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Evaluation of Practice and Awareness of the Safety Profile of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) among Dental Practitioners: A Cross-Sectional Study

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ABSTRACT

Non-steroidal anti-inflammatory drugs (NSAIDs) are the common medications used by dental practitioners to relieve dental pain and control post-operative signs of inflammation. NSAIDs, irrespective of their benefits, have a lot of hazards because of misuse and faulty prescriptions by dentists. The aim of this study is to evaluate the current use of NSAIDs during dental practice and to evaluate the association of the level of education and years of experience of dental practitioners with the awareness of the safety profile of NSAIDs. This observational cross-sectional study was conducted in Benghazi city between August and October 2024. The sample size is composed of 341 dentists. Participants were selected randomly from approximately every dental clinic in Benghazi. The questionnaire is composed of sections including assessment of drug use and drug-precautionary awareness. It is structured with checklist answers and was formulated in English. It is filled by the dentists during a visit to their dental clinics on the basis of an interview. The Statistics Package for Social Science Version 21 (SPSS) software was used for transferring and analysis of data. The results showed that the females accounted for the majority (60.7%). General practitioners represented 67.7% of the participants. About 61.0% of the dentists had clinical experience of less than 10 years. Ibuprofen and Ketoprofen were the most prescribed NSAIDs, 67.2% and 51.6, respectively. More than fifty percent (55.4%) of the participants used to prescribe NSAIDs for less than three days. Postoperative pain and dental pain were the most common clinical indications that NSAIDs were prescribed, 71.3% and 59.5%, respectively. Pregnancy was the most cited to be contraindicated (58.9%). Awareness of avoiding NSAIDs in the case of peptic ulcer patient was associated with years of experience of the dentists (P=0.030). Participants agreed that nausea was the most side effects (45.2%). Awareness of the interaction between NSAIDs and warfarin was associated with the level of education (P=0.006). The outcomes of the study have revealed less comprehension regarding scientific background knowledge of NSAIDs. There was little effect of level of education and years of experience on the awareness of the safety profile of NSAIDs during dental practice. Therefore, a lot of efforts should be focused on improving the knowledge for making proper therapeutic decisions and minimizing the risk of serious adverse effects on the patients who attend dental clinics.

KEYWORDS: Benghazi; Dentists; Clinical experience; Level of education; NSAIDs; Safety profile.

1. INTRODUCTION

Anti-inflammatory drugs, analgesics, antimicrobials, and antipyretics are often prescribed by dental practitioners in many fields of dentistry. Analgesics and anti-inflammatory drugs are widely used over-the-counter (OTC) [(1)]. Non-steroidal anti-inflammatory drugs (NSAIDs) are the most commonly used by dental practitioners to relieve dental pain and control post-operative signs of inflammation such as in endodontic treatment and extraction of teeth. Additionally, patients have used to take NSAIDs as self-medications to relieve pain related to a toothache [(1)].

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Vane and Piper first explained the mechanism of non-steroidal anti-inflammatory drugs (NSAIDs) for inhibiting cyclooxygenase (COX) enzymes which are responsible for prostaglandins (PGs), prostacyclin (PGI_2), and thromboxane (TxA2) biosynthesis from arachidonic acid (derived from cell membrane phospholipid) [(2)]. Prostaglandins have an essential role in providing protective and regulatory physiological functions in human body systems. For instance, PGE2 leads to a decrease in gastric acid secretion, while PGE2 and PGI2 increase the production of mucus, PGE2 and PGI2 maintain renal blood flow, and bronchial smooth muscles are relaxed by PGE2 and PGI2α. Moreover, contraction of the uterus is facilitated by PGE2 which progresses to labor [(3)]. Two cyclooxygenase (COX) enzymes are involved in prostaglandins biosynthesis; COX-

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I has protective functions such as gastric protection, maintaining of renal blood flow, and regulation of vascularity, and COX-2 is involved in normal renal function and vascular prostacyclin synthesis [3]. COX-1 is present in most cells, while COX-2 is induced in inflammatory cells but not at sites of GIT and platelets. COX-2 will be produced in the site of damaged dental pulp tissue and periodontitis which induces prostaglandin synthesis that leads to the activation of a pain mechanism and inflammatory manifestations [4].

Thus, inhibiting prostaglandins may give rise to serious adverse effects that were reported in many studies, especially in long-term use [5]. NSAIDs should be avoided in pregnancy due to their potential adverse effects [5, 6]. NSAIDs have a harmful role in the deterioration of renal function and increase the risk of peptic ulceration. Moreover, asthmatic and cardiovascular patients have limitations regarding the use of NSAIDs [7]. A lot of side effects such as nausea, abdominal pain, and heartburn during intake of NSAIDs were reported in many studies [5, 8, 9]. NSAIDs were also reported to potentiate some drug interactions with other medications [10-12].

