

# LJMU Research Online

Al-Khalaileh, W, Abu Farha, R, Wazaify, M and van Hout, MC

Opthalmic drug abuse and misuse in Jordan: An Observational Study from Community Pharmacies in Amman.

http://researchonline.ljmu.ac.uk/id/eprint/10124/

Article

**Citation** (please note it is advisable to refer to the publisher's version if you intend to cite from this work)

Al-Khalaileh, W, Abu Farha, R, Wazaify, M and van Hout, MC (2019) Opthalmic drug abuse and misuse in Jordan: An Observational Study from Community Pharmacies in Amman. Research in Social and Administrative Pharmacv. ISSN 1934-8150

LJMU has developed LJMU Research Online for users to access the research output of the University more effectively. Copyright © and Moral Rights for the papers on this site are retained by the individual authors and/or other copyright owners. Users may download and/or print one copy of any article(s) in LJMU Research Online to facilitate their private study or for non-commercial research. You may not engage in further distribution of the material or use it for any profit-making activities or any commercial gain.

The version presented here may differ from the published version or from the version of the record. Please see the repository URL above for details on accessing the published version and note that access may require a subscription.

For more information please contact <a href="mailto:researchonline@ljmu.ac.uk">researchonline@ljmu.ac.uk</a>

http://researchonline.ljmu.ac.uk/

# Ophthalmic drug abuse: An observational study from community pharmacies in Amman-Jordan

Waed Al-Khalaileh<sup>a</sup>, Rana Abu-Farha<sup>b, \*</sup>, Mayyada Wazaify<sup>a</sup>, Marie Claire Van Hout<sup>c</sup>

<sup>a</sup> Department of Biopharmaceutics and Clinical Pharmacy, Faculty of Pharmacy, The University of Jordan , Amman, Jordan

<sup>b</sup> Department of Clinical Pharmacy and Therpeutics, Faculty of Pharmacy, Applied Science Private University, Amman, Jordan

<sup>c</sup> Public Health Institute, Liverpool John Moore's University, United Kingdom

ARTICLE INFO	ABSTRACT					
Keywords: Abuse Community pharmacy Eye drops Jordan Misuse Ophthalmic	<i>Background:</i> There has been a trend in the past five years in Jordan for ophthalmic anticholinergic preparations to be misused or abused. This is done mainly to experience mental altering effects such as mood changes, euphoria or hallucinations. Such products are mostly obtained from community pharmacies without a prescription. <i>Objectives:</i> This study aimed to observe the requests of ophthalmic preparations in community pharmacies in Amman, Jordan, and evaluating the most popular and frequently requested ophthalmic drops suspected of abuse. Also, it aimed to describe the current methods that Jordanian community pharmacists use to manage such requests. <i>Methods:</i> A prospective cross-sectional observational study was conducted between November 2016 and January 2017 at sixteen different community pharmacies in Amman. All ophthalmic products requested were observed during this period. <i>Results:</i> A total of 140 ophthalmic product requests for 130 customers were observed. Dry eye was the most common complaint for which the customer requested the medication (n = 30, 23.1%) and direct self-medication (ie-requesting the product by name), was the most frequent method of purchase (n = 63, 48.5%). In 19 cases (14.6%), product requests were suspected to be for non-medical (ie-abuse) purposes. Most of the suspected cases were for Pentolate <sup>®</sup> (n = 11, 57.9%), whereas 7 were for Prisoline <sup>®</sup> (36.8%) and 1 for Naphcon-A <sup>®</sup> (5.3%). The majority of observed cases were for products requested without a prescription (n = 16, 84.2%), and in 12 cases out of which, sale was refused (63.2%). <i>Conclusion:</i> More effort and enforcement of pharmacy regulation for safe dispensing is needed to reduce the abuse of ophthalmic products. Educating pharmacists and ophthalmologists would help raise awareness and control the type of drug abuse.					

