Pharmacist's Role in Non-cancer Pain Management

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Summary

Pharmacists have an important role within the healthcare system. They can offer some services to the patients including consultation, patient education and therapeutic management. Community pharmacists can assess the type and severity of pain, monitor treatment and guide medication regulation to improve the treatment of the pain.
Goals: Aim and objects was to study and analyze professional abilities and role of pharmacy employees during the noncancer pain management.
Materials and Methods: The study was quantitative investigation by using Questionnaire. 285 pharmacy employees were participated in Yerevan. The survey was conducted during the 2018 -2019. The questionnaire was developed based on the World Health Organization standard questionnaire. Study results were analysis on Statistical Package for the Social Sciences program. On each question are attached diagram or table. Questionnaire and diagrams are numbered.

Results

As a result of our research, it became clear that the list of best-selling analgesics as per customer's requirement and OTC analgesics recommended by pharmacists, have not big differences. During the investigation, we discover that pharmacists have pure, indistinct knowledge about adverse reactions of OTC analgesics.

Conclusions

Involvement of pharmacists in primary care pain management is very important and pain management training of pharmacy staffs should be encouraged.

Keywords: noncancer pain, pharmacotherapy, over-the-counter analgesic, adverse effects, pharmacy employees

Background

The International Association for the Study of Pain defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage " [1]. The global problem of pain is very significant, more attention should be paid to assessing the burden of non-fatal health outcomes [2].
Pain is a general reason for self-medication with over-the-counter (OTC) analgesics. Common risks associated with OTC pain medications use can include increased risk of drug–drug interactions and adverse effects, wrong self-diagnosis, resulting in serious illness, therapeutic errors [3]. Considering the heterogeneity of patients' knowledge and behaviour reported worldwide, inappropriate use of OTC pain medication should not be underestimated and ignored.
Whereas a lot of consumers self-medicate with OTC analgesics and are uninformed of possibly hazardous drug interactions, proper counseling on the corresponding use of these medication can help minimize adverse effects and provide positive clinical outcomes. Community pharmacists should be trained to manage self-medication and counseling with OTC analgesics [4,5,6,7].
Research in Canada shows that pharmacy employees can play an important role in the pharmacotherapeutic management of pain suffering patients by providing information, discussing barriers about pain and its treatment, and monitoring pain disability, and by appropriately managing pharmacotherapy to optimize effectiveness while minimizing adverse effects [8]. In many societies, the pharmacist is the most available health professional to the public and sometimes they are first one to talk to patients. They can be big advocates for pain relief as they discuss with patients the importance of pain treatment and direct them to the right doctor.
The survey in Virginia showed that a significant

number of responding pharmacists indicated that they had less than "good" knowledge of pain management. The measures must be taken to educate pharmacists about pain treatment, including the use of OTC analgesics, especially new methods of noncancer pain management. [9]. OTC analgesics are used very often and they are available in various brands, package sizes, formulations, and dosage. They can be used for a range of different types of pain [10]. During pain management, as a principal rule, attention should be taken, especially for over-the-counter medicine, to ensure that patients are aware of the individual side effects and risks of these medications. In pain management, pharmacists can use Acetaminophen and NSAIDs. Acetaminophen can be effective for mild to moderate pain. Risks of acetaminophen include dose-dependent liver toxicity, especially when the drug is taken at high doses, with alcohol, or by those with liver disease [11].

NSAIDs such as aspirin, ibuprofen, and naproxen can provide significant pain relief for inflammation, such as from arthritis, bone fractures or tumors, muscle pains, headache, and acute pain caused by injury or surgery. Nonselective NSAIDs (those that inhibit the activity of both the cyclooxygenase [COX]-1 and COX-2 enzymes) can be associated with gastritis, gastric ulcers, and gastrointestinal (GI) bleeding. Conversely, COX-2 inhibitors have fewer GI adverse effects. The use of NSAIDs may be associated with renal insufficiency, hypertension, and cardiac-related events [12].

The goal of the research: the aim of this work is to study the role of pharmacy employees in the treatment of noncancer pain and to identify gaps in education in self -medication of pain management with OTC analgesics.

