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PERCEPTION OF COMMUNITY PHARMACISTS AND PHARMACY TECHNICIANS IN SANA`A- YEMEN ABOUT RISKS OF USE OF HERBAL PRODUCTS DURING PREGNANCY AND BREASTFEEDING

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ABSTRACT

Similar to chemically synthesized drugs, herbal medicines can be potentially harmful if not used correctly. Unfortunately, the public as well as healthcare professionals are often misled to believe that all natural treatments are inherently safe. The objective of this study was to assess the perception and knowledge of community pharmacists and pharmacy technicians in Sana'a-Yemen about the risks of herbal products during pregnancy and breastfeeding. A questionnaire composed of 246 questions regarding the risks of a sample of 246 herbal medications available in the drug market was distributed to 186 community pharmacists and pharmacy technicians. The results showed that 65% of the participants had an overall incorrect perception about risks of herbal medications. This finding was close to that reported in India and Emirates.

KEYWORDS: Herbal, Risks, Pregnancy, Breastfeeding, Community pharmacists, Yemen.

INTRODUCTION

Herbal products are preparations made from crude drugs or extracts of leaves, flowers, seeds, barks, roots, rhizomes or the whole herb of one or more plants.[1] Traditionally there have been preparing as simply by decoction, maceration or other methods at home or at herbalist

shops. Similar to synthetic drugs, many of these products are nowadays manufactured by pharmaceutical or dietary supplements companies in the form of tablets, capsules, ointments etc. They are available in community pharmacies and are dispensed without the need of medical prescription. Despite the fact that they are marketed as "food integrators", majority of these products are used as alternative treatment for alleviating a number of health problems such as heart diseases, diabetes, high blood pressure and even certain types of cancer.[2,3]

The consumption of herbal products is increasing steadily throughout the world.[3] It is frequently stated in the scientific literature that 80% of people in Asian and African countries (or sometimes that 80% of the world's population) use traditional medicine to meet their primary healthcare needs.[4] Accordingly, the market for herbal products is expected to reach $111 billion by the end of 2023.[3]

The major driving force for the use of herbal products is the perception that 'they are safe because they are natural and have fewer side effects than prescription drugs. However, various studies and researchers have high lightened their possible side effects, if taken incorrectly, in excessive amounts or in combination with some medicines.[2] There are many examples that can demonstrate the harmfulness of herbal medicines. For instance, Aloe (Aloe Vera) a causative agent in hepatotoxicity[5], Ginger(Zingiber officinale) that increases the risk of bleeding or potentiate the effects of warfarin therapy[6], Cardamom (Elettaria cardamomum) that causes serious dermatitis from skin exposure to the plant[7], Aristolochia species which contain the genotoxic, nephrotoxic and carcinogeneic constituents" aristolochic acids"[8,9], Ephedra (Ephedra sinica) which produces a number of serious cardiovascular and central nervous systems adverse effects[10] and Aconitum species that causes severe cases of cardiac toxicity manifesting as ventricular tachycardia and fibrillation and eventually leading to death.[11]

The prevalence of herbal medicine utilization in pregnancy ranges between 7% and 55% in different geographical, social and cultural settings, and ethnic groups.[12] Injudicious use of herbs or interaction of these herbs with prescribed medications can have unknown effects in pregnancy or cause serious complications in the fetus.[13] Some herbs may contain substances that can cause miscarriage, premature birth, uterine contractions, or injury to the fetus. Few studies have been done to measure the effects of various herbs on pregnant women or fetuses. Therefore, pregnant women are urged not to take any herbal products without talking to their health-care provider first. Examples of herbs that are absolutely contraindicated

during pregnancy are Saw Palmetto (Sabal serrulata) because it has hormonal activity, Dong Quai (Angelica archangelica) due to its stimulant and relaxant effect on uterine and Blue cohosh (Caulophyllum thalictroides) owing to its labor-induction effect.[14] The common pregnancy- related problems, including nausea, vomiting, constipation, and heartburn are cases that usually result in pregnant women self-medicating using over-the-counter (OTC) medications, seeking prescribed medications, or using herbs. However, the use of herbs may expand beyond those cases especially in some African and Arabian countries of populations with low-income and reduced levels of education.[15,16]