# Introduction

Abuse of Over-the- Counter (OTC) and prescription medications is an international issue.<sup>1</sup> OTC medications are those that can be bought from pharmacies or other retail outlets without a prescription.<sup>1</sup> Although the sale of OTC medications from community pharmacies may help individuals to self-treat minor ailments, save time and effort of both patients and physicians, some of these medicines can be misused or abused, which subsequently may lead to other complications such as addiction.<sup>2</sup>

It is important to differentiate between misuse and abuse terms when talking about prescription or OTC drugs.<sup>3,4</sup> In the literature, abuse is defined as "any intentional, non-therapeutic use of a drug product or substance, even once, for the purpose of achieving a desirable psychological or physiological effect", while misuse is defined as "the use of the drug for legitimate medical reason, yet, to use it wrongly either in terms of dosage or duration".<sup>5</sup> By definition, any medication can be misused, but only few have the abuse potential, such as those with mind-altering or body-shaping properties.<sup>3</sup> The most commonly reported prescription medications to be abused worldwide are stimulants such as methylphenidate and central nervous system (CNS) depressants such as sedatives (benzo-diazepines) or some -anticonvulsants like clonazepam.<sup>6</sup> Moreover,

opioid-containing medications (that are sold without prescription in some countries like the UK), cough and cold remedies containing first generation antihistamines (e.g. diphenhydramine and chlorpheneramine), sympathomimetics (e.g. pseudoephedrine) and dextromethorphan are the top OTC products reported to be abused.<sup>2</sup>

In Jordan, just like other countries in the region, with the exception of controlled drugs, the general public can buy almost any medication (both OTC and prescription) from the community pharmacy without having a prescription.<sup>7</sup> This availability combined with relatively low price and accessibility of community pharmacies may contribute to the abuse of more and different kinds of OTC and prescription drugs.<sup>7</sup>

A recently published scoping review described the abuse of topical ophthalmic anesthetics in 54 different publications world-wide (e.g. Brazil, USA, Italy, Turkey etc). It highlighted that such abuse had been reported in case series, case reports, and reviews and primarily had focused on toxicity and related complications of such product.<sup>8</sup>

In Jordan, ophthalmic products that contain medications used to treat minor ailments that can be diagnosed in the community pharmacy (e.g. antihistamines used for allergic conjunctivitis like antazoline, or sympathomimetics for itchy red eye like naphazoline) can be obtained without a prescription. On the other hand, prescription-only-ophthalmic preparations contain medications that are used to treat internal eye conditions and need to be diagnosed by a doctor (e.g. anticholinergic drugs used as mydriatic drugs (tropicamide, cyclopentolate) or beta blockers (timolol) or prostaglandins (latanoprost) used for glaucoma or conrticosteroids (efemoline) used for internal eye inflammation.

Ophthalmic anticholinergic preparations (e.g. tropicamide, cyclopentolate) are widely used to induce mydriasis and/or cycloplegia during eye examination.<sup>9,10</sup> The abuse of anticholinergic drugs, which has become well known especially in the 1980s, is related to their effect in causing euphoria and hallucination. The main reported reasons for abuse were: relaxing, getting high, induce pleasure, boosting energy, and eliminating depression.<sup>9–11</sup>

Cycloplegic agents like cyclopentolate and tropicamide can enter the systemic circulation and reach to all systems easily by absorption through cornea and then the ocular drainage system.<sup>9</sup> Because of their dangerous systemic side effects, any small amount of these agents could lead to harm if misuse or abuse happens.<sup>11</sup> Several other types of ophthalmic drugs were mentioned in literature to be liable for abuse. These included topical anesthetic drugs (TADs),<sup>12–15</sup> topical ophthalmic decongestants,<sup>16</sup> and topically applied Non-steroidal Anti-Inflammatory Drugs (NSAIDs).<sup>12–17</sup>

Anecdotal reports in the past five y ears in J ordan r evealed a n upward trend of ophthalmic drugs abuse (i.e. - used to experience mental altering effects), with many products obtained from pharmacies without prescription.<sup>18</sup> To date, there has been only one study that investigated ophthalmic drug abuse from the perspective of 220 community pharmacists in Jordan.<sup>18</sup>. This previous study involved questionnaires eliciting pharmacist self-report of suspected abuse of ophthalmic medications, which relied on pharmacists self-reporting of the suspected abuse of ophthalmic medications. A total of 178 pharmacists (80.9%) reported the abuse of some ophthalmic drugs, and they indicated that most of the ophthalmic products were obtained without a prescription (n = 136; 61.8%). However, in this current study, we aimed to investigate this issue from a different angle by observing the requests of ophthalmic preparations in community pharmacies, evaluating the most popular and frequently requested ophthalmic drops suspected of abuse in community pharmacies and describing the main methods observed by the researcher and used by pharmacists to deal with suspected requests.