Material and methods

This is a descriptive cross sectional sociological research conducted in Yerevan (Armenia) by the Department of Pharmaceutical Management of the YSMU. The study was carried out among 285 pharmacy employees selected randomly and invited to participate. During the 2018 – 2019 participants completed an anonymous self-administered paper-based questionnaire. The questionnaire was written in Armenian, the questionnaire contained both closed and open questions. Number of questionnaires distribution in Yerevan was determined by The Survey System Version 11.0. taking into account the number of the drugstores, the reliability coefficient t=1.96, the first type error is with 5% probability ($\alpha = 0,05$), and the evaluation accuracy is 5% ($\Delta = 5\%$), p=0.5. The questionnaires are developed based on WHO standard survey questionnaires, taking into account the specificity of the work . Data obtained as a result of surveys were registered in statistical SPSS software package (version 12.0). Three questions from questionnaire were used to evaluate the pharmacists' perceived learning needs and their preferences regarding the OTC analgesics and their adverse reactions.

Results

The results of the questionnaire survey carried out among 285 pharmacy employees with different ages, education and work experience. During the survey was found out that 14% of respondents did not pay attention to the customer's favorite analgesics and could not answer to this question, which is a very disturbing situation.

On the question which are the best-selling analgesics as per customer's requirement, responses were divided into two groups according to composition of the medicines: single-agent medicines (80%) and combined medicines (20%). Responses which are contain medicines with one active ingredient were grouped according to the active substance. So, the answers were classified as follows: nimesulide 28%, ketoprofen 24%, ibuprofen 23%, diclofenac 13%, metamizole sodium 7% etc. (see Fig. 1).

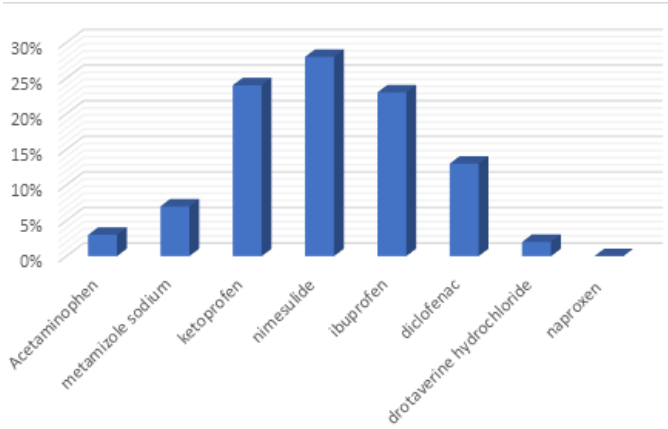

Fig.1 Best-selling analgesics (with one active substance) as per customer's requirement by pharmacy employees.
Source – study results.

During the investigation, we have separated the fixed-dose combination analgesics group, which is shown in the tabel 1.

Fixed-dose combination medicines (brand name)	Composition	Customer's requirement (%)
1. Ascofen	Acetylsalicylic Acid, Caffeine, Acetaminophen	36%
2. Spazmalgone	Metamizole sodium monohydrate, Pitofenone hydrochloride, fenpiverinum bromide	15%
3. Tempalgin	Metamizole sodium monohydrate, Triacetonamine	14%
4. Citramon	Acetylsalicylic acid, Acetaminophen , Caffeine	9%
5. Caffetin	Acetaminophen, Propyphenazone, Caffeine and Codeine	7%
6. Pentalgin	Metamizole sodium, Acetaminophen, Caffeine. Phenobarbital, Codeine	7%
7. Solpadein	Caffeine, Codeine, Acetaminophen	5%
8. Capsicam	Nonivamide, Dimethyl sulfoxide, Benzyl nicotinate	4%
9. Next	Ibuprofen, Acetaminophen	3%

Table 1. Best-selling combined analgesics as per customer's requirement by pharmacy employees Source – study results.

