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Clinical pharmacist role in improving the knowledge and outcomes in patients using isotretinoin: A randomized, controlled study☆

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ABSTRACT

Objective: To evaluate the role of a clinical pharmacist in improving knowledge and outcomes among isotretinoin users.
Methods: Patients were randomly assigned to an intervention group (received education about isotretinoin by a clinical pharmacist in addition to the physician) and a control group (received routine education by the physician), then followed for three months. Patients' knowledge about isotretinoin optimal use, and side effects and their management and other outcomes were measured in both groups at baseline and at follow up after three months using a validated questionnaire.
Results: Two-hundred and three patients completed the study; 103 were in the intervention group and 100 in the control group. The knowledge improvement between baseline score and follow-up score was greater in the intervention group (mean = 2.835 ± 1.329) compared to the control group (mean = 0.530 ± 0.784) with mean differences = −2.30495, $P < 0.001$.
Conclusion: Implementing clinical pharmacy services in dermatology clinics can positively increase patients' level of knowledge about isotretinoin, which could reduce the severity of its side effects. Therefore, improving patients' quality of life, and improvement in acne.
Practice implications: Implementing clinical pharmacist services to patients using isotretinoin is feasible in an outpatient setting. Clinical pharmacist counseling and education improve the medication knowledge among patients who use isotretinoin.

1. Introduction

Acne vulgaris (AV) is a chronic inflammatory disorder of the sebaceous glands [1]. AV is considered the eighth most prevalent disease worldwide, affecting about 9.4% of the population [2], and represents the third most prevalent skin condition [3]. Many factors are involved in the development of acne, such as increased sebum production, hormones dysregulation, stress, diet, follicular

☆ The trial is registered at ClinicalTrials.gov (identifier: NCT05839223).

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hyperkeratinization and inflammation [4]. AV is classified according to severity into mild, moderate, and severe [5].

Isotretinoin is a vitamin A derivative, which was first approved by the US FDA in 1982 [6]. It is indicated for severe and moderate acne that does not respond to other therapies [7]. Isotretinoin remains the most effective antiacne treatment, resulting in long-lasting remission and significant improvement. It affects sebum production, acne lesions and scarring, cellular differentiation, and many others. Furthermore, it has anti-inflammatory properties [8].

Several side effects are associated with isotretinoin that ranges from mild to life threatening. These side effects include dry mouth, nose, and eyes, decreased night vision, dry skin, muscle aches, joint pains, increased sunburn susceptibility, tiredness, and headaches [9]. Side effects like mood change, insomnia, hair loss, abdominal pain, and skin fragility are less common. Other miscellaneous adverse effects are hypertriglyceridemia, decreasing serum high-density lipoprotein levels (HDL), elevating serum cholesterol, and increasing liver enzymes [10]. However, the most significant side effect is teratogenicity [11].

A recent study showed that the knowledge of Jordanian patients who used isotretinoin was moderate and one third of them were not aware of the teratogenicity side effect of the medication [12]. Another study in Saudi Arabia showed that most patients do not have sufficient knowledge about isotretinoin, do not know how to deal appropriately with the side effects, and there are no specific risk minimization tools other than warnings in product leaflet [13]. Most patients receive counseling about their medications from doctors who have insufficient time to teach the patients about their medication. Isotretinoin is considered a dangerous drug if it is misused [14,15]. The clinical pharmacist can play a major role in providing appropriate patient education and continuous follow up [16]. The role of clinical pharmacist in detecting, reporting, and preventing medication errors was investigated and proved to have an essential role in reducing medication errors in different hospital settings [17,18]. Moreover, educational programs established by clinical pharmacists significantly enhanced the knowledge, attitude, and practice of healthcare professionals toward adverse drug reaction reporting [19].

This study aimed to assess the impact of a clinical pharmacist's intervention on improving knowledge about isotretinoin optimal use, and side effects and their management and other outcomes (impact of side effects on daily life and normal activities, improvement of acne condition, and satisfaction with the provided education).

2. Methods

2.1. Study design and subjects

This study was a parallel randomized controlled multicenter trial conducted in dermatology outpatients' clinics in three different hospitals in Jordan: King Abdullah University Hospital (KAUH), Princess Basma Hospital (PBH), and Prince Rashid Hospital (PRH). The study was conducted over the period from September/2020 to February/2021. The study protocol received ethical approval from the Institutional Review Board committee at Jordan University of Science and Technology (JUST IRB # 491/2020) and the Ministry of Health of Research on Human Committee (173/2020).

Patients were initially screened for eligibility during their routine visit to the outpatient dermatology clinics. The inclusion criteria were adult patients aged 18 years and above, diagnosed with moderate or severe acne, taking standard isotretinoin dose, and willing to participate in the study and do a follow-up. The exclusion criteria were patients with any contraindication to isotretinoin who cannot take the medication, like pregnant women and women who intend to become pregnant, breastfeeding women, and patients with any renal or hepatic compromise or any pre-existing hyperlipidemia patients. All patients met the inclusion criteria were invited to participate in the study. The patients were informed about the study objectives, their voluntary participation, and that withdrawal from the study was possible whenever they wanted. The patients were included in the study after they signed the informed consent form. The recruited patients were randomly allocated into intervention and control groups with a 1:1 ratio. Randomization using a simple technique was adopted; even numbers were assigned for intervention and odd numbers for control. The clinical pharmacist was responsible for randomization, enrolment, and assignment of patients into study groups (intervention vs. control), bassline measurements, providing pharmaceutical education about isotretinoin for the intervention group, and follow up phone calls for both groups. The patients and healthcare providers did not know who was enrolled in the intervention or control group.

