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Nonsteroidal Anti-Inflammatory Drugs and Analgesics Use by Kidney Transplant Recipients

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Statistical Analysis C
Data Interpretation D
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Background: Nonsteroidal anti-inflammatory drugs (NSAIDs) and analgesics are the most commonly used drugs and are increasingly available over-the-counter (OTC). In certain groups of patients, including kidney transplant recipients, their use may be complicated by adverse effects or drug interactions. The aim of our study was to assess the causes and frequency of OTC NSAIDs or analgesics use, as well as the awareness of related side effects.

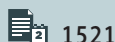
Material/Methods: We enrolled 94 randomly selected kidney transplant recipients, who represented 5% of all kidney transplant recipients at our center. An anonymous survey consisting of 23 multiple-choice questions was administered voluntarily and anonymously.

Results: In all, 63% of study patients confirmed taking the OTC painkillers; 22% of these patients took these drugs at least several times a week, and 4% took these drugs daily. For 38% of the study kidney transplant recipients, NSAIDs or analgesics were reported to be the only way to manage their pain. In addition, 30% of study patients were unaware of the risks associated with these drugs, despite the fact that 89% of the study patients consider physicians the best source of information.

Conclusions: Our study found that 63% of kidney transplant recipients regularly took OTC painkillers and 30% were unaware of the potential adverse effects. This necessitates continuous, ongoing education of kidney transplant recipients about the risks of OTC NSAIDs or analgesics use.

MeSH Keywords: Analgesics • Anti-Inflammatory Agents, Non-Steroidal • Awareness • Data Collection • Kidney Transplantation • Nonprescription Drugs

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Background

Pain adversely impacts the quality of life [1,2], and thus, people search for effective methods of controlling pain. Nonsteroidal anti-inflammatory drugs (NSAIDs) or analgesics are the most frequently used pain relievers [3]. These drugs are becoming increasingly available over-the-counter (OTC) and are widely advertised to be safe and effective for the treatment of common illnesses [4–6]. However, when used inappropriately, these drugs may cause adverse effects, including gastrointestinal bleeding, or nephro-, hepato-, myelo-, or oto-toxicity [7–10]. Children and elderly are particularly vulnerable to the adverse effects associated with these drugs. Moreover, chronic diseases, dehydration, overdosing, or concomitant medication with other nephro- or hepato-toxic agents, including immunosuppression, may additionally predispose patients to the adverse effects of these drugs [11]. Patients after solid organ transplantation belong to the high toxicity-risk group [12]. However, it is not clear how many transplant patients regularly take or abuse OTC NSAIDs and analgesics. Since many transplant centers have no structured education programs with respect to OTC NSAIDs and analgesics use, kidney transplant recipients are advised on an individual patient-physician basis.

The purpose of this study was to assess in kidney transplant recipients the frequency of use and the reasons for using OTC NSAIDs or analgesics, as well as patient awareness of related adverse effects.

Material and Methods

This was a retrospective, descriptive, and quantitative study using a 23-questions survey (Appendix 1). The study design did not require approval from the local ethics committee. Participation in this study was voluntary and anonymous, therefore, written informed consent was not obtained from the patients. In all, 94 study participants (5%) were randomly selected from 1,905 kidney transplant recipients who remained under post-transplant care at our department. The patients were approached by a registered nurse during routine outpatient visits and completed the survey in her presence. To reduce the likelihood of hypothesis guessing, the interviewees were kept blind to the research hypotheses.

Results

The characteristics of study participants are presented in Table 1. The survey revealed that 63% of patients used NSAIDs or analgesic drugs. Of these patients, 64% purchased these drugs OTC. Figure 1 presents the frequency of NSAIDs or analgesics use, whereas Figure 2 depicts the time from the last dose to the

Table 1. Characteristics of 94 kidney transplant recipients.

Gender (male/female)	53/41
Time from transplantation to survey (years)	23 to 2
Primary kidney disease:	
Glomerulonephritis	43
Autosomal recessive polycystic kidney disease	17
Unknown etiology	12
Diabetic kidney disease	9
Reflux nephropathy	4
Nephroangiosclerosis	2
IgA Nephropathy	2
Nephrolithiasis	1
Alport syndrome	1
Amyloidosis	1
Mixed connective tissue disease	1
Bilateral renal artery stenosis	1

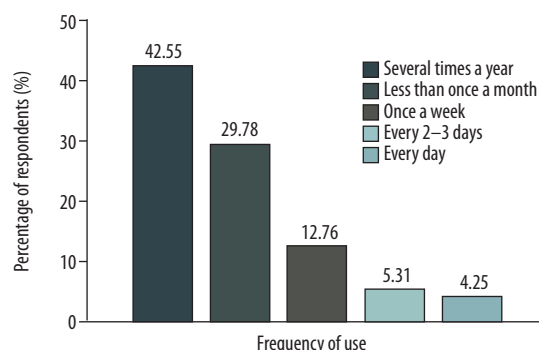


Figure 1. The frequency of the over-the-counter nonsteroidal anti-inflammatory drugs or analgesics use by kidney transplant recipients.