#### Methods

## Study design, setting, subjects and data collection

This study adopted a prospective cross-sectional observational design. Data collection took place between November 2016 and January 2017 through 16 pharmacy in different regions of Amman, the capital of Jordan. The selection of pharmacies was based on the convenience and consenting to participate by the pharmacy manager of each community pharmacy. Nevertheless, effort was made to try and approach pharmacies in diverse geographical locations in Amman.

All customers (all age groups/both genders) of the community pharmacy asking for one or more eye drops/preparations during the observational period were recruited after consenting verbally to be interviewed and no customer refusal for interviews was reported.

During the study period, two researchers had observed ophthalmic drug requests for one week duration in each pharmacy. Some of the pharmacies were observed during shift A work (from 9am to 3 pm) while others were observed during shift B (from 3 pm to 12 am). Informed consent forms were obtained from all community pharmacists, after describing that the aim of this study was to measure the ophthalmic drug abuse among customers in community pharmacies. To minimize the social desirability effect (ie- Hawthorne effect), the researchers noticed the interaction between customers and pharmacist standing beside the pharmacist on the dispensing counter, wearing lab coats to look like another pharmacist works in the same pharmacy. A collaboration was made between the researchers and the main pharmacist to detect the abuser among customers according to pharmacists' prior knowledge with them.

Immediately following the observation and after the sale had been made, customers were approached and asked to be interviewed by the researcher. Customers were interviewed to obtain any additional information thought to be important to the research, and the information was written at the end of the data collection form."

# Data collection form

The data collection form in this study was anonymous and based on a one validated and piloted by Wazaify and colleagues (2017).<sup>18</sup> The form had been designed to gather the following information without mentioning any identifying information of customers or pharmacists:

- A. Customer demographic data (age, gender and academic qualification); obtained by interviewing the customers
- B. Name of the ophthalmic product, quantity, indication and duration of use; obtained by observing the customer-pharmacist interaction
- C. Way of requesting the medication (on prescription, direct self-medication (ie-asking for product by name), indirect self-medication (ie-presenting symptoms and asking for pharmacist's advice); obtained by observing the customers
- D. Pharmacist's role in customer counseling (if any), obtained by observing the customer-pharmacist interaction. This section involved a free-text to note down any information provided by the pharmacist regarding the use, dose, the duration of use, administration of medication, and how to manage side effect.
- E. Pharmacist's reaction towards suspected cases of drug abuse, the main signs that led the pharmacist and/or researchers to suspect (e.g. the pattern and frequency of requests, pharmacists' familiarity with customers and the large quantity requested), obtained by observing the customer-pharmacist interaction
- F. General information about the participating pharmacy (e.g. Location: whether in a mall, main-street or a side small street, Type: chain or independent pharmacy), obtained by interviewing pharma-

cists to see if these factors could affect the number of suspected cases of abuse or the number of requests.

G. Pharmacist demographic data (age, gender, and experience), obtained by interviewing pharmacists

#### Ethical considerations

This study was approved by the IRB of Jordanian Ministry of Health (Reference number: MOH REC170001). In addition, verbal consents were obtained from customers to be interviewed as well as from pharmacists to use their demographic data. Written and signed consent form was obtained from the pharmacy mangers to take part in this study.

#### Statistical analysis

All data were coded and entered into the Statistical Package for Social Sciences (SPSS) database (version 23, IBM Corporation, Armonk, NY, USA). Descriptive data were summarized as counts and percentages for categorical variables and mean and SD for continuous variables.

# Results

# Baseline characteristics of study participating customers and recruited pharmacists/pharmacies

Sixteen out of nineteen pharmacies approached agreed to take part in the study, resulting in a response rate of 84.2%. The reason for rejection was that the responsible pharmacists were not interested in this kind of research studies. Ten pharmacies (62.5%) were located in west Amman and on a main road. Most of the pharmacists working in these pharmacies were female (n = 10, 62.5%) and one half (n = 8, 50%) were between 20 and 30 years old. Social demographic details of involved pharmacists/pharmacies participating in the study are summarized in Table 1.

During study period, a total of 130 different customers were interviewed, most of whom were male (n = 79, 60.8%) and between 21 and 40 years (n = 81, 62.3%). More of the observations (n = 111, 85.4%) were recruited from independent pharmacies and working shift A (ie-9 am-3pm; n = 75, 57.7%). Demographic characteristics of the study participating customers are presented in Table 2.

