

## Patient's Knowledge and Use of Oral Non-Steroidal Anti-Inflammatory Drugs in a Rheumatology Clinic

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### ABSTRACT

**Introduction.** We evaluated the knowledge of non-steroidal anti-inflammatory drugs (NSAIDs) including their dosage, side effects, contraindications, and drug interactions among the patients in an outpatient rheumatology clinic.

**Methods.** Patients in a rheumatology clinic completed a short survey assessing their knowledge of over-the-counter NSAIDs.

**Results.** The survey was provided to 400 participants and 275 (68.5%) were using over-the-counter (OTC) NSAIDs. The majority of the participants identified their commonly used NSAID. Almost a third were unaware of the contraindication of NSAIDs such as peptic ulcer disease, chronic kidney disease, and hypertension. Nearly 53.9% participants denied having any discussion of OTC medications with their providers. Two-thirds of the respondents reported seeing only the medication packaging for the dose determination (67.8%).

**Conclusions.** The gap in patient knowledge of the potential side effects and the lack of discussion of OTC medications by the providers may be predisposing the patients to preventable side effects from NSAIDs. *Kans J Med* 2019;12(4):132-135.

### INTRODUCTION

In 1897, Felix Hoffman synthesized acetylsalicylic acid (ASA) and the first non-steroidal anti-inflammatory drug (NSAID) was discovered.<sup>1</sup> NSAIDs are among the most commonly used medications owing to their anti-pyretic, anti-inflammatory, and analgesic properties.<sup>2</sup> Due to their easy availability, more than 30 million people worldwide use NSAIDs every day. NSAIDs account for almost 60% of the over-the-counter (OTC) analgesic market in the United States. OTC medications are used commonly in the adult population for analgesic effects.

NSAIDs are considered as relatively safe medications by the general population given their easy availability and having over-the-counter status.<sup>3</sup> However, they come with a broad spectrum of side effects. Side effects of NSAIDs usually are related to the inhibition of prostaglandins and thromboxane A-2. They involve many organ systems including gastrointestinal (GI), renal, and vascular systems. They can lead to gastric and duodenal ulceration by altering the mucosal integrity of the gastrointestinal tract, as well as worsening of hypertension and congestive heart failure. Other side effects include acute and chronic renal toxicity.

Up to 40% of NSAIDs users have GI side effects including reflux and dyspepsia.<sup>4</sup> About 30 - 50% of users have endoscopic lesions of subepithelial hemorrhages, erosions, and ulcerations. In the kidneys, NSAIDs lead to reduced plasma flow and disrupt the compensatory vasodilation at the glomerular level by inhibiting renal prostaglandins.<sup>5</sup> NSAIDs also cause acute interstitial nephritis (AIN) in the kidney, characterized by the presence of inflammatory infiltrate in the renal interstitium. AIN accounts for about 15% of the unexplained causes of acute kidney injury.

The effect of NSAIDs on the systolic blood pressure and increasing the overall mortality among the patients with coronary artery disease also has been studied in randomized trials. Bavry et al.<sup>6</sup> followed chronic versus non-chronic NSAID users and found that, at the mean follow-up of 2.7 years, the primary outcome of all-cause mortality, nonfatal myocardial infarction, and non-fatal stroke occurred at a rate of 4.4 events/100 patient-years in chronic NSAID users versus 3.7 events/100 patient-years in non-chronic NSAID users (95% CI 1.19 - 1.82,  $p = 0.0003$ ). The study also reported an increase in cardiovascular mortality in the chronic NSAID user group (95% CI 1.70 - 3.01,  $p \leq 0.0001$ ).

Patients in rheumatology clinics commonly suffer from joint pain and stiffness and widely use OTC NSAIDs for symptomatic management due to their anti-inflammatory and analgesic effects.<sup>7</sup> However, the knowledge of the medication dosage and the potential side effects along with drug interactions is poor among the majority of the patient population. Mullan et al.<sup>8</sup> found about one-third of their study participants could not identify the maximal daily dose and were unaware of drug contraindications. Less than half of the study participants recognized the potential side effects of the NSAIDs.