NSAIDs can be identified according to the type of cyclooxygenase (COX) enzymes that were inhibited. Acetylsalicylic acid (Aspirin) is a non-selective COX inhibitor, but has more potential to be a selective COX-1 inhibitor. Piroxicam, Indomethacin, Ketoprofen, Diclofenac, Naproxen, and Ibuprofen are non-selective COX inhibitors. Meloxicam is selective COX-2 inhibitors, noting that Celecoxib is a highly selective COX-2 inhibitor [13-15]. Naproxen also has low selectivity to inhibit COX-2 [16]. Differently, NSAIDs can be identified clinically based on the duration of action; short-acting with rapid onset, such as Ketoprofen, Ibuprofen, Diclofenac Na and Aspirin (half-life is less than 6 hours), and long-acting NSAIDs such as Naproxen, Meloxicam, and Celecoxib (half-life is more than 10 hours). In acute pain, short-acting NSAIDs are more suitable. Conversely, for chronic conditions, long-acting is preferred [17].

Misuse and prescription of NSAIDs in the wrong way with a lack of thorough knowledge regarding their maximum daily dose, indications, contraindications, drug interactions, and side effects will lead to serious sequelae [18]. Therefore, our guide to using NSAIDs properly without any complications is based on the recorded medical history of the patient as well as on the experience and scientific background of health professionals.

To date, no studies have been found in the literature in regard to the knowledge of the proper use of NSAIDs in the city of Benghazi among dentists. Therefore, the current study was designed to evaluate the current awareness regarding the use of NSAIDs during dental practice and to evaluate the association of the level of education and years of experience of dental practitioners with the awareness of the safety profile of NSAIDs.

2. MATERIAL AND METHODS

2.1. Study design

This observational cross-sectional study was conducted in Benghazi city between August and October 2024. Informed consent was taken from all participants for agreement to fill out the questionnaire. The questionnaire was formulated in English and was filled by the dentists in approximately 2 minutes during a visit to their dental clinic on the basis of an interview. Participants were selected randomly from approximately every dental clinic in Benghazi. The questionnaire was filled with check-list answers and composed of three sections, including personal information, manner of practicing NSAIDs, and knowledge of the safety profile regarding NSAIDs.

2.2. Sample size calculation

The sample size was composed of 341 participants representing dentists working in dental clinics in Benghazi and was calculated according to Krejcie and Morgan Table (19). The sample size was affirmed by using the Raosoft online calculator (www.Raosoft.com) (20), assuming that approximately 3000 dentists work in the dental clinics. The confidence level of 95% with a 5 % marginal error was taken into consideration to achieve the value of the sample size.

2.3. Statistical Analysis

The statistics package for Social Science version 21 (SPSS) software was used for transferring and analyzing data. Results of the study were presented in descriptive analysis as frequencies (n) and percentages (%). Analysis of qualitative data was done using the Chi-squared test. A two-tailed P value of less than 0.05 was considered a significant association.

3. RESULTS

A total of 341 questionnaires were collected over two months. Females accounted for the majority (60.7%). General practitioners represented 67.0% of the participants. About 61.0% of the dentists had clinical experience of less than 10 years. The age group of (31-40) was the predominant (48.1%), (Table 1).

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Table 1. Demographic and professional data of dentists in Benghazi (n = 341)

Variable	Frequency (%)
Gender	
Male	134 (39.3 %)
Female	207 (60.7 %)
Age	
25-30	112 (32.8 %)
31-40	164 (48.1 %)
41-50	45 (13.2 %)
51-60	11 (3.2 %)
>60	9 (2.6 %)
Nationality	
Libyan	331 (97.1 %)
Non-Libyan	10 (2.9 %)
Education	
Bachelor degree	231 (67.0 %)
Master degree	93 (27.3 %)
PhD	14 (4.1 %)
Diploma	3 (0.9 %)
Clinical Rank	
General Practitioner	231 (67.7 %)
Specialist	110 (32.3 %)
Years of experience	
<10 years	208 (61.0 %)
10-20 years	97 (28.4 %)
> 20 years	36 (10.6 %)

3.1. The clinical practice of NSAIDS

Ibuprofen and Ketoprofen were the most prescribed NSAIDs by participants, 67.2% and 51.6, respectively, followed by Naproxin, Diclofenac K, and Diclofenac Na (36.1%, 26.1%, and 19.6%), respectively, (Table 2).

More than fifty percent (55.4%) of them have been prescribed NSAIDs for less than three days (short period) and 44.0% have been prescribed NSAIDs up to seven days.

Postoperative pain, dental pain, and odontogenic infections were the most common clinical situations in which NSAIDs were prescribed (71.3%, 59.5%, and 49.6%), respectively. NSAIDs were used in the treatment of temporomandibular joint pain by approximately twenty percent (20.8%) of dentists. Participants who have been prescribed NSAIDs with antibiotics sometimes account for 51.3%. Over sixty (63.6%) of the participants had prescribed proton pump inhibitors as needed with NSAIDs (Table 2).