Pharmacists' OTC analgesics recommendations
According to survey 12% of the pharmacy employees were unable/avoided to respond to this question. When discussing the responses received from survey, listed medicines , again, were divided into two groups: single-agent medicines (81%) and combined medicines (19%):
Considering the responses of pharmacists about OTC analgesics recommendations and preferences were the following: ketoprofen 29%, ibuprofen 23%, nimesulide 18%, diclofenac 15%, naproxen 5%, drotaverine hydrochloride 4%, acetaminophen 3%, metamizole sodium 2%, meloxicam 1% (see Fig 2).
The research reveals that the analgesics mentioned in advice of pharmacy employees and consumers preferences are practically the same. Responses were grouped again according to the active ingredient.

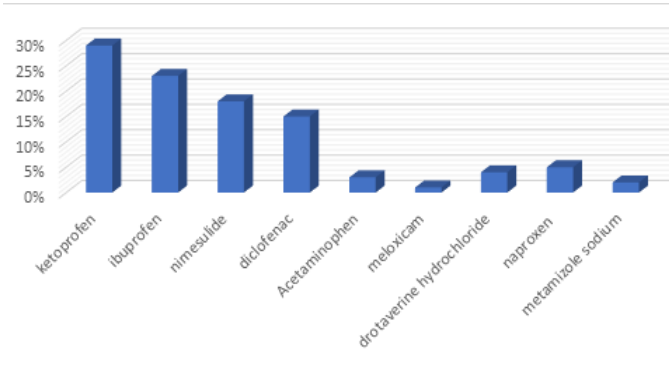

Fig. 2 Pharmacists' OTC analgesics recommendations.
Source – study results.

Pharmacy employees also suggested fixed-dose combination analgesics such as:

Fixed-dose combination medicines (brand name)	Composition	Pharmacy employees suggestion (%)
1. Spazmalgone	Metamizole sodium monohydrate, Pitofenone hydrochloride, fenpiverinum bromide	23%
2. Next	Ibuprofen, Acetaminophen	19%
3. Ascofen	Acetylsalicylic Acid, Caffeine, Acetaminophen	17%
4. Caffetin	Acetaminophen, Propyphenazone, Caffeine and Codeine	11%
5. Pentalgin	Metamizole sodium, Acetaminophen, Caffeine. Phenobarbital, Codeine	8%
6. Tempalgin	Metamizole sodium monohydrate, Triacetonamine	8 %
7. Citramon	Acetylsalicylic acid, Acetaminophen , Caffeine	7%
8. Solpadein	Caffeine, Codeine, Acetaminophen	7%

Table 2. Combined analgesics suggested by pharmacy employees
Source – study results.

As shown in picture in case of fixed-dose combination analgesics the preferences of pharmacy employees are slightly different from those of consumers.

Pharmacists' perceptions of analgesic adverse reactions

Based on survey data 24% of respondents are unaware of side effects of OTC analgesics.
The listed side effects are grouped as follows (see Fig. 3).

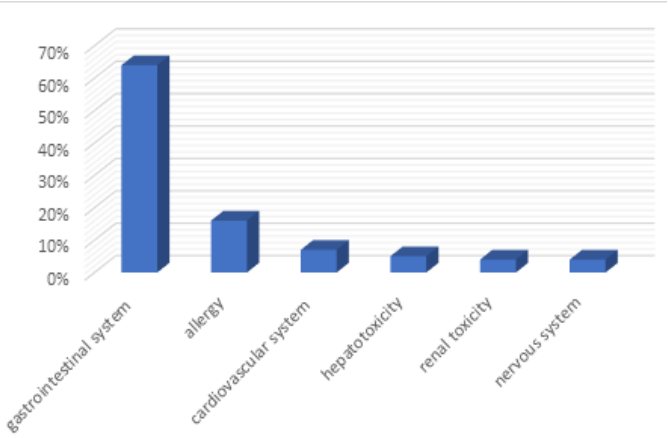

Fig. 3 Pharmacists' perceptions of analgesics side effects.
Source – study results.

Effects on the gastrointestinal (GI) system include the following side effects listed by pharmacy employees: stomach pain, nausea, stomach ulcer, meteorism, constipation, dyspepsia, epigastric burning, vomiting, digestive disorder, diarrhea.
With regard to the effects on the cardiovascular system, pharmacy employees listed the following side effects: tachycardia, arrhythmia, increased blood pressure and the nervous system effects include dizziness, headache, and so on.