Cham et al.<sup>9</sup> conducted a study of patients in the emergency department and the patients were asked about the use of OTC medications. Of 213 patients, 143 admitted using NSAIDs. Female patients were more aware of the drug side effects. The use of ibuprofen was greater among the younger population and in patients with no primary care physician. Green et al.<sup>10</sup> surveyed 294 physiotherapists and found 62.6% of the participants were incorrect or unsure about where and how to obtain most NSAIDs. Participants also demonstrated lack of thorough knowledge of the risks and contraindications of the NSAIDs.

In this study, we evaluated the knowledge of NSAIDs including their dosage, side effects, contraindications, and drug interactions among the patients coming to the outpatient rheumatology clinic of Carle Foundation Hospital, the main tertiary care center in the city of Urbana-Champaign, Illinois.

## METHODS

Following approval from the institutional review board committee, the study was conducted between April 2018 and December 2018. Patients, non-pregnant and aged 18 years and over, who presented to the rheumatology clinic for follow-up or as new patients during were invited to take part in the study. Participants were selected regardless of gender and race. Those who agreed to participate in the study and had a clear mental capacity to fill in the survey were included in the study. Individuals who did not read or speak English or were unable to complete the survey unassisted were excluded from the study. A consent form, in the form of a cover letter, explaining the study in brief was attached with the survey. The survey was anonymous and patients were informed that their decision to participate in the study or not would not affect the treatment provided.

Volunteering patients were asked to complete a 10-minute, paper-based survey. Completed surveys were collected by the clinic nurse. The survey included demographic questions related to age, gender, education, and household income. The survey also included questions developed by the authors:

1) Do you take any of the following medications? Multiple choice options included: ibuprofen, naproxen, or aspirin (other than 81 mg).

2) Do you know the side effects of these medications? If yes, participants were asked to check the side effects from the following options: indigestion, headache, dizziness, drowsiness, fluid retention, kidney problems, and liver, heart/circulation problems.

3) Have you ever discussed the side effects of oral NSAIDs with your doctor or pharmacist? And have you ever read the directions or warnings written on the medication bottle/box? Yes or No responses were required for these questions.

4) How do you determine the proper dose of over-the-counter medications? Patients were asked to check from the following options: pharmacist, consultation with their doctor, ask the nurse, see the back of the medication bottle, take it as needed without determining the dose.

5) Do you have any of the following or have you ever had any of the following problems? Patients were asked to check the answers from the following choices: kidney problems (such as chronic kidney disease), asthma, high blood pressure, use of any blood thinners, history of heart disease (such as angina, coronary artery disease, chest pain with exertion), or stomach problems (such as peptic ulcer disease, gastritis, or history of GI bleed).

6) Patient knowledge regarding over-the-counter medication was asked in the form of yes or no responses for the final four questions of the survey: oral NSAIDs can cause stomach problems such as heartburn and even stomach ulcers, over-the-counter pain medications can cause problems in the kidney including kidney failure, over-the-counter pain medications can increase blood pressure and also can increase the risk of heart attacks and strokes, and over-the-counter pain medications have to be taken with meals.

Sample size was calculated at 400 with the aim to have 95% confidence interval to be about 5% and the actual percentages to be 50%. Statistical analysis software (SAS Version 9.4) was used to analyze the data.

## RESULTS

**Demographic Information and Health Literacy Level.** The average age of the eligible patients was 55.7 years ( $\pm 14.9$ ). Females predominated (72.4%) compared to males (27.6%). Most participants were white (86.7%). A total of 61.2% of the participants had college or higher education. The majority (66.7%) had an annual income below \$50,000. A total of 68.9% of the participants reported having used at least one OTC NSAID.

