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Attitude of Libyan Pharmacist

InWesternRegionof Libya Toward ZantacWithdrawal

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ABSTRACT

Post-marketing drug withdrawals can be associated with various events, ranging from safety issues such as reported deaths or severe side-effects, to a multitude of non-safety problems including lack of efficacy, manufacturing, regulatory or business issues. During the last century, the majority of drugs voluntarily withdrawn from the market or prohibited by regulatory agencies was reported to be related to adverse drug reactions. Understanding the under lying mechanisms of toxicity is of utmost importance for current and future drug discovery. A questioner review about Libyan pharmacist attitude toward Zantac withdrawal in the western region of Libya. Thedata then was evaluated by Microsoft Excel software for analysis.The total number of responses received was 67, and these responses were from different cities in the west of Libya during 6months study 2020. Highlighting the different sources of knowledge regarding the withdrawal decision, 64.1 % got the information through social media. 32.8 % of the pharmacists after getting the information regarding Ranitidine withdrawal returned it to the company from which bought it. 83.6% of the pharmacist when asked about ranitidine cause of drawing clarified that the ranitidine contains carcinogenic substances. 37.3% of participants mentioned that pharmacovigilance means the detection of problems related to drugs after marketing and use by patients. The aim of this work is to know whether Libya really has drug control and how to deal with medicines that are withdrawn from the market by international organizations andto analyze the knowledgeand attitudeof Libyan pharmacists in western region of Libya about Zantac withdrawn from the market. From

the results of a questionnaire conducted in the western regions about knowledge and attitude of Libyan pharmacists toward Zantac withdraw from the market, we concluded that a small percentage of Zantac products have been withdrawn and the doctors are still prescribing and pharmacists are dispensing ranitidine, whether it is OTC or POM.

Key words: withdrawal**,** pharmacovigilance, ranitidine, attitude, Libya

INTRODUCTION

The main goals of drug development are effectiveness and safety. Because all drugs can harm as well as help, safety is relative. The difference between the usual effective dose and the dose that causes severe or life-threatening side effects is called the margin of safety. A wide margin of safety is desirable, but when treating a dangerous condition or when there are no other options, a narrow margin of safety often must be accepted. If a drug's usual effective dose is also toxic, doctors do not use the drug unless the situation is serious and there is no safer alternative.[(1)]Before a medicine is authorized for use, evidence of its safety and efficacy is limited to the results from clinical trials, where patients are selected carefully and followed up very closely under controlled conditions. This means that at the time of a medicine's authorization, it has been tested in a relatively small number of selected patients for a limited length of time.[(2)]After authorization the medicine may be used in a large number of patients, for a long period of time and with other medicines. Certain side effects may emerge in such circumstances. It is therefore essential that the safety of all medicines is monitored throughout their use in healthcare practice.[(2)]Monitoring the safety of medicines, which is also known aspharmacovigilance, includes all activities related to the detection, assessment, understanding and prevention of adverse effects and other possible drug-related problems, and taking action to reduce the risks and increase the benefits of medicines. It is a key public health function.[(3)] This monitoring is carried out in a number of ways, including review and evaluation of suspected adverse reaction reports,

published literature, epidemiological studies and additional clinical trial results

As the pharmaceutical industries throughout the world are moving ahead towards becoming more and more competitive, regulatory agencies are being established in various countries across the globe. Regulatory agencies and organizations play a vital role to meet the requirements of legal procedures related to drug development process.The major challenges of these regulatory agencies and organizations around the world are to ensure the safety, quality and efficacy of medicines and medical devices, harmonization of legal procedures related to drug development, monitoring and ensuring compliance with statutory obligations. They also play a vital role to ensure and increase regulatory implementation in non-regulated parts of the world for safety of people residing there. [(4)]In the present scenario, pharmaceuticals are considered as the most highly regulated industries worldwide. The regulatory body ensures compliances in various legal and regulatory aspects of a drug. Every country has its own regulatory authority, which is responsible to enforce the rules and regulations and issue the guidelines to regulate drug development process, licensing, registration, manufacturing, marketing and labeling of pharmaceutical products.

