
ORIGINAL ARTICLE

Awareness about misuse of analgesics and anti-inflammatories and their complications on liver, heart and kidney among Saudi Arabia population

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ABSTRACT

Nonsteroidal anti-inflammatory drugs (NSAIDs) widely used in management of pain and inflammation from different causes. Some study in UK stated that about 20 million prescriptions containing NSAIDs, and 15% of the people taking NSAIDs over the age of 60 years. Paracetamol and NSAIDs have dangerous adverse effects when misused and without respect to safety rules. The aim of this study is to estimate the most analgesic used and estimate the awareness of Saudi people about the complications on liver, heart and kidney after commonly used analgesics. The data were collected through questionnaire (26 questions on four sections) distributed among Saudi people online. The results showed that 496 Saudi participants; most of them from males; and their age range from 21-25 years (35.5%) with university level (73.4%). Their source of knowledge mainly from physician (49.2%) followed by leaflet, university subjects, pharmacist (36.7%, 32.7%, 29%) respectively. About 67% used analgesic for treatment of headache and the most analgesics used were paracetamol (71%), Ibuprofen (25%). Some side effects were happened upon chronic use of painkiller such as stomach pain (45%), Kidney pain (31.5%), stomach ulcer & pulse disturbance (17.9%), hypertension (8.1%) and foot edema (3.8%). About 28.2% prefer to use herbal medicine as analgesic while, 78.5% who used only one analgesic. From our results we can conclude that there was a high utilization of NSAIDs with Saudi population especially paracetamol. So, we should target public awareness campaigns about the appropriate usage the medications and future studies should be conducted.

Key Words: NSAIDs, Painkiller, Misuse, Adverse effects, Saudi Arabia.

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INTRODUCTION

There are more than one billion NSAIDs prescriptions per year and about 30 million people received NSAIDs every day in the world [1]. Study by Shin and his colleagues in UK showed that about twenty million prescriptions containing NSAIDs and 15% of the people >60 years received NSAIDs [2]. A previous review in 2015 by Ungprasert reported that there was a risk of acute kidney diseases as a result of using NSAID, but did not significance for using COX-2 inhibitors or traditional NSAIDs with higher COX-2 selectivity such as meloxicam or diclofenac [3]. Other review study done in 2018 showed that some of NSAIDs might cause morbidity in some patients starting from changing of bowel motion, diarrhea, inflammation in bowel, to chronic blood loss with iron deficiency anemia [4]. Most of NSAIDs could produce more adverse effects on GIT and should increase patient's awareness of these adverse effects. NSAIDs have a great role in relieving pain especially in cancer, bone problems, dementia prevention, improve muscle performance and urinary incontinence. On the other hand, NSAIDs can also increase the risk of stroke and geriatric psychiatric. So, these risks and benefits should be balanced carefully especially in the elderly patients to optimize overall outcomes [5]. Another review specifically focused on myocardial, vascular and renal risks of COX-2-selective meloxicam allowed a broad definition of renal

outcomes and it didn't find an increased renal risk [6]. Other report noted weak associations upon using NSAIDs with acute kidney diseases but other studies reporting the largest risks being with older patients [7]. The risk of cardiac arrest associated with use of the most common types of NSAIDs such as ibuprofen was associated with an increased risk of cardiac arrest, while diclofenac, naproxen was not associated with cardiac arrest. No significant associations between cardiac arrest and use of COX-2 selective inhibitors, rofecoxib and celecoxib [8]. Paracetamol was found to be safe in patients with chronic liver disease but in reduced dose. NSAIDs should be avoided because of their risk of hepatorenal syndrome, gastrointestinal hemorrhage and renal disease. Most opioids had adverse effects in patients with liver cirrhosis due to increased risk of hepatic encephalopathy. They should be given in lower doses and less frequency, also, should be avoided in patients with a history of encephalopathy or addiction [9]. Other study said that NSAIDs may have a role in cancer prevention and cancer promotion [10]. Study in KSA, 2018 stated that the ten most used drugs in Saudi Arabia from 2010-2015 were antibiotics and analgesics, followed by proton pump inhibitors and anti-diabetics, followed by antihyperlipidemic agents and erectile dysfunction treatments [11]. The aim of this study is to estimate the most analgesic used and estimate the awareness of Saudi people about the complications on liver, heart and kidney after commonly used analgesics.