A concern for breastfeeding women who are taking medications is the transfer of medicines into breast milk. Medicines circulating in the maternal bloodstream can potentially be transferred into human breast milk, exposing breastfed infants to medicines that may potentially be harmful. Another concern is the effect of medication on the quantity and quality of breast milk produced, which may impact on the exclusivity, duration and success of breastfeeding. Herbals galactagogues used to increase breastmilk supply are commonly used during breastfeeding. Examples of these herbs are fenugreek (Trigonella foenum-graecu), blessed thistle (Cnicus benedictus) and fennel (Foeniculum vulgare). However other herbs may be used for other reasons. For instance, garlic (Allium sativum) to boost immunity during cold, chamomile (Matricaria chamomilla) for stress relaxation, Ginger (Zingiber officinale) for general health enhancement, and cranberry (Vaccinium macrocarpon) for urinary tract infection.[17] The safety of some of those herbs has not been established.[18]

It should be mentioned that, unfortunately, herbal drugs and related products are introduced into the market of poor countries without any mandatory safety or toxicological evaluation. Many of these countries also lack effective machinery to regulate manufacturing practices and quality standards.[19]

Hence, the role of physicians and pharmacist to educate patients about risks of herbal products is absolutely vital to ensure patients rationally use of those products and prevent their potential misuse or abuse.

MATERIALS AND METHODS

Herbal products and risk distribution

A survey of herbal products available in 320 community pharmacies at 5 different areas of Sana`a, the capital of Yemen, was conducted within the period from December 6th 2019 to

February 14th 2019. Products that contained at least one medicinal plant even if contained synthetic drugs were included while those for cosmetic purposes were excluded in this study.

The results of the survey revealed that 404 different trade names of herbal products were available in those pharmacies. Then, among those products, if two or more containing the same medicinal plants, only a single product was selected regardless the variation in dosage forms or strengths of the constituents. As a result, the number reduced to 246 products which were then classified into 7 categories, based on their therapeutic- indication classes, into products for CNS, CVS, respiratory, GIT, renourinary, hepatic and topical disorders. The distribution % of each category among the surveyed products was determined.

The risk of each product during pregnancy and breastfeeding was assessed using WHO monographs of selected medicinal plants.[20] For products containing medicinal plants that are unviable in the WHO reference, the information on the medicinal plant was obtained from the websites of reliable information sources were used. These sources included, consecutively, the websites of the national center for complimentary and integrative health (NCCIH) / (NIH) National institute of health, USA[21]., the European medicine agency (EMA)[22] and the Medicines and healthcare products regulatory agency (MHRA), UK.[23]

Products were considered to have a risk during pregnancy and breastfeeding if pregnancy and/or breastfeeding was contained under the title of “contraindications” and/or “precaution with distinct warning statements such as “should be avoid”, “is not recommended”, “safety has not been established” or “No sufficient data of safety” during pregnancy/breastfeeding, For products containing two or more medicinal plants, the whole product was considered risky if at least one of those medicinal plants had a risk on pregnant or breastfeeding women.

Perception of participants

A questionnaire, prepared by the research team, was distributed to 300 community pharmacists and pharmacy technicians working at the time of the study in community pharmacies at 5 different areas of Sana`a. Unfortunately, only 186 participants completed the questionnaire. The questionnaire consisted of questions about 50 herbal products selected from the surveyed herbal products. The number of products in each therapeutic indication class was based on its distribution % while the individual products of each category were selected randomly. Each question was made as simple as possible and focused on the participant`s knowledge about safety of one product during pregnancy and breastfeeding with

two answer options: “Safe”, “Risky”. The questionnaire was left with the participant for 2 hours in order to allow the participant to use any source of information for the questions he/she was not sure of. The research team didn’t advice any participant to use a specific source of information.