Market withdrawal simply means a withdrawal of a product from the market in a country or countries which has or is reasonably expected to have an adverse effect (which is material) on sales of such product respectively. [(5)]According to the FDA, drug is removed from the market when its risks outweigh its benefits. A drug is usually taken off the market because of safety issues with the drug that cannot be corrected, such as when it is discovered that the drug can cause serious side effects that were not known at the time of approval. The FDA also takes into account the number of people taking a drug being considered for removal so as to not harm those patients.[(6)]

Drugs or medicines may be withdrawn from commercial markets because of risks to patients, but also because of

commercial reasons (e.g. lack of demand and relatively high production costs). Where risks or harms is the reason for withdrawal, this will usually have been prompted by unexpected adverse effects that were not detected during Phase III clinical trials, i.e. they were only made apparent from post marketing surveillance data collected from the wider community over longer periods of time. [7]

MATERIALS AND METHODS

Identical questionnaires were used . Questions determined knowledge and attitude of Libyan pharmacist about Zantac withdrawn from the market. Interviewees were also questioned about their knowledgeconcept of pharmacovigilance and also asked about their procedure that they have taken in the remainingmedicine boxes in their pharmacies.

With the current conditions that we faced due to Corona virus, which led to the imposition of ban and the closure of all educational institutions, which forced us to distribute the questionnaire online to the pages of pharmacists and pharmacies on social media.

- Questionnaire conditions:
  Choose one of the answer provided for each question.

-We hope you will answer all questions in questionnaire sheet.

1. **Name of the city:**
2. **Years of experience**:
   a) Less than 1 year
   b) From 1 to 5 years
   c) From 5 to 10 years
   d) More than 10 years
3. **Workplace:**
   a) Community pharmacy

b) Hospital pharmacy

4. Other answer

5. The concept of pharmacovigilance may mean:

a) Optimal safe, effective and economical use of drugs.

b) Monitoring therapeutic effect of medications .

c) Detection, understanding, evaluation and prevention of drug side effects.

d) The detection of problems related toadrug after its marketing and use by patients.

6. How did you know about ranitidine withdrawal decision?

a) Social media

b) Partner in the job

c) The institution you work for

d) Other answers.....

7. When you knew of the decision of RANITIDINE withdrawal, what is the procedure that you have taken in the remaining medicine boxes in your pharmacy

a) Returned it to the company from which it was purchased

b) Got ride of the medicine by putting it in the garbage

c) Did not abide by decision, with continuing to dispense the medicine to patient

d) Other answers.....

8. Why was *RANITIDINE* removed fromthe market?

a) As result of the increase in side effects in the last years

b) The appearance of more effective and safe alternative medicines

c) It contains carcinogens

d) Other answers.....

9. What is the substance thatis responsible for carcinogenicity?

a) Expedient

b) Nitrosamine compounds

c) N. nitrosodimethylamine " NDMA"
d) N. nitrosodiethylamine " NDEA"
e) Other answers.....

10. Who is responsible for issuing such decision in Libya?

a) Ministry of health
b) Pharmacists syndicate
c) Food and drug control center
d) Doctors syndicate
e) Other answers.....

11. If you receive a doctor's prescription that contains *RANITIDINE* :

a) You dispense the medicine because the doctor knows the condition
b) Don't dispense it and explain to patient about the seriousness ofthe drug
c) The patient is advised to return to the doctor
d) Give the patient an alternative medicine to RANITIDINE
e) Other answers.....

RESULTS

A total 67 of responses was received, from different cities in the west of Libya during a 6 months study 2019-2020.

From figure 1the following were noted: around 88 % of the participants included in the current study were working in community pharmacies, and only 9 % were working in hospital pharmacies while 3% were working in both community and hospital pharmacies.

