



Dentists knowledge about over the counter-NSAIDs: An emerging need for NSAID-avoidance education

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ABSTRACT

Objectives of the study: Non-steroidal anti-inflammatory drugs (NSAIDs) belong to a group of drugs used in the management of pain. The aim of this study is to assess dentists' knowledge of NSAIDs risks and to determine the most prescribed NSAIDs by dentists.

Materials and Methods: We collected information concerning the dentists' knowledge of NSAIDs use and adverse effects. A questionnaire consisting of 22 questions was distributed to 123 Albanian dentists reached in different dental clinics, out of which only 87 agreed to participate. Only 70.73% of the distributed questionnaires were completed.

Results: Respondents demonstrated poor knowledge of NSAIDs. Most of the respondents did not respond correctly to the questions with 39.08% of incorrect answers regarding the implications of NSAIDs in elderly patients and only 3.44% responded correctly to the contraindication of NSAIDs. The most common prescriptions were ketoprofen, ibuprofen, followed by ketorolac, aspirin, and diclofenac.

Conclusions: Dentists who participated in the survey have limited knowledge of NSAIDs use, contraindication, and safety limitation which can affect patients' safety and well-being. Dentists should pay particular attention to informing patients on NSAIDs use and should also keep updated on NSAIDs, through continuing education programs.

INTRODUCTION

Non-steroidal anti-inflammatory drugs (NSAIDs) belong to a group of drugs that display anti-inflammatory, analgesic, and anti-pyretic effects. They are among the best selling drugs all over the world and are sold over the counter. However, the use of NSAIDs is also associated with several adverse effects both in healthy individuals and in those with risk factors. NSAIDs inhibit the cyclooxygenase (COX) activity competing with the arachidonic acid (AA) for the COX active site, inhibiting the prostaglandin production, but are not capable of inhibiting the formation of other inflammatory mediators, such as leukotrienes or platelet-activating factor (Goodman, 2018;

Vonkeman, 2010; Wehling, 2014) (Fig. 1). After the discovery of the COX-2 isoform, a second generation of NSAIDs became available, the COX-2 selective inhibitors or COXIBs, which were developed to prevent the gastrointestinal (GI) side effects associated with the use of traditional NSAIDs. Unfortunately, the COXIB story is a rise and fall story, because several COXIBs were withdrawn from the market after evidence of increasing the risk for myocardial infarction and stroke (Bresalier *et al.*, 2015; Solomon *et al.*, 2005).

NSAIDs are associated with several adverse effects, including gastrointestinal and cardiovascular system, the renal system (such as cystitis, hematuria, hyponatremia, nephritis syndrome, oliguria, renal failure, etc.), the neurological system (aseptic meningitis, confusion, depression, headache, insomnia, etc.), hematologic system (anemia, aplastic anemia, leucopenia, etc.), the dermatologic system (photosensitivity, pruritus, purpura, rash, urticaria, etc.), the respiratory system [dyspnea, hyperventilation (salicylates)]. NSAIDs can also cause hypersensitivity or other symptoms such as blurred vision, conjunctivitis, fever, pancreatitis,

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and so on. Some shared adverse effects of NSAIDs are reported in Table 1 (Goodman, 2018).

Dentists are among the health professionals who commonly describe NSAIDs to their patients to manage pain and inflammation. NSAIDs are routinely prescribed for different dental problems associated with pain such as pulpal and periapical disease, tooth extracting, root canal infections, or oral implant surgery. The choice to use a certain NSAID should depend not only on the severity of pain but also on patients' risk factors and medical conditions. However, the lack of knowledge on NSAIDs side effects, such as gastrointestinal, cardiovascular events, renal failure, headache, dizziness, as well as on NSAID contraindications, can also bring to NSAID-related death. Based on the actual situation in Albania, we thought that assessing dentists' knowledge and attitudes specifically on NSAIDs could give us some indications of whether there is a need to raise awareness on this topic. Despite some studies conducted in different countries on NSAIDs knowledge and prescription in dentistry, especially in pulpal and periapical pathologies (Segura *et al.*, 2014), in oral implant surgery (Datta *et al.*, 2015) and among dentistry students (Guzmán *et al.*, 2012), we found no studies assessing the knowledge on NSAIDs prescription and risk factors among Albanian dentists. The aim of the study is to assess dentists' knowledge on the use, risks, and characteristics of NSAIDs, in order to evaluate whether

there is a need to receive further education in NSAIDs camp to improve the well-being of their patients.