To calculate the sample size, the following assumptions were employed: 30% effect size (difference in adherence to recommendation between control (50%) and intervention group (80%)), alpha = 0.05, beta = 0.8, and enrollment ratio = 1. The minimum required sample size was 45 patients in each group. The sample size was intended to be 100 patients at least in each group, to adjust for any dropout and increase the statistical power. These assumptions were determined based on a similar study [20]. The sample size was calculated by OpenEpi, Version 3, open-source calculator—SSCohort/RCT [21].

The primary outcome was patients' knowledge on optimal use, side effects and the management of the side effects of isotretinoin, while the secondary outcomes were the improvement of acne condition, the impact side effects on daily life and normal activities, and patients' satisfaction with the provided education.

2.2. Study outcomes measurements at baseline

Patient knowledge was measured through a set of questions adapted from a validated questionnaire used previously to measure patient knowledge on isotretinoin in Jordan [12]. Arabic and English questionnaire versions were taken from this study, and the Arabic form was used for data collection. The adapted questionnaire was reviewed for content validity by experts in the field. Minor changes were made based on their comments. Also, a pilot study was performed (n = 10) to test easy understanding and clarity of the questions in relation to the research objective and to ensure the usability of the data-collection method.

The baseline questionnaire consisted of two sections comprised of questions related to demographics, and patient knowledge of isotretinoin. Close-ended questions (10 questions) that measured patient's knowledge and their awareness of isotretinoin use in terms of side effects (dryness, teratogenicity, possible abnormality in lab tests, constipation, shortness of breath, and joint pain) and how to manage them, patient's knowledge about the need for a prescription to use the drug, the need of monitoring tests, how to use isotretinoin properly, and if they have knowledge about precautions in certain situations. The degree of knowledge and awareness of correct practice was calculated as a total score; the knowledge score could take the values of 0 (no knowledge) to 10 (perfect knowledge).

The follow up questionnaire consisted of the 10 knowledge questions, in addition to five questions about clinical improvement in acne after initiating the treatment from the patient's view, the effect of the side effects on daily life and normal activities, and patients satisfaction with provided information (if they needed more information about the medication, and side effects and how to manage them, and if they think they needed more follow up).

2.3. Study intervention and follow up

The recruited patients in the intervention group received pharmaceutical care/education provided by the clinical pharmacist about the followings: i) the importance of adherence to the drug and recommendations of proper use, ii) the correct method of taking it, iii) the periodic laboratory tests (lipid, liver, and pregnancy test), iv) common and serious side effects and how to properly manage/avoid them, and v) precaution/warnings about the medication. In addition to the verbal communication, written information (educational brochure) containing the most important points mentioned in the medication leaflet about the safe use of isotretinoin was given to patients by the end of the session. On the other hand, patients in the control group received regular healthcare evaluation by the physician (dermatologist). They were seen by the clinical pharmacist for data collection purposes only using the baseline questionnaire without providing any education. The time spent with patients took about 15–20 min for the control group and 30–35 min for the intervention group. Three months after the first visit (baseline), patients in both groups were followed up via mobile phone to collect information about knowledge (using the same knowledge questionnaire) and other outcomes using the five questions. To maintain our ethical role as healthcare providers, patients in both groups were provided with educational material verbally at the end of the study.

2.4. Statistical analysis

Per protocol analysis was used in this study. Descriptive statistics of categorical and continuous variables were calculated. The frequency and percentage were calculated for categorical variables, while mean and standard deviation were calculated for continuous variables. The differences in participants' responses were examined using the Chi-square test (between intervention and control groups) and McNamara's test (between baseline and follow-up encounters of the same group) for the categorical outcomes. The statistical significance was set at p-value ≤ 0.05. The analysis was carried out using SPSS version 23.

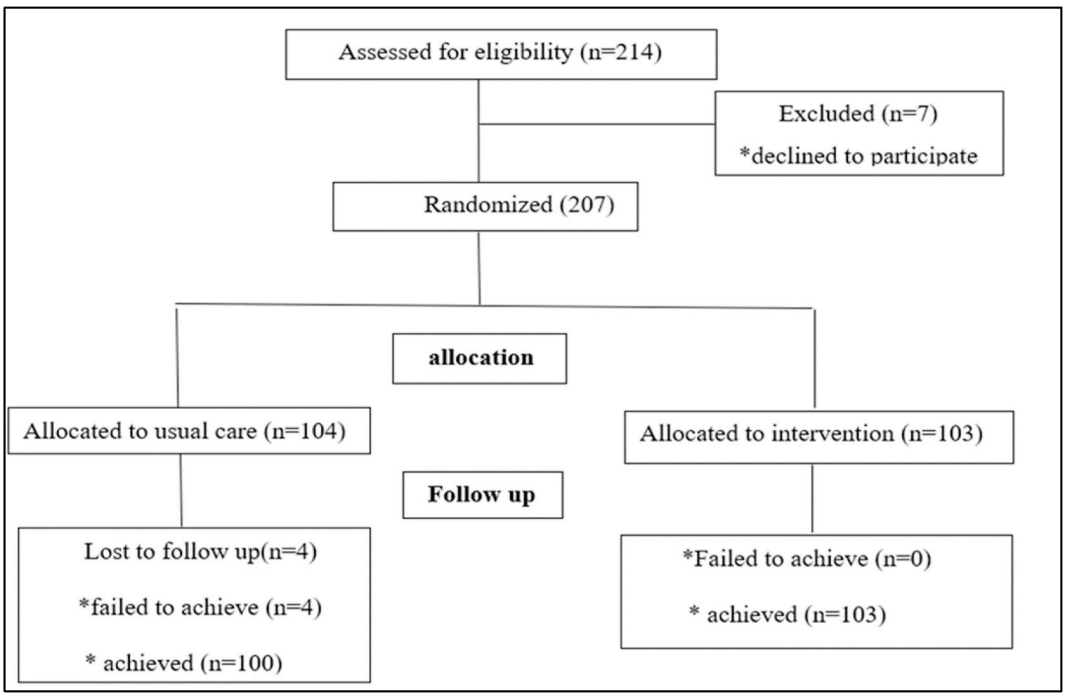

Fig. 1. Patient recruitment flowchart.