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Table 2. Clinical practice of dentists in Benghazi (n = 341)

Clinical Practice	Frequency (%)
In your current practice, how many times do you prescribe NSAIDs?	
Always	24 (7.0 %)
Frequently	80 (23.5 %)
Sometimes	202 (59.2 %)
Rarely	32 (9.4 %)
Never	3 (0.9 %)
Which types do you prescribe during dental practice (Yes)?	
Ketoprofen	176 (51.6 %)
Ibuprofen	229 (67.2 %)
Naproxen	123 (36.1 %)
Diclofenac Na	67 (19.6 %)
Diclofenac K	89 (26.1 %)
Aspirin	11 (3.2 %)
Piroxicam	3 (0.9 %)
Meloxicam	1 (0.3 %)
In which situations do you use NSAIDs (Yes)?	
TMJ pain	71 (20.8 %)
Infections	169 (49.6 %)
Post-operative	243 (71.3 %)
Dental pain	203 (59.5 %)
What period do you often prescribe?	
Short [less than 3 days]	189 (55.4 %)
Intermediate [between 3 and 7 days]	150 (44.0 %)
Long [more than 7 days]	0 (0.0 %)
Never	2 (0.6 %)
In your current practice, how often do you prescribe NSAIDs with Antibiotics (Yes)?	
Always	26 (7.6 %)
Frequently	74 (21.7 %)
Sometimes	175 (51.3 %)
Rarely	58 (17.0 %)
Never	8 (2.3 %)
Do you prescribe Omeprazole (proton pump inhibitor) with NSAIDs (Yes)?	
Always	10 (2.9 %)
Sometimes	217 (63.6 %)
Never	114 (33.4 %)

Ibuprofen was preferred to be used more by dentists with 10 to 20 years of clinical experience as well as those with less than 10 years (70% and 69.2%, respectively, *P* value = 0.026). Participants with more than 20 years of experience and a higher academic degree preferred to use Diclofenac Na. Years of experience and level of education of the dentists were highly significantly associated with the prescribing of Diclofenac Na (*P* value = 0.000 and 0.004, respectively) (Table 3).

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Table 3. Association between types of NSAIDs used by dentists in Benghazi with years of experience and level of education (n = 341)

Type of NSAIDs (yes)	<10 years (%)	10-20 years (%)	>20 years (%)	*P* value
Ketoprofen	108 (51.9)	50 (51.5)	18 (50.0)	0.977
Ibuprofen	144 (69.2)	68 (70.1)	17 (47.2)	0.026*
Naproxen	75 (36.1)	35 (36.1)	13 (36.1)	1.000
Diclofenac Na	31 (14.9)	19 (19.6)	17 (47.2)	0.000*
Diclofenac K	59 (28.4)	22 (22.7)	8 (22.2)	0.491
Aspirin	9 (4.3)	1 (1.0)	1 (2.8)	0.284
Piroxicam	0 (0.0)	2 (2.1)	1 (2.8)	0.079
Meloxicam	0 (0.0)	1 (1.0)	0 (0.0)	0.390

Type of NSAIDs (yes)	Diploma (%)	BDS (%)	MSc (%)	PhD (%)	*P* value
Ketoprofen	0 (0.0)	125 (54.1)	44 (47.3)	7 (50.0)	0.233
Ibuprofen	2 (66.7)	155 (67.1)	64 (68.8)	8 (57.1)	0.853
Naproxen	2 (66.7)	92 (39.8)	26 (28.0)	3 (21.4)	0.071
Diclofenac Na	0 (0.0)	34 (14.7)	28 (18.3)	5 (35.7)	0.004*
Diclofenac K	1 (33.3)	60 (26.0)	24 (25.8)	4 (28.6)	0.978
Aspirin	0 (0.0)	8 (3.5)	8 (3.2)	0 (0.0)	1.000
Piroxicam	0 (0.0)	2 (0.9)	1 (1.1)	0 (0.0)	1.000
Meloxicam	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0.323

*** <0.05 is a statistically significant association.**

3.2. Awareness of the safety profile of NSAIDS

Pregnancy was the most cited to be contraindicated (58.9%) followed by renal diseases, allergy to other medications, peptic ulcer, liver disease, and asthmatic patients (49.3%, 41.6%, 39.0%, 37.8%, and 35.5%), respectively. Dentists' qualifications and years of experience were associated with the avoidance of giving NSAIDs to peptic ulcer patients (*P* value = 0.022 and 0.030), respectively. Additionally, dentists who have been practicing dentistry for more than 20 years emphasized NSAIDs cannot be used for patients with ulcerative colitis, breast-feeding and celiac disease (38.9%, 36.1%, and 19.4%) with *P* value (0.032, 0.040, and 0.012), respectively, (Tables 4 and 5).