MATERIALS AND METHODS

Study design, participants

The study was based on a survey and compromised dentists reached in their private dental clinics subjected to state regulation. The process of participant inclusion is shown in Figure 2. We assessed 129 dentists for eligibility, which led to the exclusion of 6 dentists (4.65%). The remaining 123 were asked to participate and 87 (70.73%) of these agreed to participate. The study population comprised dentists completing a 10-minute paper-based survey within normal opening hours at their own private clinics in the period of November 2018–March 2019. Dentists recruited in the study were from five different cities in Albania. The following inclusion and exclusion criteria were applied:

Inclusion and exclusion criteria

Inclusion criteria for dentists

- Dentists actively exerting their profession at the time of conduction of the study.
- Dentists who voluntarily accept to participate in the study.

Exclusion criteria for dentists

- Retired dentists.
- Dentist not working in clinic.

Arachidonic Acid in Membrane Phospholipids

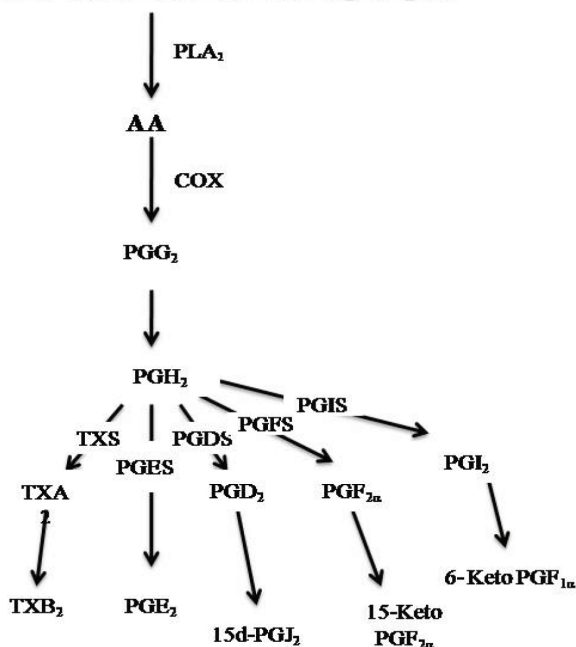


Figure 1. Arachidonic acid pathway. Arachidonic acid is a substrate for different pathways and enzymes giving rise to several metabolites. Prostaglandins and thromboxane are produced via the COX-pathway. Abbreviations: PLA₂ = phospholipase A₂, AA = arachidonic acid, COX = cyclooxygenase, PGG₂ = prostaglandin G₂, PGH₂ = prostaglandin H₂, TXS = thromboxane synthase, TXA₂ = thromboxane A₂, TXB₂ = thromboxane B₂, PGES = prostaglandin E synthase, PGE₂ = prostaglandin E₂, PGDS = prostaglandin D synthase, PGD₂ = prostaglandin D₂, 15d-PGJ₂ = 15-deoxy-D12,14-prostaglandin J₂, PGFS = prostaglandin F synthase, PGF_{2α} = prostaglandin F_{2α}, 15-keto PGF_{2α} = 15-keto prostaglandin F_{2α}, PGIS = prostaglandin I synthase, PGI₂ = prostacyclin, 6-keto PGF_{1α} = 6-keto prostaglandin F_{1α}.

Table 1. Some shared adverse effects of NSAIDs (Goodman, 2018).