3. Results

3.1. Demographics of respondents

A total of 207 patients using isotretinoin were randomly recruited to participate in the study. Four patients missed answering phone at follow-up, so they were excluded from the study. The response rate was 96.7%, and 203 patients completed the study and were included in the final analysis, as shown in Fig. 1.

Most of the respondents were females (88.2%), and the mean age for them was (21.52 ± 2.92). There were no significant differences in baseline demographic and clinical characteristics of the study participants between both groups except for monthly income

Table 1
Baseline demographic and clinical characteristics of the study population.

Characteristics	Total		Intervention group		Control group		P-value
	n	%	n	%	n	%	
Gender							
Female	179	88.20	91	88.30	88	88	0.939
Male	24	11.80	12	11.70	12	12	
Age							
16–20	86	42.40	41	39.80	45	45	0.628
21–25	100	49.20	51	49.50	49	49	
26–30	13	6.40	7	6.80	6	6	
31–35	4	1.90	4	3.90	0	0	
Marital status							
Single	196	96.90	98	95.10	98	98	0.265
Married	7	3.10	5	4.90	2	2	
Educational level							
School	21	10.30	10	9.70	11	11	0.562
College	4	2	2	1.90	2	2	
Bachelor	173	85.20	87	85	86	86	
Postgraduate studies	5	2.50	4	3.90	1	1	
Profession							
Student	146	71.9	74	71.80	72	72	0.525
Unemployed	25	12.3	10	9.70	15	15	
Non-medical profession	16	7.9	10	9.70	6	6	
Medical profession	16	7.9	9	8.70	7	7	
Residential area							
Irbid	158	77.80	80	77.70	78	78	0.949
Alzarqa'a	3	1.50	2	1.90	1	1	
Almafraq	13	6.40	7	6.80	6	6	
Amman	19	9.40	9	8.70	10	10	
Jerash	4	2	2	1.90	2	2	
Ajloun	5	2.50	2	1.90	3	3	
Maan	1	0.50	1	1	0	0	
Monthly income							
Below 500	28	13.80	17	16.50	11	11	0.032
500–100	111	54.70	47	45.60	64	64	
Above 100	64	31.50	39	37.90	25	25	
Health insurance							
Yes	197	97	99	96.10	98	98	0.428
No	6	3	4	3.90	2	2	
Strength and dose of isotretinoin per day							
10	2	1	2	1.90	0	0	0.612
20	55	27.10	26	25.20	29	29	
30	26	12.80	14	13.65	12	12	
40	117	57.60	60	58.30	57	57	
60	3	1.50	1	1	2	2	
Period since starting the current isotretinoin course (months):							
Newly diagnosed	42	20.70	22	21.40	20	20	0.603
First month	42	20.70	23	22.30	19	19	
Second month	51	25.10	26	25.20	25	25	
Third month	57	28.1	29	28.20	28	28	
Fourth month	11	5.40	3	2.90	8	8	
Body mass index							
Under 18.5	23	11.40	11	10.80	12	12	0.783
18.5–24.9	143	70.40	70	68.60	73	73	
25–29.9	28	13.90	15	14.70	13	13	
30–34.9	7	3.50	5	4.90	2	2	
35–39.9	2	1	1	1	1	1	
Total	203	100	103	50.7	100	49.3	

with P-value = 0.032, Table 1. Most patients in both study groups (99%) had no chronic disease.

3.2. Patients' knowledge about isotretinoin use

Patients' knowledge about isotretinoin treatment for both groups at baseline and at follow-up is shown in Table 2. At baseline, overall patients' average knowledge score was moderate (6.5 out of 10), and only eight patients from both groups answered the ten questions correctly.

There was no significant difference in overall knowledge score between the intervention and control groups, with a mean of (6.47 for the intervention vs. 6.57 for the control group). While results at follow-up showed a significant difference in the mean score between the intervention and control group (9.3 vs. 7.1, P-value <0.001). The average difference in the overall knowledge score (before and after the education process) was 1.6995 ± 1.589; P-value< 0.001.

Table 3 shows patients' knowledge within each group at baseline and follow up. The percentage of correct answers was significantly higher at follow-up compared to the baseline for most knowledge questions in the intervention group with P- value < 0.05. On the other hand, the percentage of correct answers were significantly higher at follow up compared to baseline for the five out of ten knowledge questions in the control group. And the average difference in overall knowledge was statistically different between the intervention and control group (2.835 ± 1.329 for the intervention and 0.530 ± 0.784 for the control group).

3.3. Patient's opnion on the improvement of acne condition, impact of the side effects on daily life and normal activities, and satisfaction with the provided education

Additional questions were asked at follow-up regarding patients' opinion about acne improvement, the impact of side effects on their daily activities, and their satisfaction with provided drug information. As shown in Table 4. There were statistically significant differences in all these three dimensions between the intervention and control groups.

There was a significant difference between the intervention and control group with regards to the impact of side effects on normal activities, P-value<0.001; 76.6% of patients in the intervention group reported no effect or a weak effect on daily activity compared to 48% of the control group.

About 47% of the intervention group reported excellent improvement in their acne compared to 30% from the control group, P-value = 0.048.

Table 2
Patients knowledge regarding the use of isotretinoin between intervention group and control group at baseline and at follow up.