Discussion

Pharmacists must play a essential role in educating patients about the appropriate OTC pain medications and inform them of the correct way to take it and the right timing between doses, report about side effects and contraindications. As shown in the survey most consumers in Armenia prefer nimesulide, which is a nonsteroidal anti-inflammatory drug (NSAID) with relative specificity for COX-2. This is quite disturbing because nimesulide use is associated with an approximately twofold increased risk for hepatotoxicity. The association between nimesulide use and related hepatotoxicity is supported by comprehensive disproportionality analysis, showing an increased rate of reported hepatic adverse events

with nimesulide, compared with other NSAIDs [13,14]. The pharmaceutical policy of countries regarding Nimesulide are very different, for example Nimesulide has never been marketed in some countries such as the USA and Australia, in Thailand, only the tablet form of the medicin is available; the suspension form was withdrawn. In India, tablet and gel forms have been available , in spite of the fact that some hepatic adverse reactions have been reported with nimesulide to the Indian National Pharmacovigilance Centre. Nimesulide is marketed in Brazil as a prescription medicine. The drug is available as tablets, paediatric suspensions, suppositories and paediatric drops [15,16]. In the Republic of Armenia, nimesulide is registered as a medicine for internal use and is included in the list of prescription drugs [17], but this government decision and the fine established by the Code of Administrative Offenses do not prohibited pharmacies from selling nimesulide without a prescription. Other preferred analgesics, such as ketoprofen and ibuprofen, may also have a hepatotoxic effect if the therapeutic dose exceeds Defined Daily Dose (DDD) and the duration of treatment is not applied correctly.

Based on above mentioned, in the Republic of Armenia pharmacist must carefully educate and guide patients in managing and controlling their pain through safe pharmacotherapy approach.

It is also disturbing that nimesulide is in the third place in the list of recommended analgesics of pharmacy staff. Therefore, it can be said that pharmacy staff do not have sufficient knowledge to perform pain management with relatively safe medications. Pharmacy staff's training needs are also indicated by their ignorance about analgesics (12%), lack of attention to analgesics purchased by consumers (14%), and general ignorance of analgesic side effects and incomplete knowledge (24%). Pharmaceutical services must be in accordance with the World Health Organization (WHO) guidelines on Good Pharmacy Practice, for which they must have the appropriate education, knowledge and skills.

Many countries place importance on the pharmacist involvement in pain management. For this reason, some countries have developed guidelines about the management of pain for pharmacists, for example in Malaysia in 2018 , Ministry of Health Malaysia with contribution from Pharmaceutical Services Programme was supplemented "Pain medication therapy management"guideline for pharmacists [18]:

Conclusion

Community pharmacists are in the best position to provide advice that will maximize pain regulation and target the most appropriate analgesic therapy for patients with pain. For this purpose government must plan and perform continuous professional development strategies to improve current and future performance. Pharmacy employees have the need for improved pharmacy education on the efficacy and safety of analgesics used at OTC dose and duration when advising on the treatment of pain.

They must complete the necessary training to update their knowledge and skills in pain management. Pharmaceutical education must help counter the stereotypes, myths, misunderstandings, that disturb better care. Programs should be more oriented on practical skills and make sure that the programs fulfill the criteria of high quality education.

References

1. International Association for the Study of Pain (IASP) IASP terminology, December 2017. Available from: https://www.iasp-pain.org/Education/Content.aspx?ItemNumber=1698#Pain.
2. GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2106: a systematic analysis for Global. Pubmed 2017 Sep 16;390(10100):1211-1259. doi: 10.1016/S0140-6736(17)32154-2. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28919117.
3. American College of Preventive Medicine. Over the counter medications: use in general and special populations , therapeutic errors, misuse, storage and disposal. A Clinical Reference. 2011.
4. Perrot S, Cittée J, Louis P, Quentin B, Robert C, Milon JY, Bismut H, Baumelou A. Self-medication in pain management: The state of the art of pharmacists' role for optimal Over-The-Counter analgesic use. Eur J Pain. 2019 Nov;23(10):1747-1762. doi: 10.1002/ejp.1459. Epub 2019 Aug 7.
5. Paul Gavaza, P. Brittany Vickery. Gaps in the Pharmacist's Pain Management Role. Practical pain management. 13 Articles in Volume 18, Issue #6, September 5, 2018.