Participants agreed that nausea was the most common side effect (45.2%), followed by abdominal pain, allergic reaction to NSAIDs, heartburn, and vomiting (39.3%, 36.7%, 29.0%, and 22.3%), respectively. Awareness of heartburn as a side effect that may be caused by using NSAIDs was highly significantly associated with the level of education and years of experience (*P* value = 0.000 and 0.001), respectively. Furthermore, level of education was significantly associated with awareness of abdominal pain as one of the frequent side effects (*P* value = 0.004), especially in those with a degree of PhD and Diploma (64.3% and 100%), respectively, (Tables 4 and 5).

Warfarin was reported by 27.6% of the dentists to have interaction with NSAIDs, followed by oral contraceptives and beta blockers (14.1% and 13.8%), respectively. Dentists with an MSc degree have a significant awareness regarding interactions of warfarin with NSAIDs (40.9%, *P* value = 0.006). Years of experience were associated with the awareness of Ranitidine interaction (*P* value = 0.032), (Tables 4 and 5).

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Table 4: Association of awareness of safety profile of NSAIDs with years of experience regarding dentists in Benghazi (n = 341)

Awareness	Total no	<10 years (%)	10-20 years (%)	>20 years (%)	*P* value
Awareness of side effects of NSAIDs (Yes)					
Abdominal pain	134 (39.3)	73 (35.1)	48 (49.5)	13 (36.1)	0.052
Nausea	154 (45.2)	91 (43.8)	44 (45.4)	19 (52.8)	0.603
Heartburn	99 (29.0)	46 (22.1)	36 (37.1)	17 (47.2)	0.001*
Diarrhea	47 (13.8)	26 (12.5)	15 (15.5)	6 (16.7)	0.680
Dyspnea	21 (6.2)	12 (5.8)	4 (4.1)	5 (13.9)	0.107
Vomiting	76 (22.3)	47 (22.6)	21 (21.6)	8 (22.2)	0.983
Rise in blood pressure	3 (0.9)	2 (1.0)	0 (0.0)	1 (2.8)	0.308
Allergy to NSAIDs	125 (36.7)	73 (35.1)	38 (39.2)	14 (38.9)	0.756
Awareness of contraindications for using NSAIDs (Yes)					
Pregnancy	201 (58.9)	116 (55.8)	59 (60.8)	26 (72.2)	0.163
Angina	31 (9.1)	12 (5.8)	12 (12.4)	7 (19.4)	0.013*
Myocardial Infarction	47 (13.8)	30 (14.4)	11 (11.3)	6 (16.7)	0.667
Stroke	38 (11.1)	21 (10.1)	11 (11.3)	6 (16.7)	0.511
Peptic ulcer	133 (39.0)	70 (33.7)	44 (45.4)	19 (52.8)	0.030*
Asthma	121 (35.5)	67 (32.2)	39 (40.2)	15 (41.7)	0.284
Renal insufficiency	168 (49.3)	104 (50.0)	42 (43.3)	22 (61.1)	0.178
Liver diseases	129 (37.8)	74 (35.6)	38 (39.2)	17 (47.2)	0.392
Allergy to other medications	142 (41.6)	78 (37.5)	45 (46.4)	19 (52.8)	0.122
Heart failure	55 (16.1)	34 (16.3)	11 (11.3)	10 (27.8)	0.072
Hypertension	91 (26.7)	57 (27.4)	26 (26.8)	8 (22.2)	0.810
Crohn's disease	40 (11.7)	24 (11.5)	9 (9.3)	7 (19.4)	0.267
Ulcerative colitis	76 (22.3)	40 (19.2)	22 (22.7)	14 (38.9)	0.032*
Celiac disease	26 (7.6)	11 (5.3)	8 (8.2)	7 (19.4)	0.012*
Breast feeding	92 (27.0)	46 (22.1)	33 (34.0)	13 (36.1)	0.040*
Awareness of drug-interaction of NSAIDs with other medications (Yes)					
Warfarin	94 (27.6)	51 (24.5)	32 (33.0)	11 (30.6)	0.278
Oral hypoglycemic	21 (6.2)	13 (6.3)	5 (5.2)	3 (8.3)	0.792
Beta blockers	47 (13.8)	29 (13.9)	12 (12.4)	6 (16.7)	0.811
ACEIs	21 (6.2)	11 (5.3)	8 (8.2)	2 (5.6)	0.598
Oral contraceptives	48 (14.1)	22 (10.6)	19 (19.6)	7 (19.4)	0.067
Prednisolone	16 (4.7)	7 (3.4)	5 (5.2)	4 (11.1)	0.129
Ranitidine	12 (3.5)	7 (3.4)	1 (1.0)	4 (11.1)	0.032*
Diuretics	20 (5.9)	13 (6.3)	3 (3.1)	4 (11.1)	0.202

*** <0.05 is a statistically significant association.**

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Table 5: Association of Awareness of safety profile of NSAIDs with level of education regarding dentists in Benghazi (*n* =341)

