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Analysis of Adverse Reaction of Analgesics, Antipyretics and Non-Steroidal Anti-Inflammatory Drugs Prescribed by Physicians of Health Care Facilities in Podilskyi Region during 2015

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ibuprofen;
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Abstract.

The problem of medicines rational use exists all over the world. It concerns particularly analgesics, antipyretics and non-steroidal anti-inflammatory drugs (NSAIDs). In Ukraine the side effects caused by non-steroidal antiphlogistics rank the second place according to the prevalence among all registered cases.

The objective of the research was to analyze adverse drug reaction report forms concerning adverse reactions caused by the use of NSAIDs, analgesics, antipyretics, and were submitted during 2015 to the Vinnytsia regional unit of the State Expert Center of the Ministry of Health of Ukraine.

The conducted research showed that 1460 cases of adverse reactions (AR) or lack of efficacy of medication (LOE) were registered in Vinnytsia region in 2015. Among all registered cases of AR with proven causal relationships (94.4%) caused by NSAIDs, there were 42.4% of AR caused by diclofenac sodium, 24.2% caused by **ibuprofen**, 10.6% caused by paracetamol, 9.1% caused by analginum (metamizole sodium) and 7.6% caused by nimesulide.

The classification of patients according to age showed inhomogeneity in these medications prescription: ibuprofen and acetaminophen were taken mostly by teenagers, analginum was taken by young people and older people took mostly nimesulide. Diclofenac retained the stable position of "the gold standard" in the treatment and was evenly administered to patients of all ages.

In addition, diclofenac and nimesulide were determined to be mostly prescribed to patients with rheumatologic pathology and ibuprofen, paracetamol and analgin were prescribed for the treatment of acute respiratory viral infections (hyperthermal syndrome). It should be noticed that allergic reactions dominated among the manifestations of adverse reactions of the studied drugs.



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Problem statement and analysis of the recent research

According to the requirements of the World Health Organization (WHO, 2004) concerning modern medication, the efficiency, safety, affordability and acceptability for the patient are the most important criteria to assess the ratio of risk/benefit of drugs and eventually the effectiveness and safety of pharmacotherapy.

The problem of medication rational use exists all over the world. According to the WHO (1985) more than 50% of medication is prescribed irrationally, and more than half of all patients take the medication incorrectly. This concerns also analgesics, antipyretics and non-steroidal anti-inflammatory drugs (NSAIDs), particularly. The variety of curative properties of medicinal drugs of this pharmacological group has led them to the category of drugs which are prescribed in most cases, because every third inhabitant of the planet uses NSAIDs. The number of registered medicinal drugs of this group exceeds 350 different trade names and constitutes more than 155 pharmaceutical forms [3, 9, 11]. The adverse reactions caused by NSAIDs rank second in frequency among all registered cases in Ukraine [2, 3, 4, 5, 10, 13, 14].

Adverse reactions caused by NSAIDs therapy were indicated in many publications. However, the study of the safe and rational pharmacotherapy on the basis of objective determination of the safety profile of non-steroidal antiphlogistics most commonly used in clinical practice, which were registered during 2015 in Podilskyi region, was conducted by us for the first time [2, 9, 11, 15].

The objective of the research was to analyse the adverse drug reaction report form (RF, form 137/o) concerning adverse reactions (AR) or lack of efficacy (LOE) registered during 2015 by the Vinnytsia regional unit of the State Expert Center (SEC) of the Ministry of Health of Ukraine, and to describe the structure of the adverse reactions caused by the use of NSAIDs, analgesics and antipyretics.

Materials and methods of the research

According to the objective, we conducted the analysis and evaluation of the RFs about the cases of adverse reactions to the most commonly used in clinical practice NSAIDs reported by health care facilities in Podolsk region during 2015, what actually became the object of study.

Results of the research and their discussion

1460 cases of AR or LOE of medication in case of its medical application were registered in 2015 (as of 12/31/2015) in the Podilskyi region. Among all registered cases of AR with proven causal relationships (94.4%) caused by NSAIDs, there were 42.4% of AR caused by diclofenac sodium, 24.2% caused by **ibuprofen**, 10.6% caused by paracetamol, 9.1% caused by analginum (metamizole sodium) and 7.6% caused by nimesulide (Fig. 1).

Undoubtedly, such a significant number of AR to NSAIDs, analgesics and antipyretics was connected with the high frequency of these medicinal drugs prescription in clinical practice by the physicians of Podilskyi region in 2015.