System	Adverse effects of NSAIDs
Gastrointestinal	Abdominal pain, bleeding, constipation, diarrhea, dyspepsia, dysphagia, eructation, esophageal structure/ulceration, esophagitis, flatulence, gastritis, melena, nausea, perforation, pyrosis, stomatitis, ulcers, vomiting, xerostomia
Platelets	Inhibited platelet activation, propensity for bruising, increased risk of hemorrhage, platelet dysfunction, thrombocytopenia
Renal	Azotemia, cystitis, dysuria, hematuria, hyponatremia, interstitial nephritis, nephritis syndrome, oliguria, polyuria, renal failure, renal papillary necrosis, proteinuria, salt and water retention, hypertension, worsening of renal function in renal/cardiac/cirrhotic patients, ↓effectiveness of antihypertensives and diuretics, hyperkalemia, ↓urate excretion (especially with aspirin)
Cardiovascular	Edema, heart failure, hypertension, MI, palpitations, premature closure of ductus arteriosus, sinus tachycardia, stroke, thrombosis, vasculitis
Neurologic	Anorexia, anxiety, aseptic meningitis, confusion, depression, dizziness, drowsiness, headache, insomnia, malaise, paresthesias, tinnitus, seizures, syncope, vertigo
Reproductive	Prolongation of gestation, inhibition of labor, delayed ovulation
Hypersensitivity	Anaphylactoid reactions, angioedema, severe bronchospasm, urticaria, flushing, hypotension, shock
Hematologic	Anemia, agranulocytosis, aplastic anemia, hemolytic anemia, leukopenia
Dermatologic	Diaphoresis, exfoliative dermatitis, photosensitivity, pruritus, purpura, rash, Steven-Johnson syndrome, toxic epidermal necrolysis, urticaria
Respiratory	Dyspnea, hyperventilation (salicylates)
Other	Alopecia, blurred vision, conjunctivitis, epistaxis, fever, hearing loss, pancreatitis, paresthesias, visual disturbance, weight gain

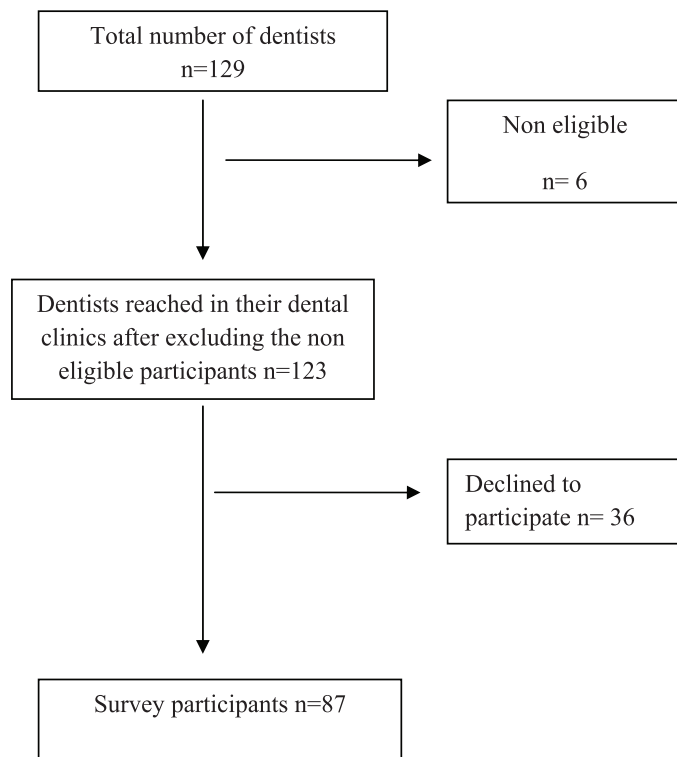


Figure 2. Selection of the participants. Flow chart describing the selection of dentists for the survey.

Survey questionnaire

If the dentists agreed to participate, they were given a questionnaire-based surveyed to fill. One validated questionnaire was designed for dentists for the purpose of the study to assess their knowledge on NSAIDs use, risk, side effects, maximum daily doses, and so on.

The questionnaire included a combination of original questions containing both qualitative and quantitative data and its validity was assessed by two experts. The questionnaires consisted of 22 questions and were distributed to 123 Albanian dentists reached in different dental clinics. Both multiple-choice questions and open (free text) questions were used. From the total 123 distributed questionnaires, 87 (70.73%) were completed and returned. Inclusion criteria restricted participation to dentists reached in different private dental clinics willing to voluntarily complete the questionnaire. Questions were designed to identify respondents' knowledge including NSAIDs use, risk, contraindication, dose, mechanism of action of NSAIDs, the most prescribed NSAIDs by the dentist, including their pharmaceutical forms, sources of information, and so on. The questionnaires were distributed by hand and returned upon completion to the researcher the same day. An English version of the questionnaire is reported below, along with a flowchart describing the selection of dentists (Fig. 2). Dentists were also asked if they had prescribed analgesics within the past months and if the patients had experienced adverse effects of their current treatment.