time of the survey. The study results showed that 8% of kidney transplant recipients indicated that they suffered from everyday pain, located in different parts of their body; and 23% reported pain more than once a month, thus explaining the observed high frequency of drug use. What should be noted is that less than 4% of these patients complained about pain localized near their transplant organ. Since the period after kidney transplantation covered a wide span (2–23 years), we used the U Mann-Whitney test with correction for continuity in our analysis. It revealed that the frequency of drug consumption did not change significantly over time. Moreover, gender and increasing age had no statistically significant impact on the frequency of drug use.

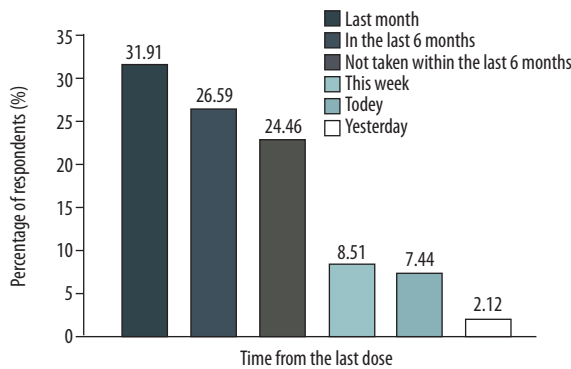


Figure 2. The time from the last dose of over-the-counter nonsteroidal anti-inflammatory drugs or analgesics to survey.

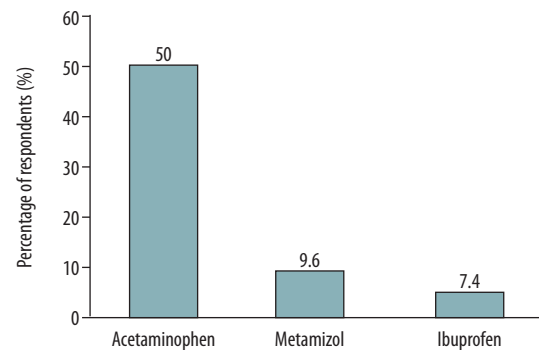


Figure 4. The most frequently consumed over-the-counter nonsteroidal anti-inflammatory drugs or analgesics by kidney transplant recipients.

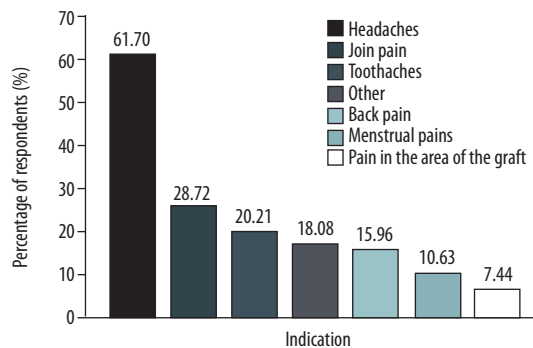


Figure 3. The reason to use over-the-counter nonsteroidal anti-inflammatory drugs or analgesics.

Figure 3 shows the reasons indicated by the study group that they used OTC NSAIDs or analgesics; reasons included headaches, join pain, toothaches, or menstrual pains. The most

frequently used OTC drugs contained acetaminophen, metamizole sodium, and ibuprofen (Figure 4). Thirty-one patients (33%) took drugs other than those presented in Figure 4, in a combination with pseudoephedrine, caffeine, or codeine. Interestingly, 63% of the study participants also used such drugs before their transplantation. These results suggest that the majority of patients with chronic kidney disease regularly take this type of medication. However, a different study design would be needed to further analyze this study result in more detail.

In our study, 82% of kidney transplant recipients confirmed reading the drug information leaflet before drug use. Most of the patients understood the risks associated with taking OTC NSAIDs or analgesics. However, 30% of the kidney transplant recipients surveyed doubted that such effects happen. Figure 5 shows the potential side effects most commonly reported by the survey respondents. Their knowledge was based mainly on what they read in the leaflets provided with the OTC drugs.