Knowledge items	Intervention group (baseline) n (%)	Control group (baseline) n (%)	P-value	Intervention group (follow up) n (%)	Control group (follow up) n (%)	P-value
knowledge about common side effects						
Yes	6 (5.8)	2 (2)	0.28	49 (47.6)	3 (3)	<0.001
No	97 (94.2)	98 (98)		54 (52.85)	97 (97)	
isotretinoin can be used during pregnancy[a]						
Yes	10 (9.7)	10 (10)	0.944	0 (0)	4 (4)	0.057
No	93 (90.3)	90 (90)		103 (100)	96 (96)	
isotretinoin can be used without prescription*						
Yes	6 (5.8)	5 (5)	0.795	0 (0)	5 (5)	0.028
No	97 (94.2)	95 (95)		103 (100)	95 (95)	
No need to have laboratory monitoring during isotretinoin use[a]						
Yes	4 (3.9)	5 (5)	0.745	0 (0)	5 (5)	0.028
No	99 (96.1)	95 (95)		103 (100)	95 (95)	
Should drink water to reduce the dryness						
Yes	99 (96.1)	98 (98	0.683	100 (97.1)	98 (98)	0.675
No	4 (3.9)	2 (2)		3 (2.9)	2 (2)	
Should use sunblock to reduce sensitivity to the sun						
Yes	99 (96.1)	99 (99)	0.121	103 (100)	99 (99)	0.493
No	4 (3.9)	1 (1)		0 (0)	1 (1)	
It is preferred to take isotretinoin with fatty foods						
Yes	70 (68)	74 (74)	0.343	103 (100)	81 (81)	<0.001
No	33 (32)	26 (26)		0 (0)	19 (19)	
Can be donate blood during isotretinoin[a]						
Yes	67 (65)	70 (70)	0.451	0 (0)	57 (57)	<0.001
No	36 (35)	30 (30)		103 (100)	43 (43)	
Woman can lactate while using isotretinoin[a]						
Yes	72 (69.9)	72 (72)	0.742	9 (8.7)	60 (60)	<0.001
No	31 (30.1)	28 (28)		94 (91.3)	40 (40)	
Can be made laser or wax during isotretinoin[a]						
Yes	66 (64.1)	55 (55)	0.188	5 (4.9)	40 (40)	<0.001
No	98 (95.1)	60 (60)		98 (95.1)	60 (60)	

The correct answer is yes unless otherwise indicated.
[a] The correct answer is no.

Table 3
Patient knowledge regarding isotretinoin use within each group at baseline and at follow up.

	Intervention group-baseline n (%)	Intervention group-follow up n (%)	P -value	Control group- baseline n (%)	Control group-follow up n (%)	P-value
Knowledge about common isotretinoin side effects						
Yes	6 (5.8)	49 (47.6)	<0.001	2 (2)	3 (3)	0.564
We can use isotretinoin during pregnancy[a]						
No	93 (90.3)	103 (100)	0.0016	90 (90)	96 (96)	0.0339
We can use the drug without prescription[a]						
No	97 (94.2)	103 (100)	0.0143	95 (95)	95 (95)	0.95
No need to have laboratory monitoring during isotretinoin use[a]						
No	99 (96.1)	103 (100)	0.0455	95 (95)	95 (95)	0.95
We should drink water to reduce the dryness						
Yes	99 (96.1)	100 (97.1)	0.705	98 (98)	98 (98)	0.98
We should use sunblock to reduce sensitivity to the sun						
Yes	99 (96.1)	103 (100)	0.045	99 (99)	99 (99)	0.317
It is preferred to take isotretinoin with fatty foods						
Yes	70 (68)	103 (100	<0.001	74 (74)	81 (81)	0.0196
We can donate blood during isotretinoin [a]						
No	36 (35)	103 (100)	<0.001	30 (30)	43 (43)	0.0008
Woman can lactate while using isotretinoin [a]						
No	31 (30.1)	94 (91.3)	<0.001	28 (28)	40 (40	0.0027
We can make laser or wax during isotretinoin [a]						
No	37 (35.9)	98 (95.1)	<0.001	45 (45)	60 (60)	0.0011

The correct answer is yes unless otherwise indicated.
[a] The correct answer is no.

Table 4
Patient's Opnion on the Improvement of Acne Condition, Impact of the Side Effects on Daily Life and Normal Activities, and Satisfaction with the Provided education.

	Intervention group n (%)	Control group n (%)	P value
In your opinion, how much is the improvement of your acne			
Excellent	48 (46.6)	30 (30)	0.048
Very good	50 (48.5)	56 (56)	
Good	5 (4.9)	5 (5)	
How does the side effects affect your daily life and your normal activities			
Big impact	0 (0)	4 (4)	<0.001
Moderate impact	24 (23.3)	48 (48)	
Weak impact	73 (70.9)	46 (46)	
No impact	6 (5.8)	2 (2)	
Do you think you needed to explain more about the drug in general			
Yes	0 (0)	52 (52)	<0.001
No	103 (100)	48 (48)	
Do you think you need more explanations about the side effects and how to avoid it			
Yes	0 (0)	71 (71)	<0.001
No	103 (100)	29 (29)	
Do you think you need more follow-up by the doctor			
Yes	18 (17.5)	44 (44)	<0.001
No	85 (82.5)	56 (56)	

Also, there are questions about patient satisfaction with the provided drug information (either through the usual care or additional care provided by a clinical pharmacist). There were significant differences between the two groups, with more satisfaction for the intervention group; 0% of the intervention compared to the control group (52% and 71%) said they needed more explanation about the drug and need more explanation about side effects and how to avoid them, respectively (P-value<0.001). In addition, 17.5% of the intervention group, compared to 44% of the control group, reported that they needed more follow-up by doctor, P-values<0.001.

4. Discussion

The average age of the study sample was 21.5 years. Most patients were aged 18–25, which is expected as AV is more prevelant in the age group 12–24 years as reported in a study in the United States [1]. Most of the participants were female (88.2%). While 11.8% were male, indicating that the female participants were more likely to develop acne, especially in adolescents, similar to the other study (93.9%) female, while 6.1% were male [13]. A possible reason for that could be that female hormone levels rise sharply during puberty, leading to acne formation. In addition, other diseases such as polycystic ovary syndrome, affect acne's appearance [22]. Also, lifestyle, stress, sensitive skin, and full coverage foundation increase acne severity for female patients [23].