Questionnaire 1: Survey on non-steroidal anti-inflammatory drugs for dentists

Question 1: Gender

Question 2: Age

Question 3: Residence

Question 4: Years of experience

Question 5: Have you prescribed NSAIDs within the past months? (YES/NO).

Question 6: On average how often do you prescribe NSAIDs in a month?

Question 7: When and for which type of dental intervention do you prescribe NSAIDs to patients?

Question 8: Have patients had experienced adverse effects of their treatment with NSAIDs? (YES/NO)

Question 9: Which are most common analgesics that you have prescribed during the last year?

- a) *Ketoprofen*
- b) *Ibuprofen*
- c) *Aspirin*
- d) *Diclofenac*
- e) *Paracetamol*
- f) *Ketorolac*
- g) *Others (naproxen, mefenamic acid, meclodenamate, piroxicam, etc)*

Question 10: Have you ever received information on NSAIDs? (Yes/No) If yes which is the main source of information?

- h) *Conference*
- i) *Congresses*
- j) *Seminars*
- k) *Open lecturers*
- l) *Continuous education courses*
- m) *Others*

Question 11: If yes when was the last time you were updated on the topic?

Question 12: Indicate the following adverse effects of oral NSAIDs

- a) *Gastrointestinal*
- b) *Platelets*
- c) *Renal*
- d) *Cardiovascular*
- e) *Neurologic*
- f) *Reproductive*
- g) *Hypersensitivity*
- h) *Hematologic*
- i) *Hepatic*
- j) *Dermatologic*
- k) *Respiratory*
- l) *Other*
- m) *None of the above*

Question 13: What is the risk of prescribing aspirin in pediatric populations?

Question 14: What is the mechanism of action of NSAIDs?

Question 15: What are the implications of taking NSAID in elderly patients?

Question 16: Have you informed patients on NSAID use, risk, side effects and interactions with other drugs? (YES/NO)

Question 17: Which is the most common pharmaceutical form of NSAIDs that you have prescribed to patients

- a) oral
- b) topical
- c) endovenous

Question 18: Have you ever switched from one NSAID to another due to different side effects? (YES/NO). If yes how often?

Question 19: Which are the most common adverse effects of overdosage of acetaminophen?

Question 20: Indicate the maximum daily doses of the most used NSAIDs in adults in your clinical practice

Question 21: Indicate maximum daily doses of the most used NSAIDs in pediatrics in your clinical practice

Question 22: Which NSAID do you prescribe in pregnant women that need dental assistance? What do you know about NSAIDs in pregnancy?

Statistical analysis

All the data obtained from the questionnaires were then electronically transferred into an excel data spreadsheet and further analyzed in R software. Descriptive statistics and frequency distributions were used to analyze the data. Content analysis was used for qualitative data. Data from closed questions were analyzed and simple descriptive statistics including frequency distributions were created.

RESULTS

A total of 123 questionnaires were distributed to the dentists reached in different dental clinics in Albania, of which 87 questionnaires were completed, representing a 70.73 % response rate. Participants could have not responded to all the questions, but there was a high return, almost for every question, whether they

were correct or not. Of the 87 dentists surveyed, 42 were females (48.27%) and 45 were male (51.72%). All of them performed their studies in Albanian Dental Schools. The mean age of the participants was 41.67 years. The baseline characteristics of the cohort are shown in Table 2. Of the respondents, 63.22% lived in Tirana and 36.78 % lived in other cities of Albania (Table 2). Their years of experience as dentists are also reported in Table 2.

Respondents were asked to list their knowledge on NSAIDs, the adverse reaction of oral NSAIDs, maximum daily doses in adult and pediatric population, mechanism of action, NSAIDs use in pregnancy, and so on. All participants stated that they have prescribed NSAIDs in the last month, with a frequency varying from 20 times/monthly to 40 times/monthly.