**Use of OTC NSAIDs and Knowledge of the Potential Side Effects.** Of 400 patients who participated in the study, 275 (68.9%) took OTC medications. Among the three NSAID options (ibuprofen, naproxen, and aspirin (other than 81 mg)), nearly two-thirds (69.3%,  $n = 190$ ) responded they took ibuprofen. Other study participants reported taking naproxen (35.3%,  $n = 97$ ) and aspirin (other than the 81 mg dosage; 16.7%,  $n = 46$ ). Patients did not report taking any other OTC NSAIDs. The following study results focused on the 275 NSAID users.

Over two-thirds (72.7%,  $n = 200$ ) of the respondents taking OTC medications acknowledged being aware of their side effects. Participants were given the list of side effects caused by NSAIDs including indigestion, headache, dizziness, drowsiness, fluid retention, kidney problems, and liver or heart/circulation problems. A total of 62.3% ( $n = 170$ ) of the patients indicated that they are aware of at least three side effects, 19.8% ( $n = 54$ ) participants were aware of more than three side effects, and 18.0% ( $n = 49$ ) did not have any knowledge of the side effects caused by the NSAIDs.

Most participants ( $n = 236$ , 86.5%) agreed that NSAIDs can cause heartburn, less than half ( $n = 115$ , 42.4%) agreed that NSAIDs should be taken with meals, highlighting that 160 patients (or 57.6%) were unaware of taking NSAIDs with meals or on a full stomach. The study participants did well in relating NSAIDs as the potential cause of kidney failure ( $n = 218$ , 79.9%). Over half ( $n = 158$ , 57.9%) of the study participants who took the NSAIDs correctly answered when inquired about the association of NSAIDs and elevated blood pressure.

A total of 53.9% of patients ( $n = 147$ ) denied having any discussion with their providers regarding the OTC NSAIDs they take, while 46.2% of patients ( $n = 126$ ) reported discussing these medications with their physician. The majority (77.7%,  $n = 212$ ) of the respondents reported reading the directions and warnings on the medication bottle/box. Nearly two-thirds (64.8%,  $n = 177$ ) of the respondents reported seeing only the bottle label for the dose determination. A total of 22.1% ( $n = 60$ ) consulted the doctor regarding the dose of OTC NSAIDs and 13.6% ( $n = 37$ ) asked their local pharmacist. There was 12.9% ( $n = 35$ ) of the respondents who reported taking OTC NSAIDs without dose determination and consultation.

**Existing Co-Morbidities in the Patient Population.** A total of 27.9% ( $n = 76$ ) of respondents reported having gastric problems such as history of peptic ulcer disease, gastritis, or GI bleed. About one-fourth of respondents reported a history of asthma (26.4%,  $n = 72$ ).

History of hypertension was reported by 26.1% of respondents (n = 71), whereas 12.5% (n = 34) reported having a history of chronic kidney disease and 11% (n = 30) had a history of coronary artery disease. Nearly two-thirds (44.3%, n = 121) reported having only one comorbidity.

**Logistic Regression Results.** “Aware of side effects” was the primary outcome for assessing the understanding of participants regarding side effects of OTC NSAIDs. After univariate analysis, controlling for age and gender, patients with more income ( $\geq$  \$35,000 - \$49,000 and  $\geq$  \$50,000) were significantly (adjusted OR 2.6 95% CI: 1.2, 5.7; adjusted OR 2.7 95% CI: 1.3, 5.5 respectively) more aware of the side effects of the OTC NSAIDs. No significant association between level of education and knowledge of side effects of NSAIDs was found. Females were almost three times (OR: 2.8 95% CI: (1.5, 5.2) more likely to read the warnings regarding over dosage as compared to males.

## DISCUSSION

NSAIDs are one of the oldest, most accessible, and most commonly used medications. Scientific advances have made healthcare providers aware of the numerous side effects of these medications, however, the discussion of the side effects of OTC NSAIDs with the patient population is not very frequent.<sup>11</sup> Ridout et al.<sup>11</sup> reported that out of 443 patients who participated in their survey, 275 respondents (62%) felt that the medication dosing and the side effects were not explained in detail by their providers or pharmacists. To specify the medications further, Wynne et al.<sup>12</sup> studied the intake of OTC NSAIDs versus the knowledge of the side effects in their patient population. The study found that patients who were not informed about the adverse effects of NSAIDs by their providers were less likely to reduce the intake of these medications in response to epigastric pain. A total of 36% of patients who suffered from GI bleed had a prior experience of epigastric discomfort, and only 11% admitted reduced compliance with the NSAID therapy when they were not informed about the adverse effects compared with the controls.