Awareness	Total no	Diploma (%)	BDS (%)	MSc (%)	PhD (%)	*P* value
Awareness of side effects of NSAIDs (Yes)						
Abdominal pain	134 (39.3)	3 (100.0)	79 (34.2)	43 (46.2)	9 (64.3)	0.004*
Nausea	154 (45.2)	2 (66.7)	100 (43.3)	44 (47.3)	8 (57.1)	0.611
Heartburn	99 (29.0)	0 (0.0)	52 (22.5)	42 (45.2)	5 (35.7)	0.000*
Diarrhea	47 (13.8)	0 (0.0)	32 (13.9)	13 (14.0)	2 (14.3)	1.000
Dyspnea	21 (6.2)	0 (0.0)	11 (4.8)	9 (9.7)	1 (7.1)	0.319
Vomiting	76 (22.3)	0 (0.0)	52 (22.5)	21 (22.6)	3 (21.4)	1.000
Rise in blood pressure	3 (0.9)	0 (0.0)	2 (0.9)	1 (1.1)	0 (0.0)	1.000
Allergy to NSAIDs	125 (36.7)	1 (33.3)	79 (34.2)	40 (43.0)	5 (35.7)	0.502
Awareness of contraindications for using NSAIDs (Yes)						
Pregnancy	201 (58.9)	2 (66.7)	142 (61.5)	50 (53.8)	7 (50.0)	0.515
Angina	31 (9.1)	1 (33.3)	17 (7.4)	12 (12.9)	1 (7.1)	0.145
Myocardial infarction	47 (13.8)	0 (0.0)	34 (14.7)	12 (12.9)	1 (7.1)	0.874
Stroke	38 (11.1)	1 (33.3)	24 (10.4)	10 (10.8)	3 (21.4)	0.225
Peptic ulcer	133 (39.0)	2 (66.7)	78 (33.8)	46 (49.5)	7 (50.0)	0.022*
Asthma	121 (35.5)	2 (66.7)	75 (32.5)	38 (40.9)	6 (42.9)	0.263
Renal insufficiency	168 (49.3)	3 (100.0)	113 (48.9)	44 (47.3)	8 (57.1)	0.378
Liver diseases	129 (37.8)	2 (66.7)	87 (37.7)	33 (35.5)	7 (50.0)	0.509
Allergy to other medications	142 (41.6)	1 (33.3)	89 (38.5)	44 (47.3)	8 (57.1)	0.287
Heart failure	55 (16.1)	1 (33.3)	38 (16.5)	11 (11.8)	5 (35.7)	0.084
Hypertension	91 (26.7)	1 (33.3)	65 (28.1)	23 (24.7)	2 (14.3)	0.632
Crohn's disease	40 (11.7)	2 (66.7)	26 (11.3)	11 (11.8)	1 (7.1)	0.090
Ulcerative colitis	76 (22.3)	2 (66.7)	46 (19.9)	25 (26.9)	3 (21.4)	0.146
Celiac disease	26 (7.6)	1 (33.3)	15 (6.5)	10 (10.8)	0 (0.0)	0.120
Breast feeding	92 (27.0)	1 (33.3)	59 (25.5)	28 (30.1)	4 (28.6)	0.783
Awareness of drug-interaction of NSAIDs with other medications (Yes)						
Warfarin	94 (27.6)	0 (0.0)	52 (22.5)	38 (40.9)	4 (28.6)	0.006*
Oral hypoglycemic	21 (6.2)	0 (0.0)	10 (4.3)	10 (10.8)	1 (7.1)	0.151
Beta blockers	47 (13.8)	0 (0.0)	33 (14.3)	13 (14.0)	1 (7.1)	0.947
ACEIs	21 (6.2)	0 (0.0)	10 (4.3)	10 (10.8)	1 (7.1)	0.151
Oral contraceptives	48 (14.1)	0 (0.0)	33 (14.3)	14 (15.1)	1 (7.1)	0.900
Prednisolone	16 (4.7)	1 (33.3)	8 (3.5)	6 (6.5)	1 (7.1)	0.083
Ranitidine	12 (3.5)	0 (0.0)	9 (3.9)	3 (3.2)	0 (0.0)	1.000
Diuretics	20 (5.9)	0 (0.0)	11 (4.8)	8 (8.6)	1 (7.1)	0.410

*** <0.05 is a statistically significant association.**

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4. DISCUSSION

Dentists have used to prescribe different types of NSAIDs regularly in dental practice to manage pain and inflammation as reported in our study. This should be based on well-scientific knowledge gained from their academic learning and clinical experience in the field. Our suspected results of the study are to find more awareness of accurate clinical manipulation of NSAIDS during clinical practice, especially among recently graduated practitioners, as a reflection of close contact with academic-based knowledge as well as among dental practitioners with more clinical years of experience in the dental field.