Dentists knowledge on NSAIDs

Of the 87 dentists surveyed 42 (48.27%) have informed at least once the patients on NSAIDs use, risk, and adverse reaction, instead of 45 (51.72%) that have not given the respective information to the patients. The most common pharmaceutical form prescribed by the dentist was the oral form versus 4.59 % of the topical NSAIDs, and 1.15 % for endovenous use. The most widely prescribed drug was ketoprofen (94.25%), followed by ibuprofen (88.51%). Paracetamol was also listed as the third most prescribed analgesic (79.31%) (Fig. 3).

Table 2. Baseline characteristics.

	Number	%
Gender		
Male	45	51.72
Female	42	48.27
Residence		
Capital City	55	63.22
Other Cities	32	36.78
Year of experience		
0–5 years	15	17.24
6–10 years	32	36.78
11–15 years	29	33.33
16–20 years	11	12.64

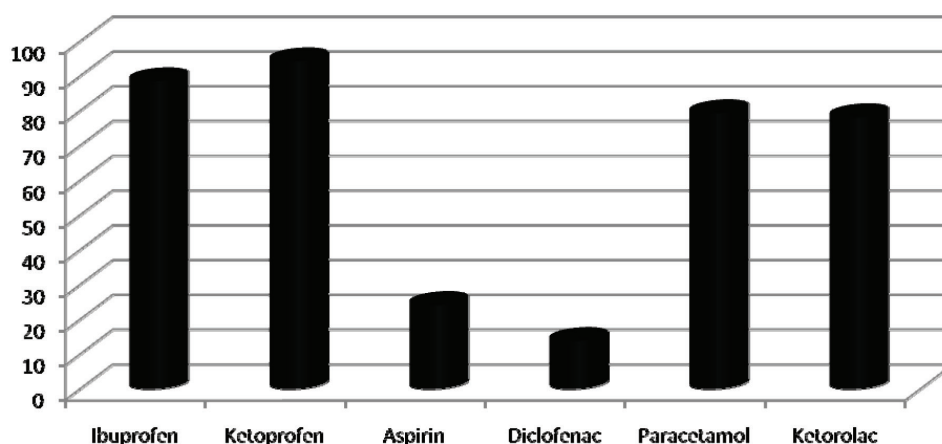


Figure 3. The most common analgesics prescribed by dentists.

Among the reasons why the dentists had prescribed NSAIDs to the patients were: extraction, implant surgery, pain, periodontitis, and infection of the teeth. Dentists were also asked if they had received information on NSAIDs use by other sources, such as conference, congresses, seminars, open lectures, continuous education courses, and so on. They indicated that the last time they were updated was during their dental studies, in the course of pharmacology, and very few of them (6.89%) have been updated through continuous education courses. Therefore, what was evident is that, considering the participants' years of experience as well, it has passed a long time since they were updated on the topic.

The group of dentists that have informed the patients on NSAIDs (42 dentists) showed lower knowledge on the side effects, and mechanism of action of NSAIDs, and maximum daily doses in adult and pediatric populations. 98.85% of the participants responded correctly to the gastrointestinal side effects of NSAIDs and 44.82% of the dentists that have informed the patients on NSAIDs risk, responded correctly to the most common adverse effects of overdosage of acetaminophen, which is the potential fatal hepatic necrosis. The ingestion of 10–15 g of acetaminophen in a single dose may bring to hepatotoxicity.

A total of 35 (40.23%) dentists had experienced a switch in NSAIDs within the past 2 years due to adverse effects.

Knowledge of the maximum daily dosage of NSAIDs

Most of the study samples responded incorrectly or simply provided no responses. In terms of dosing regimen,

Table 3. Dentist level of knowledge on NSAIDs.

	Dentist knowledge		
	Number of patients <i>n</i> (%)		
	Correct	Partially correct	Incorrect
Implication of NSAIDs in older patients	0 (0%)	53 (60.92%)	34 (39.08%)
NSAIDs in pregnancy	3 (3.44%)	79 (90.80%)	5 (5.75%)
Mechanism of action of NSAIDs	2 (2.29%)	10 (11.49%)	75 (86.21%)
Maximum daily dose in adults	7 (8.04%)	53 (60.91%)	40 (45.98%)
Maximum daily dose in pediatry	0 (0%)	11 (12.64%)	88.50%

*"Correct" = the answer was fully correct, "Partially correct" = at least one correct answer was given, "Incorrect" = none of the answers was correct.