It should be noticed that among all analysed ARs caused by the studied medicinal drugs including diclofenac, paracetamol and aspirin, the vast majority of AR was observed on the background of domestically produced medication. However, the use of nimesulide and ibuprofen caused ARs on the background of foreign production medication. Thus, the above mentioned data give the reasons to assume that there is no a direct connection between the producing country and AR frequency (Fig. 2).

The other evaluation criterion was the frequency rate of the use of analgesics, antipyretics and NSAIDs used for the patients' treatment in the Podilskyi region during 2015. The analysis showed that the ARs often occurred in case of diclofenac application in the patients with osteochondrosis

(32.1%), osteoarthritis (17.9%), neuralgia (17.9%), rheumatoid arthritis (RA) (14.3%) and in patients who were self-treated (14.3%) and as a result of acute respiratory viral infections (ARVI) – 3.6%.

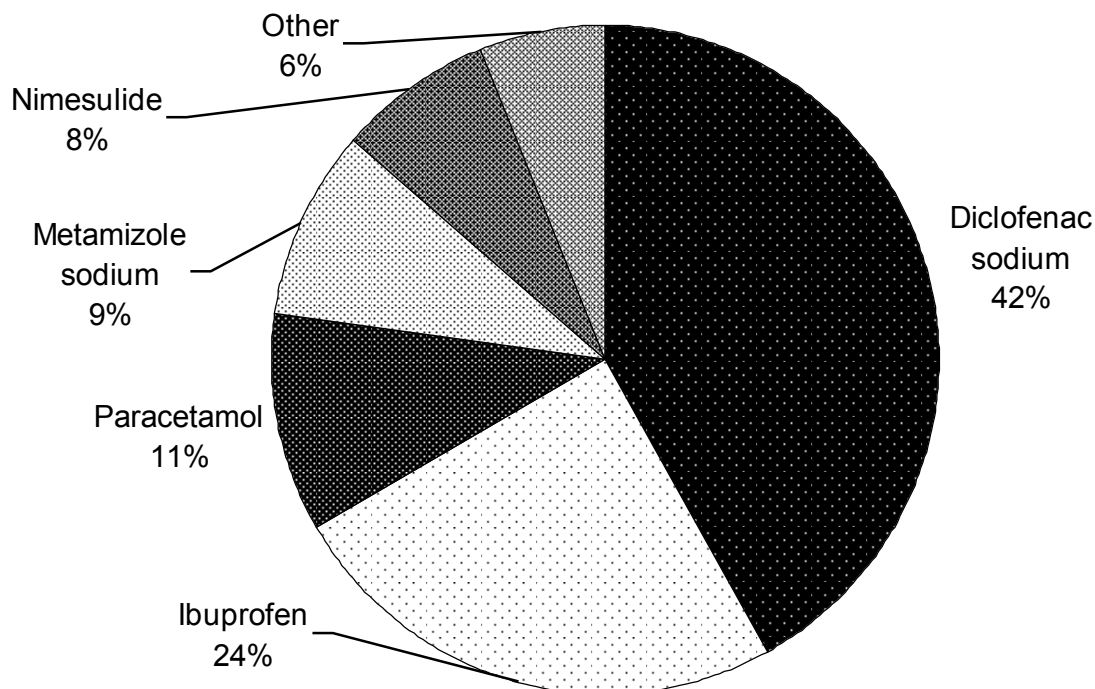


Fig. 1. Distribution of ARs caused by the use of NSAIDs and analgesics, antipyretics