6. Fendrick A Mark, Deborah E Pan, Johnson Grace E. OTC analgesics and drug interactions: clinical implications. Med Prim Care. 2008;2:2. doi: 10.1186/1750-4732-2-2 Osteopath.
7. Lynn Yeen Goh, Agnes I Vitry, Susan J Semple, Adrian Esterman, Mary A Luszcz. Self-medication with over-the-counter drugs and complementary medications in South Australia's elderly population. BMC Complement Altern Med. 2009; 9: 42 doi: 10.1186/1472-6882-9-42.
8. Ghaya Jouini,Manon Choinière,Elisabeth Martin, Sylvie Perreault, Djamal Berbiche, David Lussier, Eveline Hudon, and Lyne Lalonde. Pharmacotherapeutic management of chronic noncancer pain in primary care: lessons for pharmacists. Published online 2014 Mar 24. doi: 10.2147/JPR.S56884.
9. Mehuys E, Crombez G, Paemeleire K, Adriaens E, Van Hees T, Demarche S, Christiaens T6, Van Bortel L6, Van Tongelen I7, Remon JP7, Boussery K7. Self-Medication With Over-the-Counter Analgesics: A Survey of Patient Characteristics and Concerns About Pain Medication. 2019 Feb;20(2):215-223. doi: 10.1016/j.jpain.2018.09.003. Epub 2018 Sep 28.
10. R Andrew Moore,corresponding author Philip J Wiffen, Sheena Derry, Terry Maguire, Yvonne M Roy, and Laila Tyrrell. Non-prescription (OTC) oral analgesics for acute pain - an overview of Cochrane reviews. Cochrane Database Syst Rev. 2015 Nov; 2015(11): CD010794. Published online 2015 Nov 4. doi: 10.1002/14651858.CD010794.pub2.
11. Major JM, Zhou EH, Wong H-L, et al. Trends in rates of acetaminophen-related adverse events in the United States. Pharmacoepidemiol Drug Saf. 2016;25(5):590-598. doi:10.1002/pds.3906.
12. Evoy KE, Morrison MD, Saklad SR. Abuse and Misuse of Pregabalin and Gabapentin. Drugs. 2017;77(4):403-426. doi:10.1007/s40265-017-0700-x.
13. Jeongyoon Kwon, Seungyeon Kim, Hyejin Yoo, Euni Lee. Nimesulide-induced hepatotoxicity: A systematic review and meta-analysis. PLoS One. 2019; 14(1): e0209264. 13Published online 2019 Jan 24. doi: 10.1371/journal.pone.0209264.
14. Roberto Leone, L.A. Scuro. Risk of acute and serious liver injury associated to nimesulide and other NSAIDs: data from drug-induced liver injury case–control study in Italy. Br J Clin Pharmacol (2016) 82 238–248 238.
15. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012-. Drug Records, LiverTox: Clinical and Research Information on Drug-Induced Liver Injury. Bookshelf ID: NBK547948PMID: 31643281 Available from https://www.ncbi.nlm.nih.gov/books/NBK547948/.
16. WHO Pharmaceuticals Newsletter 2002, No. 04 http://apps.who.int/medicinedocs/en/d/Js4943e/3.html.
17. Scientific center of drug and medical technology expertise after academician E. Gabrielyan , List of prescribed drugs registered in the Republic of Armenia (30.11.2019) http://www.pharm.am/index.php/en/list-of-registred-prescription-drugs-in-republic-of-armenia/2707-list-of-registred-prescription-drugs-in-republic-of-armenia-up-to-30-11-2016.
18. Ministry of Health Malaysia Pharmaceutical Services Programme . Pain medication therapy management : guideline for pharmacy. Pages 51. Second Edition 2018.

Abbreviations

WHO- World Health Organization
SPSS- Statistical Package for the Social Sciences
OTC - over-the-counter
NSAIDs- Nonsteroidal Anti-inflammatory Drugs
COX - cyclooxygenase
GI - gastrointestinal
DDD - Defined Daily Dose