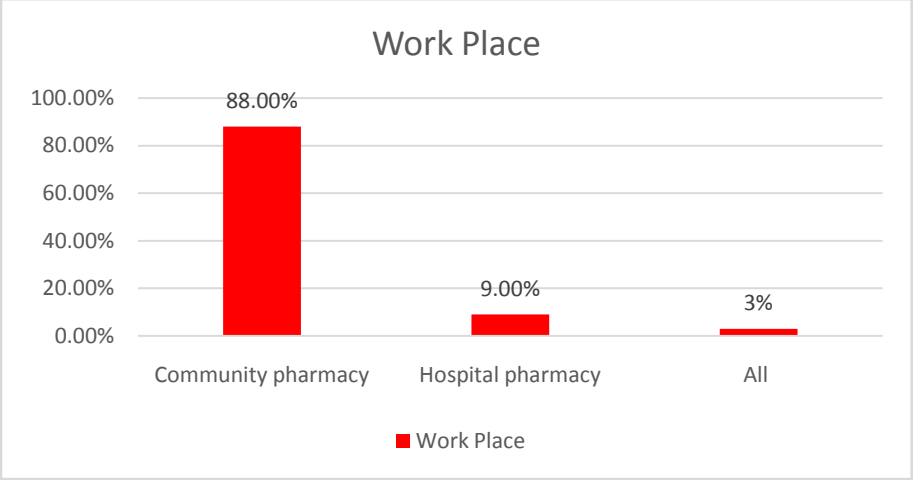

Figure 1. The percentage of participants in relation to their workplace

Figure 2 summarizes the years of experience percentage of the respondents, which highlight that more than half of participants had 1 to 5 years of experience, while 22.4 % were less than 1 year but pharmacists who have experience over five years to ten years make up 13.4% of all the participants and the least percentage was pharmacists who have experience from over ten years which were 6%.

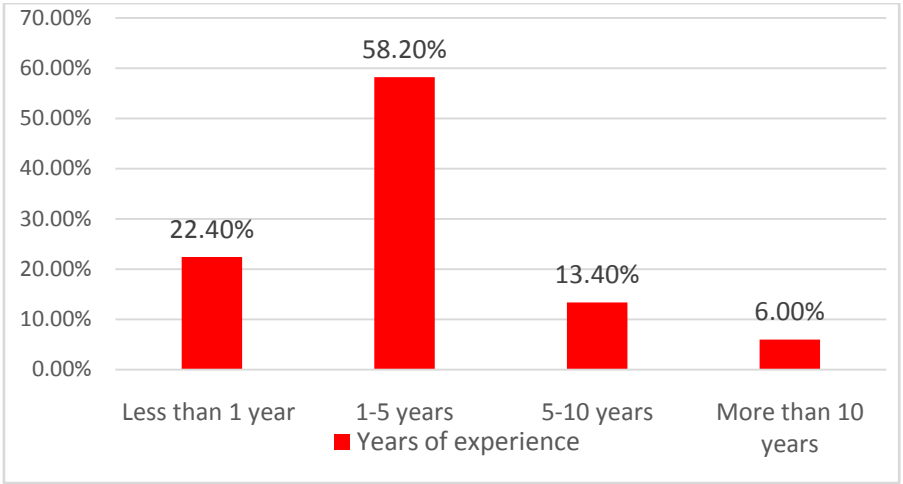

Figure 2. The percentage of pharmacists in relation to years of experience.

The concept of pharmacovigilance meaning is shown in figure 3 where 37.3% of participants mentioned that pharmacovigilance means the detection of problems related to drugs after marketing and use by patients and 28.3% stated the choice of optimal safe, effective and economical use of drugs. In addition, 25.4% said it is the detection, understanding, evaluation and prevention of drug side effects. Finally, 9% cited it is monitoring of therapeutic effect of medications.