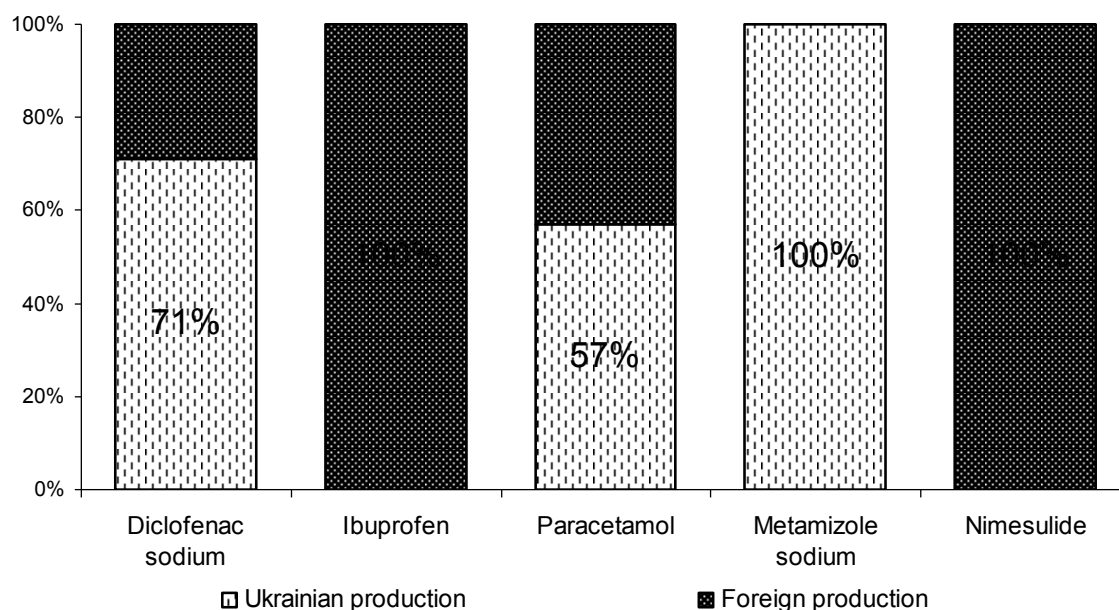


Fig. 2. The distribution of cases of AR to studied medication according to the producing country

The second largest number of AR cases was observed in patients who were prescribed ibuprofen. They were mainly registered during the treatment of ARVI (87.8%) and because of the self-treatment (12.5%). Paracetamol causing 71.4% of AR in patients with ARVI and 28.6% in patients who were self-treated ranked third. Analginum caused ARs predominantly in patients with neuralgia (33.3%), as a result of the self-treatment (33.3%) and in patients with AVRI (16.7%). Nimesulide prescribed to patients with osteoarthritis (60.0%) and patients with AVRI (40.0%) had the lowest frequency rate.

Summarizing the data, the inference should be drawn that the physicians of Podilskyi region prescribed diclofenac primarily for the treatment of rheumatic diseases, ibuprofen for the AVRI treatment, analginum for pain relief during neuralgia and osteoarthritis, as well as self-medication, nimesulide was used for osteoarthritis treatment.

The gender distribution of patients, who were prescribed the studied medication, was unequal. Diclofenac, paracetamol and analginum were usually prescribed for men in 53.6%, 57.1% and 66.7% of cases respectively, and ibuprofen, nimesulide were prescribed for women in 63.0% and 80.0% of cases, respectively (Fig. 3).

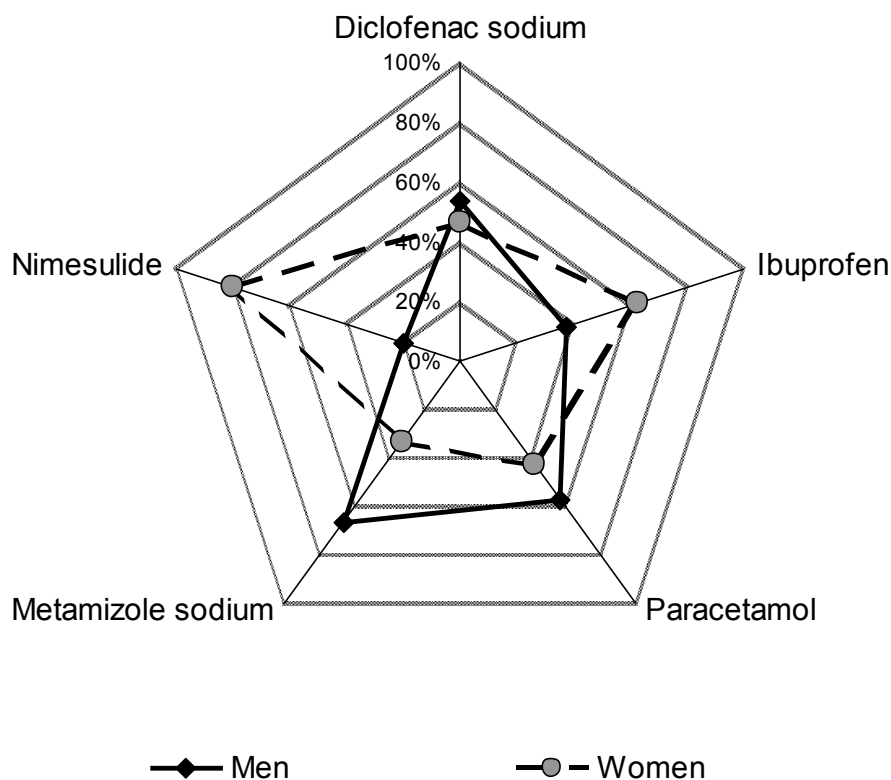


Fig. 3. The distribution of cases of AR to studied medication according to the patients' gender

The age distribution of patients treated with the studied medication (Fig. 4) was the following: diclofenac was prescribed equally to young people (at the age of 25-44) (28.6%), the middle-aged (28.6%) and the elderly (28.6%). Ibuprofen was used mainly for the treatment of adolescents (88.0%), paracetamol was taken mostly by teenagers (57.1%) and young people (42.9%), analginum was prescribed for middle-aged and young age people in 88.3% of cases, and nimesulide (40.0%) was prescribed for elderly patients.