Ibuprofen was the first line of NSAIDs used among our participants. This was in line with many studies; a multicenter, observational cohort study by Bradbury who stated that Ibuprofen and Diclofenac adhered to prescribing physicians' acceptance for managing pain in Ireland [21]. A survey conducted in Tunisia, the capital, in 2021, cited that 82% of dentists were prescribing Ibuprofen during dental practice [22]. In addition to the study by Halling et al., in Germany, that demonstrated a significant increase in prescriptions among dentists (80.1%, $P < 0.05$) [23]. Our survey revealed that more than half of recent graduate participants with years of experience of less than 10 years cited that Ibuprofen was the most used NSAIDs in dental practice, as well as those with 10-20 years of experience who have reported similar results (P=0.026), which was also described similarly in a recent study in Yemen that reported 66.6% of dentists have an experience of less than 5 years and 80.5% of dentists involved in this study were prescribing Ibuprofen for dental pain [24].

On the other hand, preferring to use Diclofenac Na was highly significantly associated with participants with more than 20 years of experience and those with a higher academic degree (P=0.000 and P=0.004), respectively. Yu's study, in 2020, was in agreement with our outcomes as it reported that Diclofenac was the most frequently prescribed analgesic along with Acetaminophen in many dental conditions and proper prescription was significantly associated with more experienced and post-graduated dentists (P value 0.004) [25]. Like other NSAIDs, the risk of adverse effects was reported to be increased when Diclofenac Na was used to relieve pain and reduce inflammation. It is a non-selective COX inhibitor, leading to inhibition of the protective function of lining mucosa of the stomach, increasing the risk of heart attack and stroke, reduction of kidney function, and association with liver toxicity [26, 27]. This may explain why dentists with less clinical experience and those with low qualifications included in our study avoid manipulating clinically with Diclofenac.

The aforementioned complications of Diclofenac Na were related to dose quantity, duration, and presence of risky patients. These adverse effects can be minimized by shortening the duration with the minimum effective dose, and may use appropriate gastro-protective agents when necessary. Alternative therapeutic options may be used when a potential risk overweighs its benefit, in addition to health care professional consultation [26].

Diclofenac potassium (K) was used by more than twenty-five percent of dentists involved in our study rather than Diclofenac Na. Diclofenac K is another type of Diclofenac that was formulated to overcome the resistance of absorption of sodium-salt preparation of Diclofenac in the acidic medium of the stomach. Diclofenac Na reaches a peak in approximately 2 hours [28]. In contrast, Diclofenac K powder sachet has an affinity for dissolving in acidic media that facilitates rapid absorption and reaching a peak within 8 minutes; in addition, Diclofenac potassium sachet can be taken safely with food [28]. These may give more preference to prescribing Diclofenac (K) than Diclofenac (Na) by the dentists in our study. Nonetheless, 75 mg intramuscular (IM) Diclofenac Na has been reported to have a significant effect in relieving acute pain after 30 minutes, in comparison with 75 mg Diclofenac K tablet [29].

In the present study, it is striking that Ketoprofen has been demonstrated by participants as the second most used NSAIDs during dental practice, despite the absence of a significant effect of years of experience and educational level on prescribing of Ketoprofen. A meta-analysis study by Sarzi-Puttini et al. showed ketoprofen was more effective over diclofenac and ibuprofen in controlling pain [30]. Additionally, pain was reported to be significantly lowered by using Ketoprofen in comparison with diclofenac after 6 hours post-surgery [31]. Studies by Sarzi-Puttini et al. also reported that Ketoprofen was reported as well-tolerated in the elderly, and was considered as a safe, rapid, and more effective NSAIDs [30, 32]. The trend of our participants to use Ketoprofen most frequently may be related to their experience of its favorable characteristics in clinical practice that was mentioned in the previous studies.

A lot of general practitioners have preferred to prescribe Naproxen in our study, more than thirty-five percent. Naproxen was reported by 78% of dentists in a study by Teoh et al. in Australia as an appropriate choice in the treatment of dental pain due to its accepted safety profile [33]. A similar trend was expressed by Şermet et al. in Istanbul, Turkey [34], which gave support to the high frequency of our results. Cooper et al. cited that in post-operative dental surgery, a single dose of Naproxen was significantly higher than Ibuprofen in relieving the pain [35]. In addition to the reported studies that demonstrated its safety for cardiovascular risk [16, 36], Naproxen was approved by the Food and Drug Administration (FDA) as the safest non-aspirin NSAIDs, due to its low selectivity for COX-2 [37]. Remarkably, cardiovascular risk was highly significantly associated with selective COX-2 inhibitors such as Celecoxib with approval by FDA [16, 32, 36, 38].