#### Table 1

Social demographic details of involved pharmacists/pharmacies participating in the study (N = 16).

Variable	Ν	%				
Age						
20-30 years	8	50%				
31-40 years	5	31.3%				
41-50 years	1	6.3%				
>50 years	2	12.5%				
Gender						
Male	6	37.5%				
Female	10	62.5%				
Experience						
<1 year	1	6.3%				
1–5 years	4	25%				
6-10 years	6	37.5%				
>10 years	5	31.3%				
Location of pharmacy						
East Amman	6	37.5%				
West Amman	10	62.5%				
The road type						
Main street	10	62.5%				
Side/sub street	6	37.5%				

# Table 2

Demographic Characteristics of study participating customers during the observational part of the study (N = 130).

Variable	Ν	%
Age		
< 20 years	13	10%
21-40 years	81	62.3%
41-50 years	29	22.3%
50-60 years	5	3.8%
>60 years	2	1.5%
Gender		
Male	79	60.8%
Female	51	39.2%
Site of recruitment		
Chain Pharmacy	19	14.6%
Independent pharmacy	111	85.4%
Shift of recruitment		
A (9am-3pm)	75	57.7%
B (3pm-12pm)	55	42.3%

\*: No observations were made during working shift C due to lack of research assistants covering this period.

## Information regarding dispensed ophthalmic products

Various ocular complaints or reasons to request ophthalmic products were noted by the observers during the study period. The top three complaints were dry eyes (n = 30, 23.1%), suspected eye infection (n = 26, 20.0%) and eye redness (n = 23, 17.7%). A summary of ocular complaints and reasons to request ophthalmic products reported by customers are presented in Fig. 1.

One hundred and forty (140) products were requested by the 130 customers during the study period. The average number of ophthalmic products requested was 8.8 products/pharmacy/week. Direct self-medication, by customer request without prescription, was the most frequent way of requesting ophthalmic products (n = 63, 48.5%), followed by doctors' prescription and pharmacists recommendations (n = 48, 36.9%; n = 19, 14.6%, respectively). The most commonly prescribed products were lubricants (e.g. artificial tears, moisturizers; n = 35, 25%), followed by decongestants & antihistamines (n = 32, 22.9%). Decongestants and antihistamines were the most commonly requested products by direct self-medication, without prescription, (n = 25/32). A description of the ophthalmic products requested or prescribed during the study is presented in (Table 3).

# Ophthalmic products abuse evaluation among study observed customers

Over the study period, 19/130 observed cases (14.6%) were suspected of drug abuse by either the researcher (n = 2) or both; the pharmacist and the researcher (n = 17). These suspected cases involved 3 ophthalmic drugs of abuse; Pentolate<sup>®</sup> (cyclopentotale) in 11 cases, Prisoline<sup>®</sup> (naphazoline and chlorpheniramine maleate) in 7 cases and Naphcon-A<sup>®</sup> (naphazoline and pheniramine maleate) in 1 case. Almost all suspected abusers were male (n = 18, 94.7%) and aged between 21 and 40 years (n = 15, 78.9%). Most of them, (n = 16, 84.2%) presented no prescription and asked for the medication by name, whereas three of them (15.8%) had brought prescription to get Pentolate<sup>®</sup> eye drops.

Pharmacists' responses to suspected drug abuse cases were diverse. In most cases (47.4%, n = 9) the pharmacist did not sell the requested product and claimed that the product was not available. In six cases, the pharmacist simply sold the drug of request (31.5%), in one case the pharmacist sold a less quantity than requested (5.3%), In one case, the pharmacist did not sell the requested product because of lack of prescription (5.3%), and in two cases (10.5%) the pharmacist did not sell the products because the drug was not actually available. The product



Fig. 1. Ocular Complaints presented by customers during the study period (N = 130). \*Others: e.g. dust in the eye, glaucoma, foreign body entry, refuse to mention.

 Table 3

 Ophthalmic preparations dispensed (with/without prescription) during the study period.