The allergic reactions, gastrointestinal tract disorders and the central nervous system disorders dominated among the ARs that occurred on the background of the studied analgesic-antipyretics and NSAIDs. The medication position according to these systemic manifestations was the following: allergic reactions occupied the first place among all recorded ARs, moreover, ibuprofen, nimesulide and analginum caused them in 100% of cases. The use of diclofenac and paracetamol was followed by allergic reactions in 60.7% and 71.4% cases accordingly. Gastrointestinal complications ranked the second according to the AR incidence. 35.7% of them were caused by diclofenac and 14.3% of cases – by paracetamol. CNS disorders were observed in 3.6% of patients in case of diclofenac use and in 14.3% of patients in case of paracetamol use.

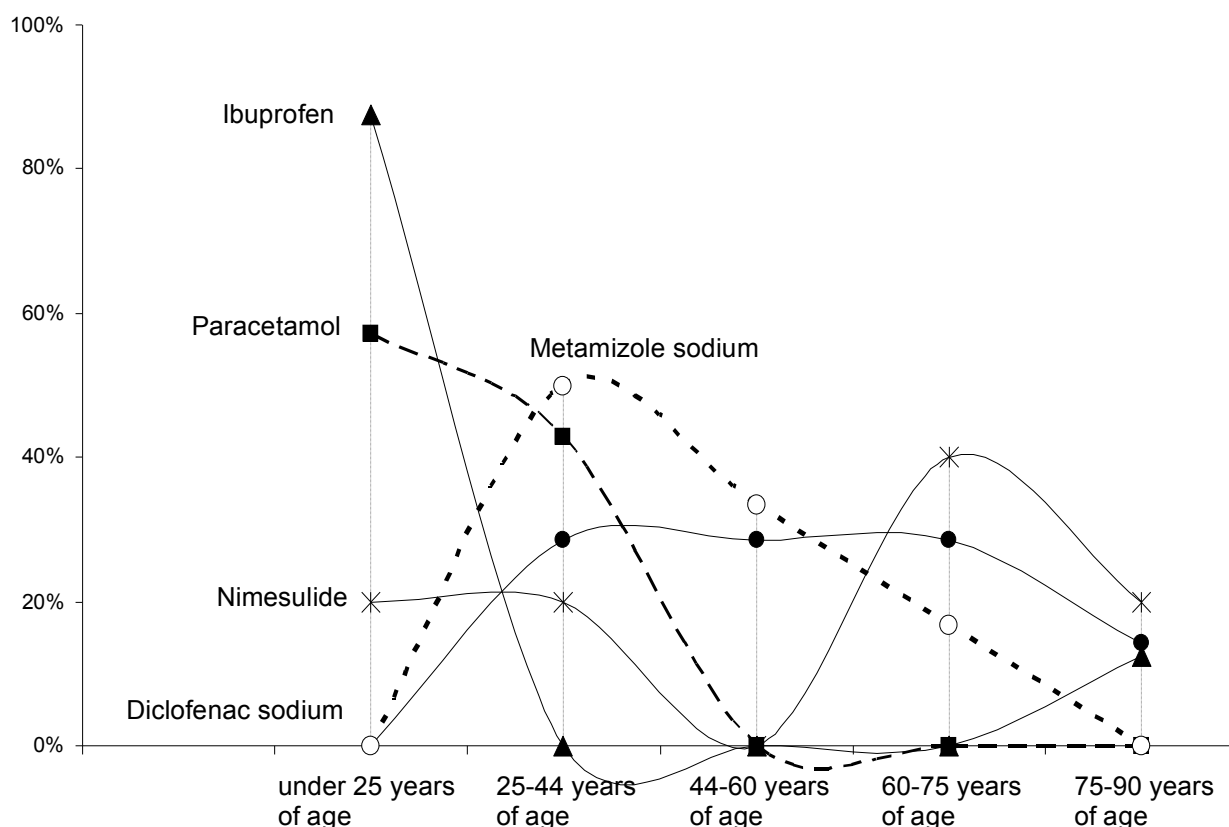


Fig. 4. The distribution of cases of AR to studied medication according to the patients' age

Patients with burdened anamnesis were not detected among the patients with studied manifestations of ARs.

