by the pharmacist, and practice of pharmacists. The survey was validated and initially piloted in 20 pharmacies in Riyadh city, with minor changes made to the final form. Final year Doctor of Pharmacy students distributed the questionnaires from March through May 2012. Three days after distributing the survey, the completed forms were collected, and an additional week was allowed for uncompleted forms. Pharmacists who did not fill out the survey within this time frame were considered non-respondent.

Descriptive statistics were used to analyze the data. The data were analyzed using the Statistical Package for Social Sciences (SPSS version 18.0, Chicago, IL, USA). The Research Committee at the Medication Safety Research Chair at King Saud University approved the study.

Results. One hundred and sixty questionnaires (100 in Riyadh, and 30 each for Buraydah and Ha'il) were distributed with a response rate of 72.5% (n=116). The median age of participants was 30 years old, with a median of 7 years of total work experience. More than half of the participants (56%) knew the correct pregnancy risk classification category for oral isotretinoin (category X). Further, most participants (78%) responded that teratogenicity is the most serious risk associated with the use of oral isotretinoin (**Table 1**). Only 6.2% of the pharmacists recommended using 2 methods of contraception (hormonal and non-hormonal methods), while a quarter of them reported that they would recommend the use of oral contraceptives only as a pregnancy prevention method for women with childbearing potential (**Figure 1**). Almost one-fifth (n=21) of the pharmacists had dispensed oral isotretinoin without a valid prescription. Approximately 45% of the pharmacists claimed to always provide counseling to patients on the risk of teratogenicity. Of those surveyed, 11% did not enquire whether the patient had performed a pregnancy test prior to dispensing oral isotretinoin (**Table 2**).

Discussion. A study showed that most (76%) women who had been exposed to isotretinoin during pregnancy had not received contraceptive counseling,

thus highlighting the importance of proper counseling in minimizing fetal exposure to isotretinoin.[7] Unfortunately, this study reveals that community pharmacists in Saudi Arabia are unaware of the proper methods of contraception. Furthermore, a recent survey in Riyadh city revealed that only 62% of dermatologists recommended the use of 2 methods for contraception for women of childbearing age during the use of oral isotretinoin.[6]

Even in countries where pharmaceutical regulations are more advanced, such as those put forth by the European Union and the U.S. regulatory agencies, cases of pregnancy exposure are still occurring. For instance, in Europe, there is limited compliance with the Pregnancy Prevention Program (PPP), which may explain the 143 reported cases of pregnancy exposure to systemic isotretinoin.[8,9] In the U.S., efforts to decrease isotretinoin exposure during pregnancy have been implemented at several stages. Initially, the PPP consisted of educational materials for patients and healthcare professionals on the risks of birth defects and surveys for users and prescribers. However, because reports of pregnancy exposure exceeded 2000 by 2002, and since it was found that pregnancy tests were not performed prior to the use of isotretinoin in 36% of female patients,[10] the PPP was replaced by the System to Manage Accutane Related Teratogenicity (SMART) program. The updated system included a medication guide and introduced pharmacists to the procedure where they are responsible for ensuring the presence of all requirements to assure proper use of the medication. However, the implementation of SMART was not associated with a reduction in pregnancy exposure or compliance with pregnancy testing requirements.[11] Accordingly, in 2006 a risk minimization program named iPLEDGE was implemented. This program mandates the registration of prescribers, pharmacists, patients, and wholesalers to an internet-based program, and that each must comply with the directions intended to prevent female pregnant patients from receiving isotretinoin.[12] However, just as important to the design of these plans, regulators need to have the ability to assess their performance.

Table 1 - Pharmacist's knowledge of the risks associated with isotretinoin (n=116).