Ophthalmic products			Description method of request			
	N	%	Prescription	Indirect self- medication	Direct self- medication	
Lubricants	35	25%	13/35	3/35	19/35	
Decongestants and antihistamines	32	22.9%	2/32	5/32	25/32	
Antibiotics	23	16.4%	17/23	4/23	2/23	
Antibiotic and steroid combination	14	10%	7/14	5/14	2/14	
Anticholinergic agents	14	10%	6/14	0/14	8/14	
Steroids	11	7.9%	8/11	1/11	2/11	
Glaucoma medications	7	5%	2/7	0/7	5/7	
NSAID	3	2.1%	0/3	1/3	2/3	
Other <sup>a</sup>	1	0.7%	1/1	0/1	0/1	

a Witch hazel (Eye Bright) Eye drop.

had been sold in 7 out of the 19 suspected cases of abuse (36.8%) and not sold in remainder (63.2%). The quantity of ophthalmic products of abuse requested by one customer ranged between 1 and 5 (mean = 1.7). Detailed information about the 19 suspected cases are presented in Table 4.

The reasons for suspected abuse of ophthalmic products were based on customers' reactions and answers during the interview (e.g. anxiety, confusion, hesitation, lying, and requesting another drug of abuse) (n = 9, 47.4%), incompatibility among the symptoms mentioned by the customers and the requested eye drop (n = 4, 21.1%), and based on prior pharmacist experience with the customer (n = 6, 31.6%).

# Discussion

The study is first of its kind in Jordan to observe ophthalmic drug abuse in community pharmacy, and has illustrated the complexities of suspected abuse of prescription and nonprescription ophthalmic preparations in community pharmacy settings in Amman. In addition, the study reports the ophthalmic products most frequently suspected of abuse and highlighted the methods used by Jordanian pharmacists to manage such requests. In this study, independent pharmacies represented the majority of our sample. This is because the majority of community pharmacies in Jordan are independent rather than chain. According to the Jordan Pharmaceutical Association (JPA), there are a total of 3214 community pharmacies in Jordan. The number of chains is 56 and estimated to have 200 branches around Jordan. All the rest are independent pharmacies.

Few studies described the problem of ophthalmic products misuse in the literature, either from the pharmacy staff perspective<sup>4,7</sup> or by measuring the general public's attitudes towards these medications.<sup>18–21</sup> Dry eye and lubricants were the most reported complaint and dispensed ophthalmic products, respectively. This may be attributed to the time in which the study was conducted, and the transition from autumn to winter. Although ophthalmic lubricants are considered safe drugs; corneal epithelial toxicity could occur as a result of using multi dosing products for long durations. This is attributable to the preservatives present, especially benzalkonium chloride.<sup>22</sup>

Several serious medical consequences like blindness have been reported in the literature due to OTC ophthalmic drug misuse.<sup>20</sup> In the present study, decongestants and antihistamines were the most frequently requested products by direct self-medication method. Soparker and workers (1997), in their study described the different patterns of conjunctivitis triggered by misusing ophthalmic decongestants. Follicular conjunctivitis, eczematoid blepharoconjunctivitis, and conjunctival hyperemia were observed with long-term usage of ophthalmic decongestants, regardless of the purpose of use (misuse or abuse).<sup>16</sup> It is concerning that in our study more than half of lubricant requests were requested through direct self-medication. Thus, it is important to educate customers about such consequences and the responsibility of customers education situates within both ophthalmologists and community pharmacist professional practice.<sup>23</sup>

During the observation period, eleven customers were suspected to abuse cyclopentolate eye drops while eight customers were suspected of abusing naphzoline under two brand names (seven cases for Prisoline<sup>®</sup>, and one case for Naphcon-A<sup>®</sup>). All of the reported products at this section in the study are classified by the Jordan Food and Drug Administration (JFDA) as OTC products except for pentolate<sup>®</sup> (cyclopentolate). The abuse of Pentolate<sup>®</sup>, Prisoline<sup>®</sup>, and Naphcon-A<sup>®</sup>, had been reported previously in Jordan from pharmacists' perspective using cross-sectional survey method.<sup>4,18</sup> However, this trend has not surfaced in community pharmacy until 5 years ago<sup>7</sup> as cheap and legal alternative to other controlled or illicit drugs.<sup>24</sup>