In this study, patients had an average knowledge score at baseline (6.5 out of 10), indicating that patients were only moderately

knowledgeable about isotretinoin and not fully aware of the potential risks associated with its use. A previous cross sectional study in Jordan using an online questionnaire found that the knowledge score was 8.1 out of 10 among isotretinoin users [12]. Another study conducted in Saudi Arabia also showed that community residents were not sufficiently aware of isotretinoin proper use and its risks [13].

As isotretinoin has many adverse effects and contraindications, all patients should be well-versed in every aspect of it. Only 84.2% of patients were aware that teratogenicity is one of the side effects of isotretinoin. M. Lelubre et al. found similar rates in Belgium, reporting that 87.9% of female patients clearly understood isotretinoin teratogenicity [24].

A small percentage of participants (5.4%) believed they could use isotretinoin without a prescription, and 10.8% of the patients took it without a prescription at least once. These results follow another study that reported 10.4% of participants took isotretinoin from pharmacies, friends, or other family members without a prescription [13], indicating the lack of enforced regulations to prevent the dispensing of isotretinoin without a prescription in Jordan.

Around one third of participants did not know that isotretinoin is preferred to be taken with meal, the physician or the dispensing pharmacist should advise the patient to take it with food, especially with a fatty meal to enhance absorption [25]. Moreover, two-thirds of participants did not know that they should not donate blood during treatment. Also, 71% of patients did not know that isotretinoin may enter breast milk, and thus a woman cannot breastfeed her baby while using isotretinoin. Additionally, isotretinoin increases the risk of scarring when waxing or using laser hair removal [26]; however, 59.6% of patients did not know that they cannot use them during treatment. These results indicate that the patients were not receiving effective education at routine care.

Previous studies have shown that good patients' understanding about isotretinoin is essential to increase compliance and reduce adverse effects [12,13,27]. The American Association of Health-System Pharmacists (ASHP) believes that pharmacists have a role in meeting a patient's primary care needs by providing information, education, and counseling to patients about medical care [28]. Some studies have shown the role of a clinical pharmacist in increasing the patient's knowledge about their disease, patient's commitment to their medications, improving outcomes, and accepting medicines, especially in chronic diseases such as diabetes and hypertension [29, 30]. Our study is considered the first clinical trial conducted in Jordan on acne disease, and more importantly on isotretinoin.

At follow-up, the intervention group showed significant improvement in knowledge about the drug, its side effects and their managment compared to control group. They also showed better perception of the imporvement of AV, less impac of isotretinoin side effects on daily life and normal activities and higher level of satisfaction with the provided education. These results clearly signify the importance of clinical pharmacists and their role in educating patients about their medication. There were no previous interventional studies on the role of clinical pharmacists' education about isotretinoin. However, previous interventional studies showed that education provided by clinical pharmacists had a positive impact on several health outcomes [18,29–32].

Some questions, such as knowledge about donating blood, breastfeeding a child, wax or laser, the nature of eating, and its effect on treatment, patients from both groups were interested to know the truth. This could explain the significant difference in knowledge found in the control group in these questions, another reason was that 57% of the control group compared to 45% of the intervention group saw outside sources for obtaining information about the medication.

Generally, most patients were satisfied with the quality of care they received at dermatology clinic by clinical pharmacist. Four factors were identified that contributed towards a positive patient experience with the service: ample consultation time, listening and understanding individual patients' needs, in-depth specialized knowledge, and a holistic approach. Also, the improvement of acne as perceived by patients was greater in intervention compared to control group indicating proper use, a good understanding of medication, and adherence to medication urged by clinical pharmacist during the education process. Since patients in intervention group were able to deal with side effects, most of the patients were unaffected or less affected by the side effects on their daily activities.

4.1. Strengths and limitations

The robustness of this study is strengthened by its design; randomized control trials can provide strong evidence of the actual causal effect of an intervention. The rigorous methodology allows avoiding bias related to confounding factors (through a control group) and selection bias (through randomization). Sample size was larger than a similar study [20] and was more than the double of the minimally required sample size. Only one researcher interviewed all patients in the two phases, reducing the risk of multi-interviewer bias. It is a multicenter study which allows more generalizability. Finaly, the questionnaires used in this study were validated in previous study and validated prior to the conduction of study when some changes were made on some parts.

This study had some limitations. First, we were able to follow-up patients at a single time point; multiple follow-up points would strengthen our results. Second, following up with patients by phone had a few barriers, such as lack of eye contact. Third, the physician may have been spending more time on counseling patients about the medication in response to their knowledge about the ongoing research project (the Hawthorne effect), however both intervention and control groups were receiving the physician routine care and the physician was blinded of the patients' assignments which might mute this effect.

5. Conclusion and recommendations

The study had evaluated the role of a clinical pharmacist in improving clinical outcomes in patients using isotretinoin. Results showed that the clinical pharmacist intervention has a significant effect in improving the level of knowledge about the medication. Improvement in the knowledge about isotretinoin leading to reduce severity of side effect and improve acne. This study shed light on the importance of the clinical pharmacist's role in managing patients at the dermatologic clinic.

We recommend implanting the services of a clinical pharmacist in an outpatient dermatology clinic for patients using isotretinoin

to educate them about medication, monitor them during treatment, help them managing the side effects they experience, and follow-up their compliance with instructions and medication. This will lead to improve clinical outcomes in patients using isotretinoin. Therefore, we also recommend creating awareness programs and educational sessions for healthcare professionals about clinical pharmacy and its applications to demonstrate their importance in the educational process and improving patients' outcomes.

Author contribution statement

Ruba Y. Alabadallah; Bushra M. Hijazi: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper. Shoroq M Altawalbeh: Conceived and designed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper. Muna Oqal; Basima A. Almomani: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Data availability statement

Data will be made available on request.