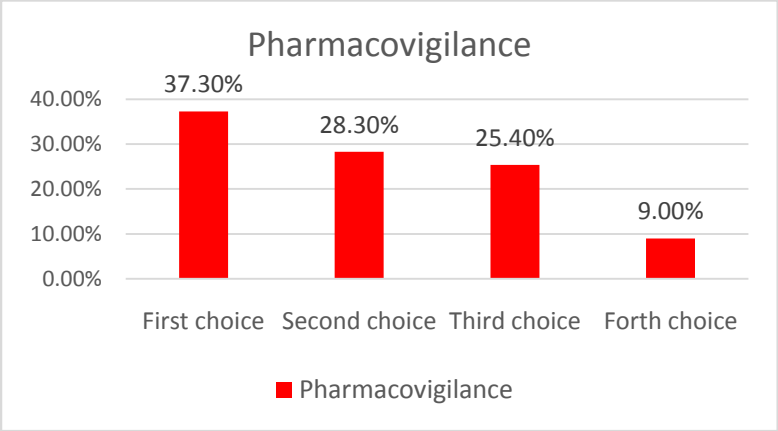

Figure 3.Knowledge of pharmacist in concept of pharmacovigilance

The fourth question asked participants about their knowledge regarding the decision of Ranitidine withdrawal from market, 97% of respondents were aware of this decision.

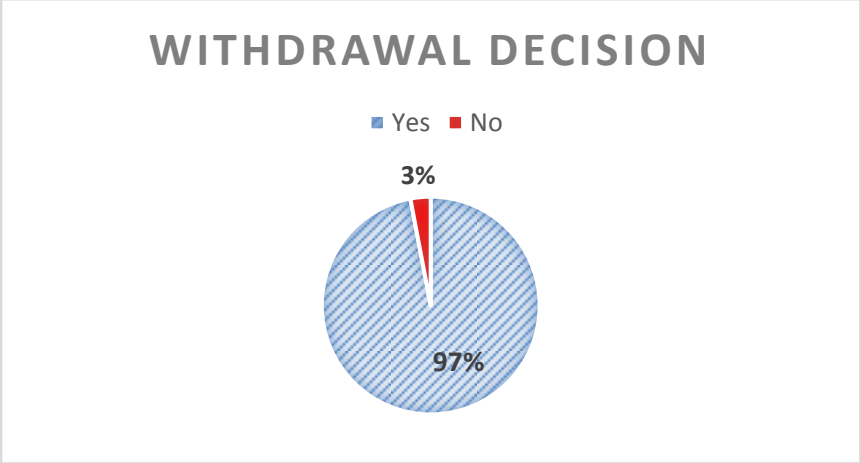

Figure 4.The percentage of pharmacists aware about decision of Ranitidine withdrawal fromthe market.

Figure 5 highlights the different sources of knowledge regarding the withdrawal decision. Whereas, 64.1 % got the information through social media but 26.9% from partner in job (maybe use colleague instead) and the rest were from institution of work 4.5 %, collage 1.5 % and from FDA guidelines was 1.5 % while 1.5 % said they did not remember the source**.**

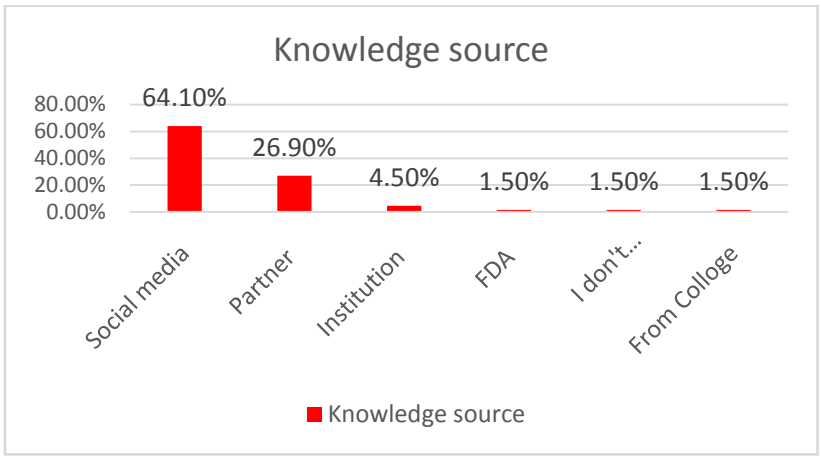

Figure 5. Sources of knowledge regarding the withdrawal decision

The procedure taken by pharmacists after getting the information regarding Ranitidine withdrawal is expressed in figure 6, where 32.8 of pharmacist return

the drug to company from which it was purchased, 31.3 were got ride the medicine by putting it in the garbagewhile 29.9 of the pharmacistscontinuing to dispense the medicine to the patient, and the other procedures were left decision to the manager 1.5 % and 4.5%.