45.98% did not know the maximum number of tablets that could be taken in a 24-hour period in adults, of which 16% indicated a higher maximum daily dose, and 84% of the respondents underestimated the daily maximum dose. These results implicate that dentists that under-estimated the daily maximum dose, did not give optimal pain management, instead of the over-estimated daily maximum dose group that could be dangerous and lead to complications and adverse drug events. When asked to indicate the maximum daily dose of NSAIDs in pediatric, 82.76% ($n = 72$) of the participants did not report any dose (Table 3), whereas 11 participants (12.64%) correctly reported the maximum daily dose of ibuprofen and 5.75% reported incorrect maximum daily doses in pediatric populations (Fig. 4).

Knowledge of the potential adverse effects of NSAIDs

Interestingly, 98.85% of the respondents recognized the side effects in the gastrointestinal system (stomach pain and stomach ulcer), unlike 18.39% ($n = 16$) that identified hepatic problems as an adverse effect, 14.94% ($n = 13$) that reported hypersensitivity, a potential adverse effect, and 5.75% ($n = 5$) that identified kidney disease as an NSAID side effect (Table 4 and

Table 4. Adverse effects of NSAIDs. The total number of dentists that indicated correctly each of the adverse effects of NSAIDs.

Adverse effects of NSAIDs	Number	%
Gastrointestinal	86	98.85
Platelets	0	0
Renal	5	5.75
Cardiovascular	2	2.29
Neurologic	0	0
Reproductive	0	0
Hypersensitivity	13	14.94
Hematologic	0	0
Hepatic	16	18.39
Dermatologic	0	0
Respiratory	0	0
Other	0	0
None of the above	3	3.45

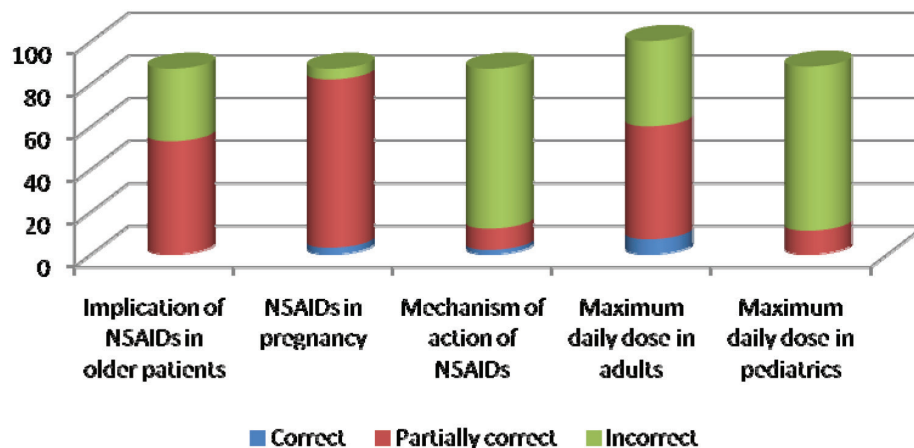


Figure 4. Dentist level of knowledge on NSAIDs.



Figure 5. The most known adverse effects of NSAIDs (the total number of dentists that indicated correctly each of the adverse effects of NSAIDs).

Fig. 5). Few respondents incorrectly believed that rheumatoid arthritis (8%) was a possible side effect.

In reference to aspirin, none of the participants reported that a major risk of prescribing aspirin in pediatric populations is its potential association with Reye Syndrome.

NSAIDs and geriatric use

When asked to indicate the implications of NSAIDs in elderly patients, none of them reported a decreased capacity of plasma albumin to bind drugs in elderly patients, resulting in higher total concentrations of unbound NSAIDs.

NSAIDs and pregnancy

Only a small proportion of respondents ($n = 3$, 3.44%) responded correctly about the NSAIDs effects in pregnancy, including also their association with the closure of the ductus arteriosus and impaired fetal circulation in utero, particularly in fetuses older than 32 weeks of gestation, out of 90.80% with partially correct answer (that did not report the closure of ductus arteriosus), and only 5.75% ($n = 5$) with totally incorrect answer.