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Ethics statement

The study protocol received ethical approval from the Institutional Review Board committee at Jordan University of Science and Technology (JUST IRB # 491/2020) and the Ministry of Health of Research on Human Committee (173/2020) and informed consents were obtained from the participants.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e20102.

References

[1] G.M. White, Recent findings in the epidemiologic evidence, classification, and subtypes of acne vulgaris, J. Am. Acad. Dermatol. (1998), https://doi.org/10.1016/s0190-9622(98)70442-6.

[2] T. Vos, A.D. Flaxman, M. Naghavi, R. Lozano, C. Michaud, M. Ezzati, K. Shibuya, J.A. Salomon, S. Abdalla, V. Aboyans, J. Abraham, I. Ackerman, R. Aggarwal, S. Y. Ahn, M.K. Ali, M.A. Almazroa, M. Alvarado, H.R. Anderson, L.M. Anderson, K.G. Andrews, C. Atkinson, L.M. Baddour, A.N. Bahalim, S. Barker-Collo, L. H. Barrero, D.H. Bartels, M.G. Basáñez, A. Baxter, M.L. Bell, E.J. Benjamin, D. Bennett, E. Bernabé, K. Bhalla, B. Bhandari, B. Bikbov, A. Bin Abdulhak, G. Birbeck, J.A. Black, H. Blencowe, J.D. Blore, F. Blyth, I. Bolliger, A. Bonaventure, S. Boufous, R. Bourne, M. Boussinesq, T. Braithwaite, C. Brayne, L. Bridgett, S. Brooker, P. Brooks, T.S. Brugha, C. Bryan-Hancock, C. Bucello, R. Buchbinder, G. Buckle, C.M. Budke, M. Burch, P. Burney, R. Burstein, B. Calabria, B. Campbell, C.E. Canter, H. Carabin, J. Carapetis, L. Carmona, C. Cella, F. Charlson, H. Chen, A.T.A. Cheng, D. Chou, S.S. Chugh, L.E. Coffeng, S.D. Colan, S. Colquhoun, K.E. Colson, J. Condon, M.D. Connor, L.T. Cooper, M. Corriere, M. Cortinovis, K.C. De Vaccaro, W. Couser, B.C. Cowie, M.H. Criqui, M. Cross, K. C. Dabhadkar, M. Dahiya, N. Dahodwala, J. Damsere-Derry, G. Danaei, A. Davis, D. De Leo, L. Degenhardt, R. Dellavalle, A. Delossantos, J. Denenberg, S. Derrett, D.C. Des Jarlais, S.D. Dharmaratne, M. Dherani, C. Diaz-Torne, H. Dolk, E.R. Dorsey, T. Driscoll, H. Duber, B. Ebel, K. Edmond, A. Elbaz, S.E. Ali, H. Erskine, P.J. Erwin, P. Espindola, S.E. Ewoigbokhan, F. Farzadfar, V. Feigin, D.T. Felson, A. Ferrari, C.P. Ferri, E.M. Fèvre, M.M. Finucane, S. Flaxman, L. Flood, K. Foreman, M.H. Forouzanfar, F.G.R. Fowkes, R. Franklin, M. Fransen, M.K. Freeman, B.J. Gabbe, S.E. Gabriel, E. Gakidou, H.A. Ganatra, B. Garcia, F. Gaspari, R.F. Gillum, G. Gmel, R. Gosselin, R. Grainger, J. Groeger, F. Guillemin, D. Gunnell, R. Gupta, J. Haagsma, H. Hagan, Y.A. Halasa, W. Hall, D. Haring, J.M. Haro, J.E. Harrison, R. Havmoeller, R.J. Hay, H. Higashi, C. Hill, B. Hoen, H. Hoffman, P.J. Hotez, D. Hoy, J.J. Huang, S.E. Ibeanusi, K.H. Jacobsen, S. L. James, D. Jarvis, R. Jasrasaria, S. Jayaraman, N. Johns, J.B. Jonas, G. Karthikeyan, N. Kassebaum, N. Kawakami, A. Keren, J.P. Khoo, C.H. King, L. M. Knowlton, O. Kobusingye, A. Koranteng, R. Krishnamurthi, R. Lalloo, L.L. Laslett, T. Lathlean, J.L. Leasher, Y.Y. Lee, J. Leigh, S.S. Lim, E. Limb, J.K. Lin, M. Lipnick, S.E. Lipshultz, W. Liu, M. Loane, S.L. Ohno, R. Lyons, J. Ma, J. Mabweijano, M.F. MacIntyre, R. Malekzadeh, L. Mallinger, S. Manivannan, W. Marcenes, L. March, D.J. Margolis, G.B. Marks, R. Marks, A. Matsumori, R. Matzopoulos, B.M. Mayosi, J.H. McAnulty, M.M. McDermott, N. McGill, J. McGrath, M.E. Medina-Mora, M. Meltzer, Z.A. Memish, G.A. Mensah, T.R. Merriman, A.C. Meyer, V. Miglioli, M. Miller, T.R. Miller, P.B. Mitchell, A. O. Mocumbi, T.E. Moffitt, A.A. Mokdad, L. Monasta, M. Montico, M. Moradi-Lakeh, A. Moran, L. Morawska, R. Mori, M.E. Murdoch, M.K. Mwaniki, K. Naidoo, M.N. Nair, L. Naldi, K.M.V. Narayan, P.K. Nelson, R.G. Nelson, M.C. Nevitt, C.R. Newton, S. Nolte, P. Norman, R. Norman, M. O'Donnell, S. O'Hanlon, C. Olives, S.B. Omer, K. Ortblad, R. Osborne, D. Ozgediz, A. Page, B. Pahari, J.D. Pandian, A.P. Rivero, S.B. Patten, N. Pearce, R.P. Padilla, F. Perez-Ruiz, N. Perico, K. Pesudovs, D. Phillips, M.R. Phillips, K. Pierce, S. Pion, G.V. Polanczyk, S. Polinder, C.A. Pope, S. Popova, E. Porrini, F. Pourmalek, M. Prince, R.L. Pullan, K. D. Ramaiah, D. Ranganathan, H. Razavi, M. Regan, J.T. Rehm, D.B. Rein, G. Remuzzi, K. Richardson, F.P. Rivara, T. Roberts, C. Robinson, F.R. De Leòn,