	Chain/ Independent	Participant gender/	Eve drop/		Used	Compliant by	Customer	Pharmacist response/ reason, if not	
#	Pharmacy	age	Quantity <sup>a</sup>	Request method	before	customer	Familiarity	sold	Suspicious reasons
1	Independent	Male 21–40 years	Prisoline <sup>®</sup> 1	By customer without prescription	Yes	Redness	Non Familiar	Sold the drug	No redness was appearing. In addition, the customer asked for Lyrica ®
2	Independent	Male 21–40 years	Prisoline <sup>®</sup> 1	By customer without prescription	yes	Redness and Itching (Allergy), for his mother	Non Familiar	Refusing to sell under the pretext of lack of medicine	Anxiety and confusion apparent during the conversation
3	Chain	Male 21–40 years	Prisoline® 1	By customer without prescription	Yes	Refuse to mention	Familiar	Refusing to sell under the pretext of lack of medicine	The way of asking, appearance and he refused to talk with the observer pharmacist
4	Chain	Male 21–40 years	Pentolate <sup>®</sup>	By customer without prescription	Yes	To induce mydriasis	Familiar	Refusing to sell under the pretext of lack of medicine	The pharmacist told that this customer always come to the pharmacy and ask for pentolate <sup>®</sup>
5	Independent	Male 21–40 years	Pentolate <sup>®</sup>	By customer without prescription	Yes	To induce mydriasis before surgery	Non familiar	The drug is not existing	The way of asking, appearance, no prescription and when we asked him about the surgery, he confused and didn't answer
6	Independent	Male 21–40 years	Pentolate <sup>®</sup>	By customer without prescription	Yes	Refused to mention	Non familiar	Refusing to sell under the pretext of the absence of a prescription	The pharmacist told that this customer came before and asked for pentolate <sup>®</sup>
7	Independent	Male 21–40 years	Prisoline® 2	By customer without prescription	Yes	Redness	Non familiar	Sold the drug	The customer came with his friend and ask for two bottles.
8	Independent	Male 21–40 years	Pentolate <sup>®</sup> 1	By customer without prescription	Yes	Dry eye and redness	Familiar	Refusing to sell under the pretext of lack of medicine	Because pentolate <sup>®</sup> eye drop not used for redness or for dry eye
9	Independent	Male 21–40 years	Prisoline <sup>®</sup> 2	By customer without prescription	Yes	Burning sensation	Familiar	Sold the drug	The pharmacist told that this customer always asked for this eye drop in large quantities.
10	Independent	Male 21–40 years	Pentolate <sup>®</sup> 1	By customer without prescription	Yes	Dry eye and redness	Non familiar	Sold the drug	Because pentolate <sup>®</sup> eye drop not use for redness or for dry eye
11	Independent	Male 21–40 years	Prisoline <sup>®</sup> 2	By customer without prescription	Yes	Refused to mention	Non familiar	Refusing to sell under the pretext of lack of medicine	Appearance and his way of asking, requesting two bottles. In addition, he mentioned all the alternatives
12	Independent	Male 21–40 years	Pentolate ® 4	By customer without prescription	Yes	To induce mydriasis before surgery	Non familiar	Refusing to sell under the pretext of lack of medicine	The customer asked for all the quantity present in the pharmacy which was 4
13	Independent	Male 41–50 years	Naphcon-A <sup>®</sup> 5	By customer without prescription	Yes	Redness	Non familiar	Refusing to sell under the pretext of lack of medicine	He was insisting to buy the drug, and left his number to call him when the drug became available
14	Independent	Male 21–40 years	Pentolate <sup>®</sup> 1	By customer without prescription	Yes	Redness (Allergy)	Non familiar	Sold the drug	Pentolate <sup>®</sup> eye drop not used for allergy
15	Chain	Male 21–40 years	Pentolate <sup>®</sup> 1	By prescription written by general doctor	Yes	To induce mydriasis before surgery	Familiar	The drug is not existing	The pharmacist told that this customer came every two days with a prescription
16	Independent	Female 41–50 years	Pentolate <sup>®</sup> 2	By prescription written by general doctor	Yes	To induce mydriasis before surgery	Familiar	Refusing to sell under the pretext of lack of medicine	The pharmacist told that this woman came frequently with different prescriptions written by ophthalmologists or general doctors
17	Independent	Male 41–50 years	Pentolate <sup>®</sup> 2	By prescription written by ophthalmologist	Yes	To induce mydriasis	Familiar	Refusing to sell under the pretext of lack of medicine	The pharmacist told that this customer was frequently coming to take this eye drop and when the pharmacist told him that there must be a prescription, he brought a prescription.