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One participant used to prescribe Meloxicam frequently. Noticeably, this participant has a degree of master's (M.Sc.) and has clinical experience of 10 to 20 years, which may reflect the understanding of using this medication. Meloxicam was reported to be more tolerated regarding the gastrointestinal system when compared with other NSAIDs [39]. Many studies reported its efficiency in relieving post-operative pain. A double-blind randomized parallel-group clinical trial study reported that a single dose of Meloxicam 15 mg had more analgesic and anti-trismus effects than using Diclofenac after extraction of a difficult tooth in the lower jaw 'third molar' [40]**.** Another recent study in 2020, revealed that administration of 15 mg meloxicam before 60 minutes of surgical removal of the mandibular third molar had a significant reduction in post-operative pain and edema (*P* value = 0.000) [41].

Piroxicam is another NSAID which is related to Meloxicam (Oxicam group). In our study, 2 participants were used to prescribe it. Piroxicam has a maximum daily dose of 20 mg, and should be prescribed for young people who have no comorbidity with other diseases and should be avoided in the elderly [42]. Nevertheless, other studies have cited that Meloxicam was more effective in pain relief and with substantial duration of action than Piroxicam and Diclofenac [39, 42].

Interestingly, our study has shown that fewer participants have used Aspirin to relieve dental pain (3.2%). As reported, chronic use of high doses leads to an increased risk of gastric ulceration and renal dysfunction [4]. In general, aspirin should be avoided in children less than 16 years of age, as it may develop Reye's syndrome [43]. Ibuprofen of 400 mg was reported to be favorable and more effective in relieving dental pain with markedly longer action than 650 mg of Aspirin [44].

More than half of our participants were prescribed NSAIDs for less than 3 days in order to reduce discomfort related to their side effects. Nausea, abdominal pain, allergy to NSAIDs, heartburn, vomiting, and diarrhea were reported by our participants as the most common side effects, respectively. The outcomes of our study were in agreement with a study by Muthanna that reported more than half (53.9%) were aware of most gastrointestinal side effects of NSAIDs [24]. Awareness of heartburn and abdominal pain were the lonely significantly associated with the degree of academic qualification (*P* value = 0.000 and 0.004), respectively. Otherwise, there was no effect of levels of education among dentists on the awareness of the side effects of NSAIDs.

In this context, vomiting, rashes, gastric pain, blurred vision, and dizziness have been reported less frequently with the use of Ibuprofen, and high doses of Ibuprofen may cause seizures, dyspnea and an increase in blood pressure [9]. For patients with hypersensitivity to Aspirin (aspirin-induced asthma), NSAIDs should be avoided, especially Ibuprofen [8]. Aside from Aspirin, all NSAIDs, when taken at normal therapeutic doses, could raise blood pressure (BP) in hypertensive patients as well as normal individuals [45, 46].

As expected, in the present study, pregnancy was the most cited to be avoided with NSAIDs (58.9%), followed by renal diseases, allergy to other medications, peptic ulcer, liver disease, and asthmatic patients, respectively. In the study of Monisha, participants avoided the use of NSAIDs during pregnancy and renal insufficiency (88% and 80%, respectively) [47]. Regarding pregnancy, The Food and Drug Administration (FDA) included most NSAIDs in category (B) during the first three months of pregnancy and as category (D) during the last three months [5], and FDA recommended avoiding the use of NSAIDs after week 20 of pregnancy [48, 49].Our participants with higher qualifications affirmed to avoid giving NSAIDs to peptic ulcer patients (P value = 0.022). Additionally, a dentist who has been practicing dentistry for more than 20 years emphasized NSAIDs cannot be used for patients with peptic ulcers (P value = 0.030). Awareness of some gastrointestinal diseases such as ulcerative colitis and celiac was associated with years of clinical experience by dentists (P value = 0.032 and 0.012), respectively.

Adverse effects were reported in many studies; long-term use of NSAIDs may cause kidney and gastrointestinal complications and many medically compromised patients may deteriorate with NSAIDs comorbidity [50, 51]. The risk of myocardial infarction as well as renal and hepatic dysfunction was elevated with chronic high doses of Ibuprofen. Ibuprofen has been reported to cause gastrointestinal bleeding, consequently potentiating the risk of gastric ulcers. In addition, renal damage, heart failure, hyperkalemia, and bronchospasm were related to high doses of Ibuprofen use [9]. A lot of studies have reported that Aspirin and NSAIDs such as Ibuprofen could have induced an attack in children and adult patients with asthma (a non-allergic mechanism) [52-54].

In the case of breastfeeding, about twenty-five percent of participants preferred not to give NSAIDs to avoid harmfulness to the infant and was significantly associated with more clinically experienced dentists (*P* = 0.040). However, no clear explanations were clarified by the participants regarding avoidance of prescription, but Donaldson and Goodchild' study revealed and explained that Aspirin with a dose of more than 100 mg was reported to develop Reye syndrome and platelet dysfunction and, in contrast, other than Selective COX-2 inhibitors, Ibuprofen, and other NSAIDs can be used for mother-feeding patients [55]. Additionally, Rigourd et al. in other studies also supported the safety of Ibuprofen and Ketoprofen for mother-feeding patients as the relative infant dose (RID) was significantly lower than 1% in both [56, 57].