L. Ronfani, R. Room, L.C. Rosenfeld, L. Rushton, R.L. Sacco, S. Saha, U. Sampson, L. Sanchez-Riera, E. Sanman, D.C. Schwebel, J.G. Scott, M. Segui-Gomez, S. Shahraz, D.S. Shepard, H. Shin, R. Shivakoti, D. Silberberg, D. Singh, G.M. Singh, J.A. Singh, J. Singleton, D.A. Sleet, K. Sliwa, E. Smith, J.L. Smith, N.J. C. Stapelberg, A. Steer, T. Steiner, W.A. Stolk, L.J. Stovner, C. Sudfeld, S. Syed, G. Tamburlini, M. Tavakkoli, H.R. Taylor, J.A. Taylor, W.J. Taylor, B. Thomas, W. M. Thomson, G.D. Thurston, I.M. Tleyjeh, M. Tonelli, J.A. Towbin, T. Truelsen, M.K. Tsilimbaris, C. Ubeda, E.A. Undurraga, M.J. Van Der Werf, J. Van Os, M. S. Vavilala, N. Venketasubramanian, M. Wang, W. Wang, K. Watt, D.J. Weatherall, M.A. Weinstock, R. Weintraub, M.G. Weisskopf, M.M. Weissman, R.A. White, H. Whiteford, S.T. Wiersma, J.D. Wilkinson, H.C. Williams, S.R.M. Williams, E. Witt, F. Wolfe, A.D. Woolf, S. Wulf, P.H. Yeh, A.K.M. Zaidi, Z.J. Zheng, D. Zonies, A.D. Lopez, C.J.L. Murray, Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010, Lancet 380 (2012), https://doi.org/10.1016/S0140-6736(12)61729-2.

[3] P. Wolkenstein, J.J. Grob, S. Bastuji-Garin, S. Ruszczynski, J.C. Roujeau, J. Revuz, R. Corona, French people and skin diseases: results of a survey using a representative sample, Arch. Dermatol. 139 (2003), https://doi.org/10.1001/archderm.139.12.1614.

[4] S.M. Tuchayi, E. Makrantonaki, R. Ganceviciene, C. Dessinioti, S.R. Feldman, C.C. Zouboulis, Acne vulgaris, Nat. Rev. Dis. Prim. 1 (2015), 15029, https://doi.org/10.1038/nrdp.2015.29.

[5] J. Kraft, A. Freiman, Management of acne, Can. Med. Assoc. J. 183 (2011) E430, https://doi.org/10.1503/cmaj.090374. LP-E435.

[6] L. Azoulay, D. Oraichi, A. Bérard, Patterns and utilization of isotretinoin for acne from 1984 to 2003: is there need for concern? Eur. J. Clin. Pharmacol. 62 (2006) https://doi.org/10.1007/s00228-006-0151-x.

[7] A.L. Zaenglein, A.L. Pathy, B.J. Schlosser, A. Alikhan, H.E. Baldwin, D.S. Berson, W.P. Bowe, E.M. Graber, J.C. Harper, S. Kang, J.E. Keri, J.J. Leyden, R. V. Reynolds, N.B. Silverberg, L.F. Stein Gold, M.M. Tollefson, J.S. Weiss, N.C. Dolan, A.A. Sagan, M. Stern, K.M. Boyer, R. Bhushan, Guidelines of care for the management of acne vulgaris, J. Am. Acad. Dermatol. 74 (2016), https://doi.org/10.1016/j.jaad.2015.12.037.

[8] A.M. Layton, W.J. Cunliffe, Guidelines for optimal use of isotretinoin in acne, J. Am. Acad. Dermatol. 27 (1992), https://doi.org/10.1016/S0190-9622(08)80252-6.

[9] M. Rademaker, Adverse effects of isotretinoin: a retrospective review of 1743 patients started on isotretinoin, Australas. J. Dermatol. 51 (2010), https://doi.org/10.1111/j.1440-0960.2010.00657.x.

[10] P. Brzezinski, K. Borowska, A. Chiriac, J. Smigielski, Adverse effects of isotretinoin: a large, retrospective review, Dermatol. Ther. 30 (2017), https://doi.org/10.1111/dth.12483.

[11] R.D. Wilson, A preventable teratology: isotretinoin, CMAJ (Can. Med. Assoc. J.) 188 (2016), https://doi.org/10.1503/cmaj.1150114.

[12] A.S. Jarab, S. Al-Azzam, S. Almutairi, T.L. Mukattash, Patients' knowledge and information needs about isotretinoin therapy use in Jordan, Int. J. Clin. Pract. (2022) 2022, https://doi.org/10.1155/2022/9443884.

[13] N.S. Younis, N.Y. Al-Harbi, Public understanding and awareness of isotretinoin use and safety in Al ahsa, eastern Saudi arabia, Ther Innov Regul Sci 53 (2019), https://doi.org/10.1177/2168479018807677.

[14] A. Saqib, M. Atif, R. Ikram, F. Riaz, M. Abubakar, S. Scahill, Factors affecting patients' knowledge about dispensed medicines: a Qualitative study of healthcare professionals and patients in Pakistan, PLoS One 13 (2019), https://doi.org/10.1371/journal.pone.0197482.