For statistical purposes, participants were grouped based on their gender, level of qualification, years of experiences and source of information they rely on.

The incorrect perception (Pi) of all participants or of a group of participant was calculated as follows:

$Pi = 100 * Qi/ (50 * n)$

where (Qi) were the cumulative number of questions answered incorrectly, (n) was the number of participants and (50) was the number of questions per a questionnaire.

The incorrect perception (Pi) was then calculated as follows

$Pi = 100 - Pc$

Calculations and statistical data analysis was conducted using SPSS program V.20. Suitable statistical methods were used to evaluate variations in sets of data with $p < 0.05$ indicating significant difference.

RESULTS AND DISCUSSION

Herbal products and risk distribution

As demonstrated in table 1, 7 therapeutic-indication classes of herbal products were found in community pharmacies. The top most two classes were the products for respiratory (45.122%) and GIT disorders (18.699%) while the classes with lowest distributions (1.22%) were the products for CVS and CNS.

The majority of products (98%) were the ones which have risks if used during pregnancy and/or breastfeeding and the difference in distributions of risky products to the safe ones was significant ($p < 0.05$).

Table 1: Statistics of herbal products (n=246) surveyed in community pharmacies of Sana`a –Yemen and their distributions of risks during pregnancy and breastfeeding.

No.	Therapeutic -indication class	f *		Total	
		Risky	Safe	f *	Distribution %
1.	CNS	2	1	3	1.220
2.	CVS	2	1	3	1.220
3.	Respiratory	111	0	111	45.122
4.	GIT	45	1	46	18.699
5.	Renourinary	43	1	44	17.886
6.	Hepatic	23	1	24	9.756
7.	Topical	15	0	15	6.098
Total		241	5	246	100
Distribution %		98	2	100	
p value		0.0049 ▲			

*: frequency; ▲Significant difference ($p < 0.05$)

Examples of medicinal plants which were found in the surveyed herbal products with known risks if used during pregnancy and/or breastfeeding, were demonstrated in table 2.

Table 2: Examples of medicinal plants that should be avoided during pregnancy and breastfeeding (20-23) which were found in the herbal products marketed in Yemen.

Therapeutic-Indication class	Medicinal plants
CNS	Zizyphi (Zizyphus jujube), Ginko (Ginkgo biloba), Radix Eleutherococci (Eleutherococcus senticosus), Ginseng (Eleutherococcus senticosus), Chinese thorowax root (Radix Bupleuri) and German Chamomile (Matricaria chamomilla)
CVS	Radix cum (Taraxacum offi cinale), Semen Hippocastani (Aesculus hippocastanum), Cum Flore (Crataegus monogyna), Cynarae (Cynara cardunculus), black myrobalan (Terminalia chebula) and Garlic (Allium sativum)
Respiratory	Semen Armeniacae (Prunus armeniaca), Radix Althaeae (Althaea officinali), Ephédra (Ephedra sinica), Eucalyptus (Eucalyptus globulus), Liquorice (Glycyrrhiza glabra), Red clover (Trifolium pretense) and Senega (Polygala senega)
GIT	Senna (Senna alexandrina), ginger (Zingiber officinale), Aloe oral (Aloe vera), Biji makassar (Brucea javanica), Chamomile (Chamomilla recutita), Cinnamon (Cinnamomum verum),Chinese goldthread (Coptis chinensis), Curcum (Curcuma longa) and Goldenseal (Hydrastis Canadensis)
Renourinary disorders	Parsley (Petroselinum crispum), Shepherd's purse (Capsella bursa-pastoris), Stone root (Collinsonia Canadensis), Couchgrass (Elymus repens) Uva-Ursi (Arctostaphylos uva-ursi), Buchu (Agathosma betulina), Saw Palmetto (Sabal serrulata) and Corn Silk (Zea mays)
Hepatic disorders	Celandine (Chelidonium majus), Dandelion (Taraxacum officinale), Yellow Dock (Rumex crispus) and Blue flag (Iris versicolor)
Topical disorders	Hamamelis (Hamamelis virginiana), Aetheroleum (Melaleuca alternifolia), Calendula (Calendula officinalis), Capsicum (Capsicum species), Roman Chamomile (Matricaria recutita), Comfrey (Symphytum officinale), Hops (Humulus lupulus), Bilberry (Vaccinium myrt), Hydrocotyle (Centella asiatica), St John's Wort (Hypericum perforatum) and Centellae (Centella coriacea).