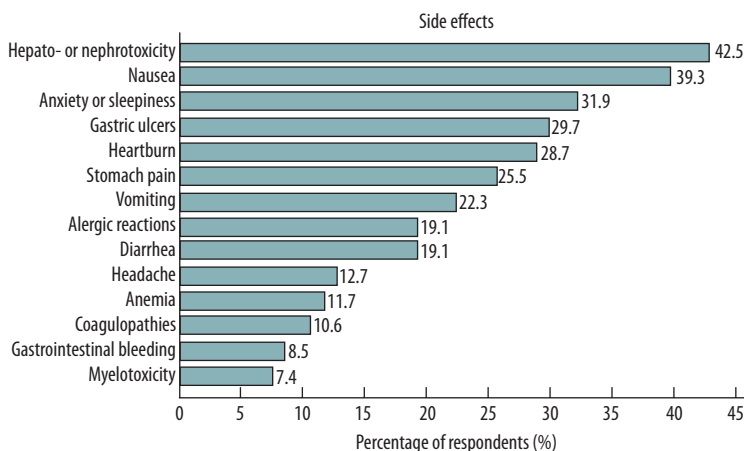


Figure 5. The awareness of related side effects of over-the-counter nonsteroidal anti-inflammatory drugs and analgesics.

The survey revealed that 89% of kidney transplant recipients identified doctors as the preferred and most reliable source of information about NSAIDs and analgesics. However, it was price, previous experience, and easy dosing that influenced the choice of the drug purchased. Half of the study cohorts indicated that advertisements did not influence their decision to buy certain drugs. In all, 38% of kidney transplant recipients in our study used only analgesics to treat their pain symptoms. Massages, physical therapy, or even waiting out the pain were mentioned as means of pain control.

Discussion

The results of our study indicated that the use of nonprescription analgesics is common among kidney transplant recipients. We found that 63% of kidney transplant recipients took OTC NSAIDs or analgesics. Moreover, one-third of kidney transplant recipients were unaware of the adverse effects associated with these drugs. Therefore, we suggest that the toxicity of these drugs should always be a clinical suspicion, especially if specific symptoms, such as edema, increased blood pressure, decreased glomerular filtration rate, or increased serum creatinine, occur. It is also reasonable to encourage all transplant practitioners to provide continuous education to their patients regarding the use of these OTC agents. This could prevent or at least diminish uncontrolled drugs use, avoid possible drug interactions, and reduce related adverse effects and unnecessary healthcare costs. Transplant recipients are a non-homogenous group of patients with multiple comorbidities and variable pre-transplant medical histories. Immunosuppression used after transplantation may cause indirect and drug-related side effects. Additional use of NSAIDs or analgesic drugs may result in overlapping symptoms. Therefore, educational programs for such patients are needed.

It is important to note that cultural or country association is related to prescription strategies by physicians or OTC purchases by patients, as well as the intensity of follow-up by healthcare workers, including patient education on supplementary medication. Each country in the European Union independently determines how medicines are sold and how patients are educated. In many countries, a pharmacy monopoly persists, but it is also common for OTC drugs sales to take place in supermarkets, petrol stations, or kiosks. In the UK, simple analgesic compounds, up to 16 tablets, requires government approval to be available outside the pharmacy. In Ireland, medications available outside of pharmacies include paracetamol, acetylsalicylic acid, and ibuprofen in restricted doses and tablet numbers. In recent years, liberalization rather than tightening of these drug rules has occurred [13].

OTC medicines and dietary supplements are often believed by consumers to be risk-free and used without consulting a

physician [14]. It was previously reported that every eighth renal transplant recipient uses some form of complementary and alternative medicine. Of these, some herbal or Chinese medicines can interfere with immunosuppressive treatment [15]. In a previous study, we found that 30% of liver or renal transplant recipients used more than one dietary supplement or herbal supplement. In addition, patient awareness of the possible side effects and interactions with immunosuppressive drugs was poor [12,16]. Given the sales volume of OTC painkillers all over the world, one can speculate that the incidence rate of related adverse effects is much higher than that of dietary or herbal supplements. Accordingly, the costs of adverse effects management are also higher. This suggests appropriate patient education is needed.

It is estimated that one-third of the world population uses OTC medicines. Among the most frequently used are those containing acetaminophen or acetylsalicylic acid [3,17,18]. Unfortunately, our findings in a kidney transplant recipient population were consistent with this data. Also, the location of the pain in our patients was similar to the pain reported in the general population. The increasing consumption of OTC NSAIDs and analgesics worldwide is partially related to effective advertising. For many people, advertisements represent the primary source of information about drugs and treatment options. Limiting advertising as a method to reduce NSAIDs and analgesics use, and the costs of related adverse effects is a matter for debate. Our results suggest that price, dosing, and patient experience, and not advertisements, contributed the most to the choice of drug purchased. Interestingly, in our study, the majority of kidney transplant recipients believed that doctors were the most reliable source of knowledge about these drugs and expected them to be a source for patient education. But recent reports identified specific areas of patient education where doctors consider nurses more competent. However, in practice, the medical information from doctors and nurses should supplement each other [19]. Therefore, we emphasize the importance of cooperation between nurses and doctors in the education of their patients. This could prevent or at least diminish uncontrolled OTC drug use, avoid possible drug interactions, reduce related adverse effects and unnecessary healthcare costs.