Knowledge	Frequency	(%)
Most serious risks of oral isotretinoin		
Teratogenicity	90	(77.6)
Hepatic side effects	79	(68.1)
Dry skin	63	(54.3)
Musculoskeletal side effects	20	(17.2)
Depression	20	(17.2)
Anemia	17	(15.0)
Do not know	1	(1.0)
At-risk patient group for using isotretinoin		
Pregnant women	110	(94.8)
Breastfeeding women	71	(61.2)
Women with childbearing potential	56	(48.2)
Children	50	(43.1)
Elderly people	22	(19.0)
Adults	9	(8.0)
Do not know	0	(0.0)

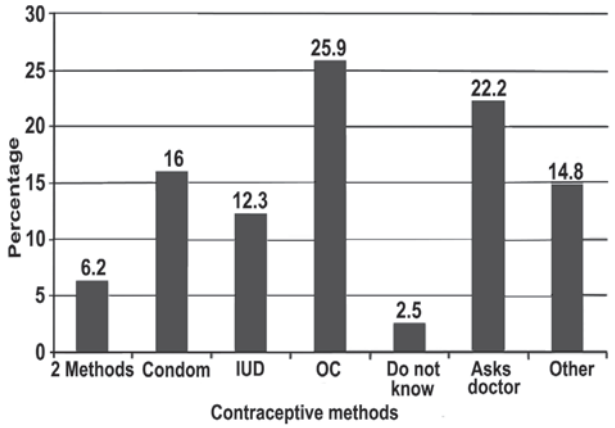

Figure 1 - Recommended methods of contraception. IUD - intrauterine device, OC - oral contraceptives

Table 2 - Pharmacists' practice when dispensing oral isotretinoin.

Pharmacists' practice	Always	Usually	Sometimes n=116 (%)	Rarely	Never
Before dispensing oral isotretinoin to a female, I ask the patient or her guardian about whether she is married or not.	66 (56.8)	17 (14.6)	15 (12.9)	6 (5.1)	11 (9.5)
When dispensing oral isotretinoin, how often do you provide counseling to a female patient or her guardian about isotretinoin risks?	52 (44.8)	31 (26.7)	25 (21.5)	6 (5.1)	1 (1.0)
I inquire about whether pregnancy tests are carried out or not before dispensing the medication	45 (38.7)	29 (25.0)	19 (16.4)	9 (7.7)	13 (11.2)
How often do patients ask about the risk of teratogenicity and the use of oral isotretinoin?	9 (7.7)	21 (18.1)	31 (26.7)	37 (31.8)	17 (14.6)

The infrastructure in developing countries may create another barrier to the implementation of RMPs similar to iPLEDGE. Thus, there is a need to enhance the knowledge of both the physicians and pharmacists on the proper use of isotretinoin and its risk of teratogenicity. Professional societies, with the support of marketing authorization holders, could have an important role in promoting the safe practice by hosting educational events. Awareness programs should also target patients as a key player in the medication utilization process. It is worth noting that, while almost half of the participants identified the correct pregnancy risk classification, a greater proportion (78%) reported that teratogenicity is a known risk of using oral isotretinoin. This discrepancy could be attributed to differences in the educational background of the participants or the ambiguity of the U.S. pregnancy risk classification system. However, this issue needs to be addressed by more research.

A limitation of our study is the lack of female pharmacists, which is due to work regulation restrictions that make the participation of female pharmacists at retail pharmacies not possible. Additionally, a more representative sampling that covers a wider geographical area would strengthen the findings of this survey.

This study demonstrated that almost 20% of pharmacists dispense oral isotretinoin without a valid prescription. However, we speculate that the proportion of those dispensing isotretinoin without a prescription in this study might actually be an underestimate, due to participants' fear of liabilities for illegitimate dispensing. Consistent with our findings for isotretinoin, another study of community pharmacists in Saudi Arabia showed that the vast majority of pharmacists dispensed antibiotics without asking for a prescription.[13] Further work is needed to determine the reasons for such noncompliance.

In conclusion, this study shows that pharmacists at private community pharmacies are not adequately aware of the proper use and risks of oral isotretinoin for female patients. Therefore, greater attention should be focused on training and educating pharmacists in order to enhance the safe use of such a high-risk product. We recommend the implementation of tools to enhance the safe use of isotretinoin, and imposing more effective regulations to limit the practice of illegitimate dispensing of prescription medicines, particularly oral isotretinoin, in Saudi Arabia.

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