In 2005, a study among the patients suffering from osteoarthritis was conducted regarding their awareness of the side effects of NSAIDs.<sup>13</sup> A total of 3,755 patients were surveyed and 35.5% of the patients were aware of the side effects of non-steroidal anti-inflammatory medications.

The results from our study highlighted the need for patient education regarding the side effects of OTC NSAIDs. Our observation indicated that OTC NSAIDs are used more frequently by the middle-aged patients and that women are more frequent consumers of NSAIDs, which is in line with similar studies.<sup>14</sup>

Our findings supported a cross sectional study by Cullen et al.<sup>15</sup> in which the patients were inquired about the adverse reactions to the common medications. Patients underrated the risk of adverse events and considered NSAIDs as low-risk medications with the lack of knowledge of the upper GI bleeding as a potential side effect. Ngo et al.<sup>16</sup> also reported the lack of knowledge among their patient population regarding the potential serious adverse effects of non-prescription analgesics such as ibuprofen. This study further highlighted that 66% of the study participants (n = 110) reported rarely or never

reading manufacturer’s printed warning instructions at the back of the medication packaging.

The relationship of exceeding the labeled maximum daily dose of medication has been linked with the patients’ health literacy level. Kaufman et al.<sup>17</sup> identified the relationship of low health literacy scores (measured by the Rapid Estimate of Adult Literacy in Medicine) with the excessive intake of acetaminophen among patients. The gap in knowledge of the adverse reactions from OTC NSAIDs and the lack of discussion of OTC medications in the provider’s office can predispose the patient to avoidable complications such as GI bleed, acute kidney injury, and hypertension.<sup>18</sup> The lack of knowledge of the dosing and the side effects of the easily available OTC medications highlight a serious public health issue that should be discussed among the healthcare providers.

In our clinic, physicians often provide reconciliation of prescribed medications for pain control, but it is seldom seen that the patients are inquired about their use of OTC medications and whether they are aware of the adverse reactions. The responsibility lies more on the physicians than the pharmacists as most of the NSAIDs are easily available outside the pharmacy.

Our study highlighted an urgent need for the discussion of OTC pain medications between the patients and their healthcare providers. The discussion should not be limited to rheumatology clinics, but also should take place with the primary care provider. Patients in our study relied on the product label for the dose determination of OTC medications. However, the maximum allowed dose can vary among patients depending on co-existing comorbidities such as chronic renal or heart failure, hypertension, and history of GI bleed. Therefore, discussion between the providers and patients is encouraged. It should provide encouragement to the patients to discuss these medications openly in their follow-up visits and may limit excessive intake of such medications. Furthermore, there is a need to identify if the information on the medication packaging is comprehensible for the patients with low health literacy.

**Limitations.** This study was limited in several areas. Participants were not asked the reason for using OTC medications and the maximum number of tablets they consume every day. Also, the interval between the tablets was not asked. The generalizability of our study findings are limited by the fact that the study was conducted in one rheumatology clinic and participants from culturally and linguistic diverse backgrounds were unable to complete the survey due to language barriers.

## CONCLUSIONS

This study highlighted that the patients using OTC analgesics have gaps in their knowledge of the side effects and the dosing of these medications. Patients often rely on the medication packaging for information of the maximum dosage and do not discuss taking those medications with their physicians. Such practices can predispose the patients to several preventable adverse reactions. This is a public health issue that needs to be addressed in outpatient primary care clinics through proper education of both providers and patients to allow open communication regarding all OTC medications, especially those with high side effect profile such as NSAIDs.

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