Conclusions

NSAIDs and analgesics are commonly used by kidney transplant recipients. However, a high proportion of kidney transplant recipients remain unaware of potentially dangerous drug interactions. The results of our study showed that dosing, previous experience, and price contributed the most to patient's OTC drug choice. Thus, appropriate education on these drugs should be provided by health professionals to minimize adverse effects and healthcare costs rather than limiting advertising and drug availability [20].

Appendix 1.

Nonsteroidal anti-inflammatory drugs and analgesics use by kidney transplant recipients.

Survey

- 1 Please, provide your birth date (day/month/year)/...../.....
- 2 Please, indicate your gender F M
- 3 Please, provide the date of kidney transplantation (day/month/year)/...../.....
- 4 Do you use analgetic drugs?
 - a. yes
 - b. no
- 5 Are these drugs available without prescription?
 - a. yes
 - b. no
- 6 If not, did you use analgetic drugs before trnasplantation?
 - a. yes
 - b. no
- 7 Please, provide the names of analgetic drugs you have used (from the most to the least frequently used)
 - a.
 - b.
 - c.
- 8 How frequently do you use analgetic drugs?
 - a. every day
 - b. every 2–3 days
 - c. once a week
 - d. less than once a month
 - e. several times a year
- 9 Do you read the leaflets attached to the drugs available without prescription before use?
 - a. yes
 - b. no
- 10 What is your average monthly expenses on the analgetic drugs ?
(at the time of study: 1 euro=4.2 PLN, 1 USD=3.3 PLN)
 - a. less than 10 PLN
 - b. 10–50 PLN
 - c. 50–100 PLN
 - d. more than 100 PLN
- 11 How frequently do/did you suffer pain?
 - a. every day
 - b. less than once a month
 - c. more than once a month
 - d. several times a year
- 12 If you use/used the analgetic drugs, what was the indication? (you may indicate more than one answer)
 - a. pain of the graft area
 - b. toothache
 - c. headache
 - d. joint pain
 - e. menstrual pain
 - f. spinal pain
 - g. other
- 13 Do/did you manage pain with analgesic drugs only?
 - a. yes
 - b. no
- 14 If not, do/did you use:
 - a. physiotherapy
 - b. acupuncture
 - c. massage
 - d. psychotherapy
 - e. herbal preparations
 - f. other.....?
- 15 Do you thing that analgesic drugs may have adverse effects? (please, indicate one answer)
 - a. definitely not
 - b. rather not
 - c. sometimes
 - d. definitely yes
 - e. rather yes
- 16 If yes, what side effects do you recognize? (you may indicate more than one answer)
 - a. heartburn
 - b. headache
 - c. arousal or somnolence
 - d. abdominal pain
 - e. nausea
 - f. vomiting
 - g. diarrhea
 - h. anemia
 - i. stomach or duodenal ulcers
 - j. gastrointestinal tract bleeding
 - k. blood clotting disturbances
 - l. liver or kidney injury
 - m. bone marrow injury
 - n. allergic reactions including asthma

17 Do/did you pay attention to the compounds of analgesic drugs you use / used?

- a. yes
- b. no

18 Do/did you consult the choice of analgesic drug with your doctor?

- a. always
- b. sometimes
- c. never

In questions 19 and 20, please grade your answers from 1 to 5. Indicate only one figure, i.e.: 1---2---3--(4)----5).

19 How strong do you believe in different sources of information about analgesic drugs?

a. doctor	I don't believe at all 1---2---3---4---5 I believe
b. advertisement/media	I don't believe at all 1---2---3---4---5 I believe
c. nurse, family, relatives	I don't believe at all 1---2---3---4---5 I believe

20 What is important for you about analgesic drugs?

a. dosing	unimportant 1---2---3---4---5 very important
b. price	unimportant 1---2---3---4---5 very important
c. previous experience	unimportant 1---2---3---4---5 very important
d. advertised drug efficacy	unimportant 1---2---3---4---5 very important

21 Which of the following diseases do you suffer from?

- a. hypertension
- b. diabetes
- c. gastric / duodenal ulcer
- d. cardiovascular disease (coronary disease, myocardial infarction)
- e. chronic kidney disease
- f. other

22 Do/did you complain about the pain of the graft area?

- a. yes
- b. sometimes
- c. no

23 When did you take analgesic drug for the last time?

- a. today
- b. yesterday
- c. this week
- d. this month
- e. in the last 6 months
- f. I didn't take analgesic drugs in the last 6 months

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