#	Chain/ Independent Pharmacy	Participant gender/ age	Eye drop/ Quantity <sup>a</sup>	Request method	Used before	Compliant by customer	Customer Familiarity	Pharmacist response/ reason, if not sold	Suspicious reasons
18	Independent	Male 41–50	Prisoloine <sup>®</sup> 3	By customer without prescription	Yes	Redness and Itching	Familiar	Sold the drug, but in less quantity, only one bottle.	Appearance and his way of asking. In addition, he requested three bottles.
19	Independent	Male 20–40	Pentolate <sup>®</sup> 1	By customer without prescription	Yes	He told that he is sick and need this drug	Familiar	Sold the drug	The Customer didn't clarify his disease and why he wants the medication

a Number of packages.

In terms of these observed cases of suspected abuse of ophthalmic products in Amman, it was notable that the majority occurred in independent pharmacies as opposed to chain pharmacies. We speculate that this trend could be due to the lack of uniform sales protocols when dealing with suspected abuse of medicinal products in independent pharmacies, as opposed to network protocols often present for employees in chain pharmacies. On the other hand, in independent pharmacies, retail pressures to generate income could influence decisions to dispense, despite suspected abuse.<sup>24</sup>

# **Study limitations**

The main limitations of this study were:

- 1. The study was conducted in a single city at Amman, capital of Jordan, and hence the results might not be generalizable to other cities in Jordan but on the other hand, every effort had been made to cover different regions of Amman to ensure representativeness.
- 2. The obtained sample size was in general small. However, the sample was higher than the minimum target sample calculated by the statistician (n = 120).
- 3. As the study researchers were females, no observations were made during working shift C, which may have affected the results. However, the researchers have fully covered both shifts, A and B in all recruited pharmacies.
- 4. The observation period, one week for each pharmacy may have not been enough and may have affected the results.
- 5. Many ophthalmic products as Pentolate<sup>®</sup> and Prisoline<sup>®</sup> were not available in the pharmacies during the observation which could underestimate the number of cases suspected of abuse, who could have obtained the products from those pharmacies.
- 6. The human error during reporting and observing cases cannot be ignored, such as inter-rater reliability between the two researchers and subjectivity in judgment. However, every effort was made during training of the researchers to maximize consistency (as described in Method section) and minimize this kind of error.
- 7. Although every effort had been made to assure pharmacists of the confidentiality and anonymity of the study and that it was done solely for research purposes by the academic team, the Hawthorne effect could not be totally negated, as some pharmacists may have behaved differently in the presence of the researchers, which may have affected the results of the study.

# Future work

This study provides a baseline data to build on in future studies; long-term study targeting different cites in Jordan with larger sample size to obtain more generalizable data. In addition, a qualitative study using in-depth interviews with customers suspected of drug absue is also recommended to better understand the main factors behind ophthalmic drug abuse.

# Conclusion

Observations in this study showed that 1 in every 6 requests of opthalmic products in community pharmacies in Amman is suspected of abuse where the product had been sold in almost 40% of suspected cases of abuse. The most commonly products suspected of abuse are anticholinergics and sympathomimetics. The study underscores the need for regulatory efforts to manage specific ophthalmic products (Pentolate<sup>®</sup>, Prisoline<sup>®</sup> and Naphcon-A<sup>®</sup>) abuse, through a more proactive role of the pharmacist rather than just refusing sale. Create a registry of those using the products and that can help pharmacists better flag excessive users of a particular product can be one suggestion. Also, Jordan Pharmaceutical Association and JFDA should develop best practices in the community pharmacy's for detection and management of all types of prescription and nonprescription drug abuse including ophthalmic medications.

# **Conflicts of interest**

Authors have no conflict of interest to report.