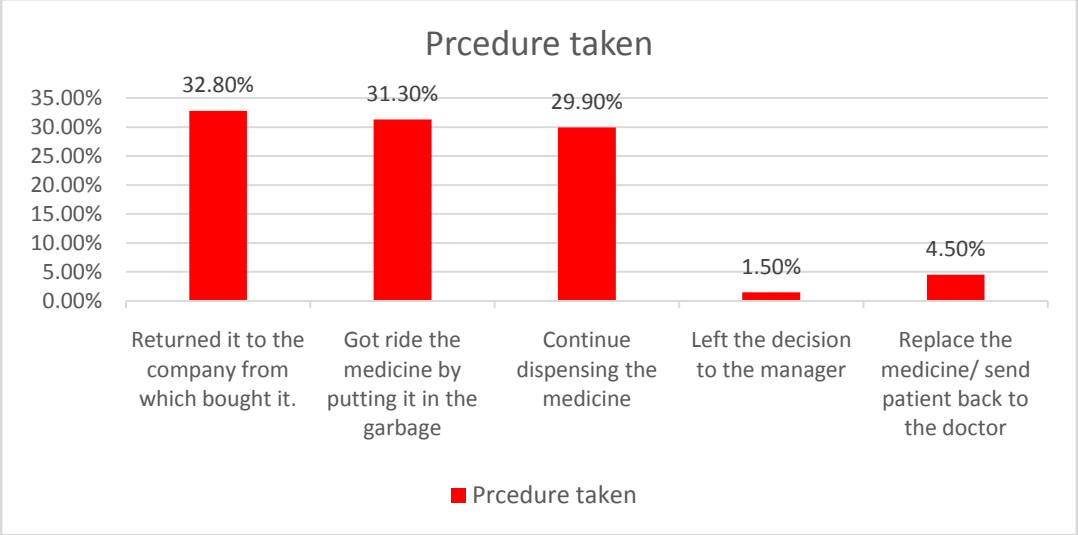

Figure 6.The procedure taken by pharmacists after getting the information regarding Ranitidine withdrawal

Figure 7 summarize the reason of Ranitidine withdrawal, where 83.6% clarified that ranitidine contains carcinogenic substances, 11.9% said that appearance of more effective and safe alternative medicines and4.5 % of them answered that asa result of the increase in side effects in the last years**.**