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In our survey, a lack of knowledge and awareness were markedly observed regarding drug-interactions with NSAIDs irrespective of Warfarin. Warfarin was expressed in our survey as the most avoided drug with NSAIDs. Similar findings described by Sharma et al. (79%) [12]. The study of Battistella et al. also confirmed the hazard of co-prescription of NSAIDs with warfarin that agreed with the avoidance reported in our study [10]. There was only a significant association between the awareness of hazards of co-administration of NSAIDs with Warfarin and the educational degrees of the dentists ($P = 0.006$).

There was controversy in some outcomes of previous studies regarding Warfarin; Battistella et al. reported that the risk of bleeding in upper GI in those taking warfarin concomitantly with non-selective and selective COX-2 inhibitors was in similar increase compared with control patients not treated with NSAIDs [10]. On the contrary, Sarzi-Puttini et al. have reported no interaction between Ketoprofen and warfarin was observed [32].

Avoidance of prescribing NSAIDs with oral contraceptive medications was the second most reported drug-interaction by our participants. The risk of venous thromboembolism in women on oral contraceptive medication was reported by Meaidi et al. to be significantly associated with concurrent use of NSAIDs [58].

Other medication-interactions with NSAIDs were cited in many studies. Angiotensin converting enzyme inhibitors (ACEIs), Calcium-channel blockers, Beta-blockers, and Diuretics have been found to have low significant interaction with NSAIDs in elderly hypertensive patients [11, 59-61]. Other studies revealed that a statistically significant increase in BP was reported when NSAIDs (other than Naproxen and Aspirin) were co-administered with Beta-blockers, angiotensin receptor blockers (ARBs) and ACEIs; NSAIDs attenuated their action while having found low effect on BP with diuretics and calcium channel blockers [54, 62].

Concurrent use of NSAIDs even in a short-term with glucocorticoids will result in an increased risk of gastrointestinal bleeding [12, 63] that was demonstrated in our study by fewer participants. Similarly, interaction with oral hypoglycemics was also reported by fewer participants as NSAIDs were reported to increase their half-life [12].

About fifty percent of our participants reported concurrent use of antibiotics with NSAIDs in some particular situations. Antibiotics could be prescribed concurrently with NSAIDs, and no evidence of the presence of adverse effects was reported [64]. Effects of NSAIDs were cited to be reduced when used with Antacids [59] which was notified and significantly associated with high years of experience in our survey ($P = 0.032$).

It is worthwhile highlighting some critical points regarding a prophylactic dose of Aspirin 75-100 mg that is commonly used by dental patients. Co-administration of NSAIDs (other than Diclofenac) with Aspirin may potentiate clot formation due to its competitive access to the site of platelet-expressed COX-1 [8]. Potential interaction with Aspirin could be reduced if Ibuprofen is taken more than 30 minutes after a prophylactic dose of Aspirin, according to FDA [54, 65].

More than sixty percent of dentists in our survey have reported that Omeprazole, a gastro-protective agent, was used with NSAIDs in some instances as needed. A Study by Bakhriansyah et al. demonstrated that non-selective COX inhibitors and selective COX-2 used with PPIs were significantly associated with a decrease in the risk of gastro-intestinal perforation, ulceration, and bleeding in comparison with non-selective COX inhibitors that used alone ($P < 0.05$) [66]. Another study revealed that ketoprofen 200 mg when administrated with omeprazole 20 mg once daily had significantly more comfortable postoperative pain [67]. Accordingly, for some systemic diseases that require long-term use of NSAIDS such as osteoarthritis, PPI is preferred to be used [63]. In contrast, short-term use of NSAIDs was more practiced in dentistry and that may not necessitate the use of PPI, unless in the case of accompanying discomfort and for those with high risk.

Finally, this survey highlighted the utilization and clinical manipulation of NSAIDs during dental practice and the work has attempted to put the level of education and period of clinical experience in focus despite the lack of sources of data in the literature concerning this issue.

5. CONCLUSION

To conclude, the study results have revealed less comprehension regarding scientific background knowledge of NSAIDs. There was little effect on the level of education and years of experience with awareness of using NSAIDs during dental practice. The safety profile of NSAIDs should be kept in consideration by physicians to reach the proper therapeutic decision. In addition, many parameters including the age and weight of the patient, medical history, intensity of pain, and understanding of pharmacokinetics and pharmacodynamics of NSAIDs will guide physicians in making the decision.

6. RECOMMENDATIONS

According to the outcomes of the study, further workshops and events are needed to close the gap and should be continued to improve the level of knowledge and practice regarding the use of NSAIDs, and to minimize the risk of a lot of serious adverse effects on the patients who attend dental clinics.

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