Diclofenac, nimesulide and paracetamol were used as monotherapy in most AR cases. Ibuprofen caused these ARs on the background of another medicinal drug prescription that was a part of the complex therapy. Only analginum caused ARs on the background of polypharmacotherapy, i.e. when 3 or more medicinal drugs were prescribed (Fig. 5).

Conclusions

1. Diclofenac and ibuprofen were the main medication causing ARs in patients of Podilskyi region in 2015.
2. ARs on the background of studied drugs were registered mainly in men with the exception of nimesulide which was predominantly used during women treatment.
3. The age distribution of patients treated with the studied drugs was the following: ibuprofen and acetaminophen were used mostly by teenagers, analginum – by young people and by elder people were treated with nimesulide.
4. Nimesulide and diclofenac were prescribed mostly for patients with rheumatic disorders, and ibuprofen, paracetamol and analgin was used in the treatment of ARVI.
5. Allergic reactions occupied the first place among all recorded ARs to the studied medication.

Prospects for further research

The analysis of adverse reactions to the studied medication indicates the importance of finding and development of new ways for improvement of analgesics, antipyretics and NSAIDs safety profile. Special attention in solving this problem should be provided to diclofenac and ibuprofen.

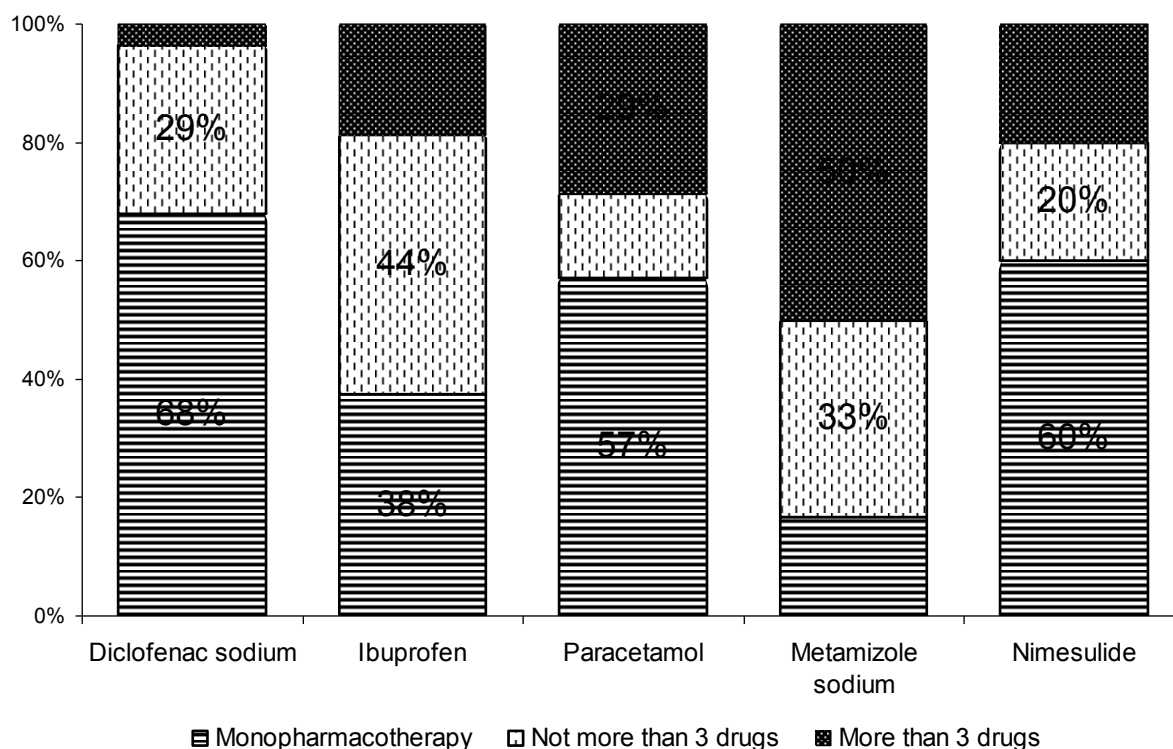


Fig. 5. The number of concomitant medication while using NSAIDs and analgesics-antipyretics

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