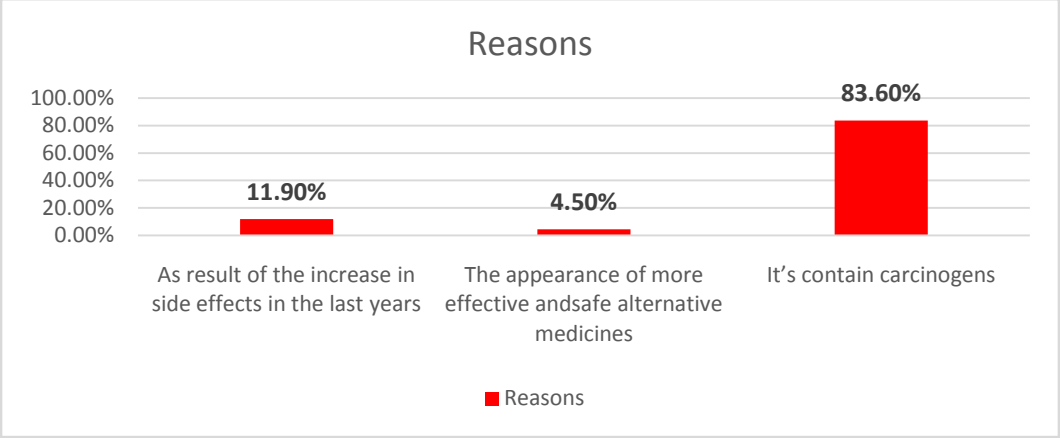

Figure 7. Shows the reason of Ranitidine withdrawal

Figure 8 states the opinion of respondents about the substance that responsible for carcinogenicity, about 60% highlighted that N. nitrosodimethylamine" NDMA" is the carcinogens substance while 23.9% said that substance that responsible for carcinogenicity is nitrosamine compounds , but 9% said that carcinogenicity result from excipients and 6% highlighted that N.Nitrosodimethylamine" NEMA, whereas 1.5 % said that do not have knowledge.

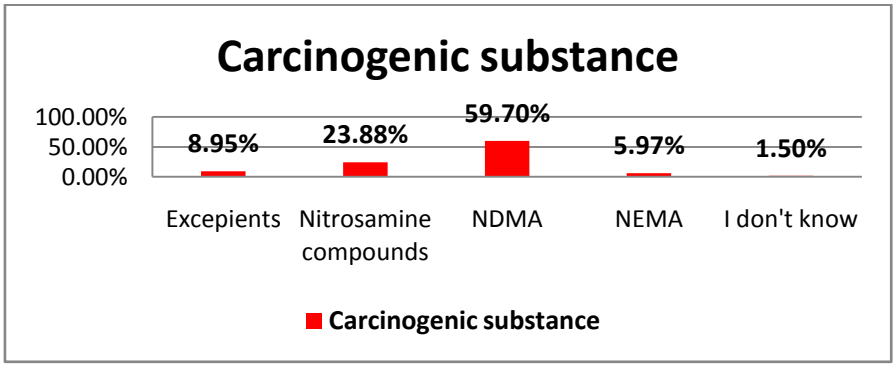

Figure 8. The opinion of respondents about the substance thatis responsible for carcinogenicity

Figure 9 showed the participants's opinion regarding the responsibility of Ranitidine withdrawal. 40.3% of the participants confirmed that the decision is the responsibility of the Food and drug control center, 33.3 % mentioned that it is the ministry of health's responsibility, while 17.9% of them said this responsibility to pharmacists syndicate, and 7.5% have referred the responsibility to the doctors syndicate.

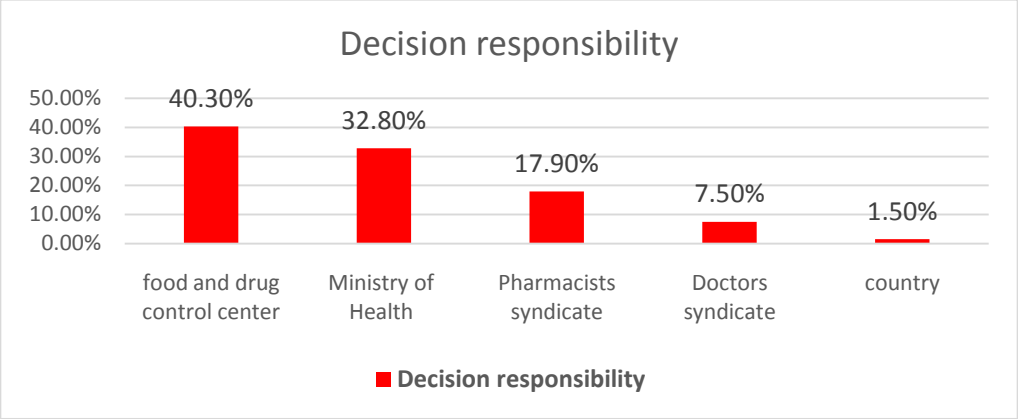

Figure 9.Responsibility for withdrawal decision in Libya

Responses to question 10 designed for assessing respondents' attitudes if they receive a prescription contain ranitidine, were presented in figure 10. Nearly 37.3% was the patient is advised to return to the doctor, 25.4% give the patient an alternative medicine to RANITIDINE,19.4% not dispensing it and explain to a patient about the seriousness of drug, while 17.9% dispense the medicine because the doctor knows the condition.