#### References

- J.E. Lessenger, S.D. Feinberg, Abuse of prescription and over-the-counter medications, J Am Board Fam Med 21 (1) (2008) 45–54.
- R.J. Cooper, Over-the-counter medicine abuse-a review of the literature, J Subst Use 18 (2) (2013) 82–107.
- G.F. Hughes, J.C. McElnay, C.M. Hughes, P. McKenna, Abuse/misuse of non-prescription drugs. Pharm World Sci 21 (6) (1999) 251–255.
- M. Wazaify, E. Abood, L. Tahaineh, A. Albsoul-Younes, Jordanian community pharmacists' experience regarding prescription and nonprescription drug abuse and misuse in Jordan–An update, J Subst Use 22 (5) (2017) 463–468.
- A. Shei, M. Hirst, N.Y. Kirson, C.J. Enloe, H.G. Birnbaum, W.C. Dunlop, Estimating the health care burden of prescription opioid abuse in five European countries, Clin Outcomes Res: CEOR 7 (2015) 477.
- NIDA, Commonly Abused drugs charts. retrieved from. charts, In: Abuse NIoD, 2014.
- A. Albsoul-Younes, M. Wazaify, A.-M. Yousef, L. Tahaineh, Abuse and misuse of prescription and nonprescription drugs sold in community pharmacies in Jordan, Subst Use Misuse 45 (9) (2010) 1319–1329.
- W. Al-Khalaileh, M. Wazaify, M.-C. Hout, The Misuse and Abuse of Ophthalmic Preparations: A Scoping Review of Clinical Case Presentations and Extant Literature, 2018.
- A.E. Darcin, N. Dilbaz, S. Yilmaz, M.K. Cetin, Cyclopentolate hydrochloride eye drops addiction: a case report, J Addiction Med 5 (1) (2011) 84–85.
- F.S. Bersani, O. Corazza, P. Simonato, et al., Drops of madness? Recreational misuse of tropicamide collyrium; early warning alerts from Russia and Italy, Gen Hosp Psychiatry 35 (5) (2013) 571–573.
- F.S. Bersani, C. Imperatori, M. Prilutskaya, R. Kuliev, O. Corazza, Injecting eye-drops: a mini-review on the non-clinical use of tropicamide, Hum Psychopharmacol Clin Exp 30 (4) (2015) 262–264.
- B. Yeniad, S. Canturk, F. Esin Ozdemir, N. Alparslan, K. Akarcay, Toxic keratopathy due to abuse of topical anesthetic drugs, Cutan Ocul Toxicol 29 (2) (2010) 105–109.

- E. Erdem, I.H. Undar, E. Esen, K. Yar, M. Yagmur, R. Ersoz, Topical anesthetic eye drops abuse: are we aware of the danger?, Cutan Ocul Toxicol 32 (3) (2013) 189–193.
- A. Sharifi, H. Sharifi, M. Karamouzian, et al., Topical ocular anesthetic abuse among Iranian welders: time for action, Middle East Afr J Ophthalmol 20 (4) (2013) 336.
- O.Y. Tok, L. Tok, I.M. Atay, T.C. Argun, N. Demirci, A. Gunes, Toxic keratopathy associated with abuse of topical anesthetics and amniotic membrane transplantation for treatment, Int J Ophthalmol 8 (5) (2015) 938.
- C.N. Soparkar, K.R. Wilhelmus, D.D. Koch, G.W. Wallace, D.B. Jones, Acute and chronic conjunctivitis due to over-the-counter ophthalmic decongestants, Arch Ophthalmol 115 (1) (1997) 34–38.
- A.J. Flach, Corneal melts associated with topically applied nonsteroidal anti-inflammatory drugs, Trans Am Ophthalmol Soc 99 (2001) 205.
- M. Wazaify, M.B. Alali, M.A. Yousef, S. Qammaz, Ophthalmic drops abuse in community pharmacy setting: a cross-sectional study from Jordan, J Subst Use (2017) 1–5.

- P. Tayanithi, P. Aramwit, Self-medicated over the counter ophthalmic solutions in central Bangkok, J Med Assoc Thail 88 (2005) S330.
- R. Kadri, S. Hegde, A.A. Kudva, A. Achar, Over the counter ophthalmic drug misuse, are we aware?, Online J Health Allied Sci 9 (2) (2010).
- R. Kadri, S. Hegde, A.A. Kudva, A. Achar, S.P. Shenoy, Self-medication with over the counter ophthalmic preparations: is it safe?, Int J Biol Med Res 2 (2) (2011) 528–530.
- G.J. Berdy, M.B. Abelson, L.M. Smith, M.A. George, Preservative-free artificial tear preparations: assessment of corneal epithelial toxic effects, Arch Ophthalmol 110 (4) (1992) 528–532.
- A.-M.M. Yousef, A.G. Al-Bakri, Y. Bustanji, M. Wazaify, Self-medication patterns in Amman, Jordan, Pharm World Sci 30 (1) (2008) 24–30.
- M. Wazaify, J. Scott, Prescription/Non-prescription medicine misuse and regulation–time for a modern, fit for purpose approach, J Pharm Pract Commun Med 3 (4) (2017) 197–199.