DISCUSSION

This study identified that many respondents who participated in the survey did not display knowledge or had limited knowledge of NSAIDs use, precautions. 3.44% of the respondents displayed correct knowledge on the use of NSAIDs in pregnancy versus 39.08% of incorrect answers on the use of implications of NSAIDs in older patients. The most widely prescribed analgesic by the dentist was ketoprofen (94.25%), followed by ibuprofen (88.51%) and paracetamol (79.31%).

Despite the lack of knowledge, respondents have prescribed NSAIDs. Perceptions and knowledge of NSAIDs should increase. Dentists should be updated on NSAIDs through conferences, courses, medical representatives, and so on, and then, the communication between dentists and dental patients should increase, in order to minimize the negative consequences of limited NSAIDs knowledge. Moreover, dentists who give advice to the patients may also be at risk of legal action in case an incident occurs, considering that even NSAIDs used for a short period of time can be associated with a higher risk of cardiovascular events, leading to death. Considering that NSAIDs are over the counter drug, it is very important to underline that many of these products are available with no health professional advice at the point of purchase.

As reported by Goodman & Gilman, free-naproxen concentrations are markedly increased in older patients, although total plasma concentrations essentially are unchanged, and the higher susceptibility of older patients to GI complications may be due in part to elevated total or free NSAID concentration (Goodman, 2018). Unfortunately, none of the participants was aware of the diminished capacity of plasma albumin in older patients, which may bring to higher total plasma concentration.

16% of the participants indicated higher maximum daily dose of NSAIDs, and these results were even more worrying when considering that 82.76% of the dentists had a completely lack of knowledge on the maximum daily dose prescribed in the pediatric population. Of greater concern, 3.45% of the respondents did not know any of the side effects of NSAIDs.

The principal strength of the study is that by obtaining first hand information on issues related to use of NSAIDs, we were able to study dentist knowledge, and NSAID treatment in details. Other strengths included the high response rate (70.73%). However, there were several limitations to our study. The sample size was small, therefore, in perspective, this study should be replicated in a larger sample increasing not only the dentist number but also replicating it for dental patients. Moreover, the possibility that some questions may be misinterpreted is another limitation of the study. By providing open questions, the respondents can answer whatever they wish. On the other hand, this information can lead to different categories of investigations. Moreover, in perspective, we should also evaluate the knowledge on the legal implications of a wrong medical prescription, as well as the difference among different dentists and dental patients' age range groups knowledge.

CONCLUSION

In Albania, there are no official statistical data on the prescription and consumption of NSAIDs in the whole population, despite some cross-sectional studies involving a certain number of patients taking NSAIDs. Despite this, also in other countries, there are only few studies reported in the literature focusing on NSAIDs dentists' knowledge. This study has highlighted the absolute need of dentist to be updated on NSAIDs, for improving the well-being of their patients. Dentists should inform patients on NSAIDs use and risks, and on the other hand, they themselves should attend different seminars to update their knowledge on NSAIDs, as they are among the most prescribed drugs together

with antibiotics from the dentists. A lack of knowledge on NSAIDs use can have implications for patients' safety, bringing to inappropriate use of these drugs, affecting patients safety. This gap in knowledge may predispose patients to adverse drug events because many dentists may exceed recommended daily doses. Dentists may also not recognize potential contraindications or simply not be aware of potential side effects, thereby making this a widespread public health issue. Based on these concerning findings, and also on the crucial role and use of NSAIDs in our daily routine, we suggest that similar studies should be conducted also in other countries recruiting a higher number of dentists and other health professionals, such as physiotherapist, pharmacist, and physicians.

AUTHORS' CONTRIBUTIONS

All the authors of this manuscript are equally responsible for the technical information communicated to the journal. All authors had an active contribution to the conception and design and/or analysis and interpretation of the data and/or the drafting of the paper and they have critically reviewed its content and have approved the final version submitted for publication.

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CONFLICTS OF INTEREST

All the authors declare that there are no conflicts on interest.

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None.

COMPLIANCE WITH ETHICAL STANDARDS

The following study is in accordance with the ethical standards of the responsible committee on human experimentation.

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