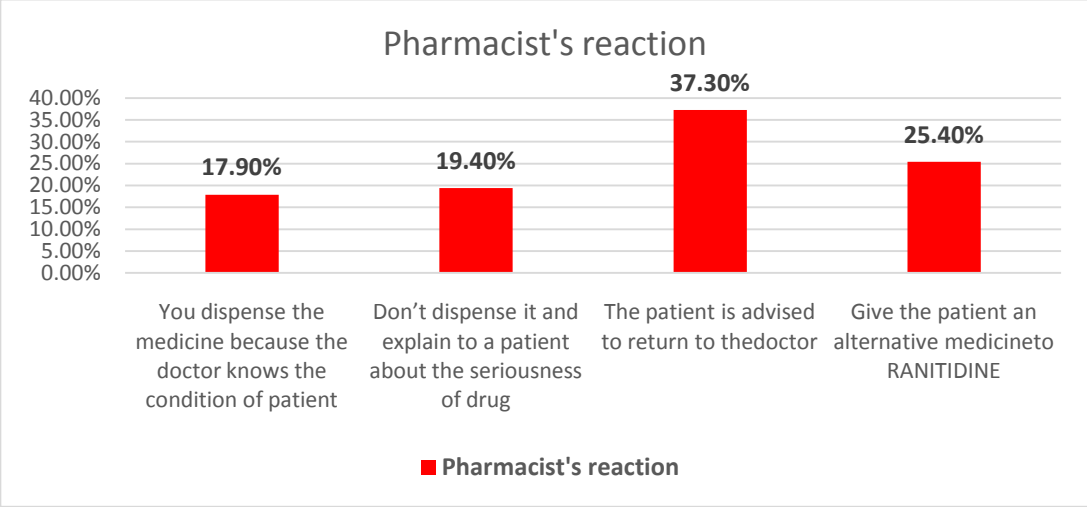

Figure 10.Pharmacist's reaction if they receive prescription that contains Ranitidine.

Discussion and conclusion

The present investigation was conducted in a 6 months period. The goal was the altitude of Libyan pharmacists about subject of Zantac withdrawal from markets at some districts from the west district in Libya.Up to our knowledge this the only research article about pharmacist attitude toward Zantac withdrawal in Libya and we do not find in any country else this is may be due to missed government role in Libya.FDA issued a decision to withdraw all medicinal products related to ranitidine from the market on date 1.April. 2020, and Libya issued a decision to withdraw ranitidine from pharmacies on date 9.April.2020 but issued a decision only without withdrawing the drug from pharmacies and some pharmacies still selling this product of the drug after this decision was issued.

From the results of a questionnaire conducted in the western regions about knowledge and attitude of Libyan pharmacists about the decision to withdraw Zantac from the market, we are concluded that a small percentage of Zantac products have been withdrawn and that the doctors are still prescribing and pharmacists are dispensing

ranitidine, whether it is OTC or POM. And basing on this, strict measures voluntary recall of already banned drugs or drugs with documented adverse effect profileshould be taken, and needed continuous safety surveillance of drugs- even very old drugs and those presumed to be quite safe. There is a need to study pharmacovigilance in Libya. Physicians should begin reporting adverse drug reaction (ADR) to the nearest pharmacovigilance center to help generate ADR database, and pharmacists and doctors should be advise patients about the availability of alternative prescriptions and over the counter (OTC) medicinesto treat their condition. This will ensure marketing of safe medicines and aid better patients care.

towards pharmaceutical companies which seem to be uninterested in

Pharmacists should remind patients taking prescription ranitidine that they should speak with their healthcare professional about other treatment options before stopping the medicine, as there are multiple drugs approved for the same or similar uses as ranitidine that do not carry the same risks from NDMA.

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