Participants' data and perceptions

Differences in the number of participants, as shown in table 3, with respect to their gender, years of experiences, level of qualification and sources of information were all found significant ($p < 0.05$). The results showed that most of participants were males, had a range of 6-10 years of experience, attaining pharmacy Bachelor degree and were dependent on physicians` prescriptions as main source of information with percentages of 96.8%, 53.8%, 57% and 50.5%, respectively.

With respect to participants` perceptions (table 3), the overall average incorrect perception of all participants was 66.969± 8.831%; (95% C.I: 62.2- 77.8%) which was significantly higher ($p<0.05$) than their overall average correct perception of 33.031 ± 8.831% (95% C.I: 28.2- 37.8%). The incorrect perception was close and not significantly different ($P > 0.05$) from that reported in in India (76.3%)[24] and United Arab Emirates (71%).[25]

Table 3: Data of Participants (n=186) and their perceptions about risk of herbal products use during pregnancy and breastfeeding.

Data		Statistics of participants			Participants` Perceptions		
		f	%	p value	Correct %	Incorrect %	p value
Gender	Male	180	98.6	< 0.001 ♣	34.3	65.7	0.483 ☼
	Female	6	3.2		37.7	62.3	
Experience (years)	1 – 5	100	37.6	< 0.001 ♣	30.7	69.3	0.922 ☼
	6 – 10	70	53.8		33.7	66.3	
	11 -15	16	8.6		28.6	71.4	
Qualification	Pharmacy Master	2	1.1	< 0.001 ♣	40.8	59.2	0.171 ☼
	Pharmacy Bachelor	106	57.0		37.1	62.9	
	Pharmacy technician diploma	78	41.9		31.5	68.5	
Source of information	Physician opinions	94	50.5	< 0.0001 ♣	8.7	91.3	0.001 ♣
	Other pharmacists	10	5.4		34.8	65.2	
	School lectures and text books.	62	33.3		31.3	68.7	
	Search on non-scientific Web sites	2	1.1		9.8	90.2	
	WHO, NIH, MHRA	18	9.7		65.1	34.9	
Average ± SD					33.031± 8.831	66.969± 8.831	< 0.0001♣
95 % C.I					28.2- 37.8	62.2- 77.8	

The statistical analysis showed that the high incorrect perception of participants obtained in this study was not attributed to the participants gender, years of experience or qualification with $p > 0.05$ in each case. However, the factor that was significantly different ($p < 0.05$)

among the participants was the source of information they rely on. Participants who reported that they use reliable sources of information such as WHO, NIH or MHRA had significantly lower incorrect perception than those who used to use other unreliable sources such as physicians opinions and web search of non-scientific websites.

On conclusion, using untrustworthy sources to get information on risks of herbal products is a major factor that lead to incorrect information the pharmacist may provide to patients during counseling sessions. This issue becomes more critical when the patient is one of the specific population of patents e.g. pregnant and breastfeeding women who are more affected by drugs risks and therefore need more awareness while selecting of a medication for them. With the availability and easiness of reaching the reliable sources of information, pharmacist have no excuse to use unreliable sources.

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