[15] M. Atif, M.R. Sarwar, M. Azeem, D. Umer, A. Rauf, A. Rasool, M. Ahsan, S. Scahill, Assessment of WHO/INRUD core drug use indicators in two tertiary care hospitals of Bahawalpur, Punjab, Pakistan, J Pharm Policy Pract 9 (2016), https://doi.org/10.1186/s40545-016-0076-4.

[16] C.J.P.W. Keijsers, J.R.B.J. Brouwers, D.J. de Wildt, E.J.F.M. Custers, O.T.h.J. Ten Cate, A.C.M. Hazen, P.A.F. Jansen, A comparison of medical and pharmacy students' knowledge and skills of pharmacology and pharmacotherapy, Br. J. Clin. Pharmacol. 78 (2014), https://doi.org/10.1111/bcp.12396.

[17] F. M.G, S. N.A, A. A.A, Detection and prevention of medication errors in the operating rooms of a pediatric surgery department in Egypt, Int. J. Pharmaceut. Sci. Rev. Res. 42 (2017).

[18] L.S. Mostafa, N.A. Sabri, A.M. El-Anwar, S.M. Shaheen, Evaluation of pharmacist-led educational interventions to reduce medication errors in emergency hospitals: a new insight into patient care, J. Publ. Health (2020) 42, https://doi.org/10.1093/pubmed/fdy216.

[19] D.M. Ibrahim, M.A. Shawki, M.H. Solayman, N.A. Sabri, Pharmacovigilance education to healthcare professionals: will it affect their performance in reporting adverse drug reactions? Int. J. Clin. Pract. 75 (2021) https://doi.org/10.1111/ijcp.14731.

[20] L. Tsur, E. Kozer, M. Berkovitch, The effect of drug consultation center guidance on contraceptive use among women using isotretinoin: a randomized, controlled study, J Womens Health 17 (2008), https://doi.org/10.1089/jwh.2007.0623.

[21] S.M. Dean Ag, K.M. Sullivan, Version, Open: Open Source Epidemiologic Statistics for Public Health (2013). OpenEpi.com, www.OpenEpi.com. (Accessed 10 July 2023).

[22] N. Skroza, E. Tolino, I. Proietti, N. Bernardini, G. La Viola, F. Nicolucci, R. Pampena, S. Zuber, V. Balduzzi, V. Soccodato, M.T. Mancini, C. Potenza, Women and acne: any difference from males? A review of the literature, in: Giornale Italiano Di Dermatologia e Venereologia, vol. 151, 2016.

[23] E. Chlebus, M. Chlebus, Factors affecting the course and severity of adult acne. Observational cohort study, J. Dermatol. Treat. 28 (2017), https://doi.org/10.1080/09546634.2017.1329500.

[24] M. Lelubre, J. Hamdani, C. Senterre, K. Amighi, M. Peres, M.P. Schneider, O. Bugnon, C. De Vriese, Evaluation of compliance with isotretinoin PPP recommendations and exploration of reasons for non-compliance: survey among French-speaking health care professionals and patients in Belgium, Pharmacoepidemiol. Drug Saf. 27 (2018), https://doi.org/10.1002/pds.4441.

[25] W.A. Colburn, D.M. Gibson, R.E. Wiens, J.J. Hanigan, Food increases the bioavailability of isotretinoin, J. Clin. Pharmacol. 23 (1983), https://doi.org/10.1002/j.1552-4604.1983.tb01800.x.

[26] L.K. Spring, A.C. Krakowski, M. Alam, A. Bhatia, J. Brauer, J. Cohen, J.Q. Del Rosso, L. Diaz, J. Dover, L.F. Eichenfield, G.C. Gurtner, C.W. Hanke, M.N. Jahnke, K.M. Kelly, S. Khetarpal, M.A. Kinney, M.L. Levy, J. Leyden, M.T. Longaker, G.S. Munavalli, D.M. Ozog, H. Prather, P.R. Shumaker, E. Tanzi, A. Torres, M. W. Velez, A.B. Waldman, A.C. Yan, A.L. Zaenglein, Isotretinoin and timing of procedural interventions: a systematic review with consensus recommendations, JAMA Dermatol 153 (2017), https://doi.org/10.1001/jamadermatol.2017.2077.

[27] M. Al-Harbi, Concerns and awareness of acne patients about isotretinoin in qassim region of Saudi Arabia, Int. J. Health Sci. 4 (2010).

[28] K.A. Galt, R.F. Demers, R.N. Herrier, ASHP statement on the pharmacist's role in primary care, Am. J. Health Syst. Pharm. 56 (1999), https://doi.org/10.1093/ajhp/56.16.1665.

[29] A. Lindenmeyer, H. Hearnshaw, E. Vermeire, P. Van Royen, J. Wens, Y. Biot, Interventions to improve adherence to medication in people with type 2 diabetes mellitus: a review of the literature on the role of pharmacists, J. Clin. Pharm. Therapeut. 31 (2006), https://doi.org/10.1111/j.1365-2710.2006.00759.x.

[30] M. Amer, N. Rahman, S.R. Nazir, A. Raza, H. Riaz, M. Sultana, S. Sadeeqa, Impact of pharmacist's intervention on disease related knowledge, medication adherence, HRQoL and control of blood pressure among hypertensive patients, Pak. J. Pharm. Sci. 31 (2018).

[31] S.W. Gillani, S.M. Gulam, D. Thomas, F.B. Gebreighziabher, J. Al-Salloum, R.A. Assadi, K.G. Sam, Role and services of a pharmacist in the prevention of medication errors: a systematic review, Curr. Drug Saf. 16 (2020), https://doi.org/10.2174/1574886315666201002124713.

[32] M. Butt, A. Mhd Ali, M.M. Bakry, N. Mustafa, Impact of a pharmacist led diabetes mellitus intervention on HbA1c, medication adherence and quality of life: a randomised controlled study, Saudi Pharmaceut. J. 24 (2016), https://doi.org/10.1016/j.jsps.2015.02.023.