MATERIAL AND METHODS

The Study will be conducted through cross-sectional descriptive study design. Data were collected from a sample of 496 participants, who answered questionnaire online from 5th of February, 2020 to 5th March, 2020. The data was collected through a well-structured questionnaire was used to address the study objectives. The questionnaire consists of 26 questions distributed in four sections. First section consist of 4 questions about participants socio-demographic, second section consist of 9 questions concerning their knowledge's about the painkiller such as the rate of using analgesics, type of analgesics used, their adverse effects and source of information, third section consist of 6 questions concerning their knowledge's about the uses of painkiller and finally fourth section consist of 7 questions about the rate of using analgesics in patients with liver, heart or kidney diseases. The questionnaire was prepared in English but prior to use in the study was translated from its original English version to Arabic. Statistical analyses were performed using SPSS version 23 (SPSS, Chicago, IL, USA). Frequencies and percentages were calculated for categorical variables.

RESULTS AND DISCUSSION

In this study the total number of participants was 496 patients. Most of male participants their ages ranged from 21-25 years (35.5%), then 41-45 years (12.5%). Most of participants from Western region of KSA 208 (41.9%) followed by North region 96 (19.4%). Other study in KSA found that 70.4% from the Central Saudi Arabia, 19.2% (Western) and 10.4% from Eastern region [12]. In other study found that 34% of the Saudi participants were between 34 - 51 years old [13]. Other study in KSA revealed that about 50% of participants their ages was between 18 and 25 years [12, 14]. Other studies done in KSA and Norway found the same percentages of the age of participants [15, 16]., but study done in USA differ from us [17]. Most of responders aged > 40 years (52.63%), followed by 26-40 years old (42.1%), 15-25 years old (5.3%) [18]. Similar results showed that 24.3%, 16.9% and 6.9% of participants their ages ranged from 26-35, 36-45 and 46-55 years old respectively [14].

In this study the level of education of the participants was varied, most of them from university level 364 (73.4%) followed by secondary level education 75 (15.1). Other study in Saudi Arabia (2019) found that about 48.5%, 34.5% & 11% of participants from university, high school & primary school level respectively [13]. Other study in KSA reported that most of participants from university degree (66.2%), followed by high school diploma (21.7%) and intermediate degree (1.4%) [18]. Study of Abougalambou showed that 72.2%, 24.3% of participants with university degree and high school respectively [12]. Other recent study in KSA 2020 said that university students were the main contributors to this study (91.1%), but postgraduate students only 8.9% [14].

Table 1 describes the participant knowledge's about painkiller either analgesic or anti-inflammatory. About 93.3% knew what are analgesic and anti-inflammatory and their source of knowledge mainly from physician (49.2%) followed by leaflet (36.7%), university subjects (32.7%), pharmacist (29%). About 19.8% of participants didn't ask the physician or pharmacist about drugs. Other study in KSA revealed that 86% & 70% received information about NSAIDs from physician & pharmacist respectively while 22% did not receive. About 25.5% were counseled by a healthcare provider on the risks of NSAIDs. Most of participants 94% and 90.5% agreed that physicians and pharmacists respectively should play an essential role in providing information regarding side effects of NSAIDs to their patients [13]. Other study

stated that they received information about analgesics from physician or pharmacist (68.1%), TV, radio, social media (12.2%), parents and friends (19.3%) [14]. More than 30% of Saudi participants took their information from physicians and 20% from pharmacists [12], which indicate great knowledge about the rational use of NSAIDs by comparing to an Indian study which did not ask the physician or pharmacist for using NSAIDs [19].

Our study showed that 62.7% of participants didn't have enough information about analgesics and anti-inflammatory, and only 8.1% didn't read the leaflet about the drugs. While the study done recently in KSA, stated that their participants had adequate knowledge and awareness about analgesic doses [14].

The current study revealed that the most analgesics used were Panadol (71%), Brufen (25%), Panadol Plus (22.6%) and Diclofenac (12.3%), but low percentages who used Aspirin (6%) and Ketofan (0.2%) (Figure 1). Other study in KSA are similar to our finding that the most commonly used drug was paracetamol (77.3%) and 95.7% of the participants use it only when needed, but 4.3% use it regularly. About 17.7% & 1.8% who used ibuprofen & aspirin respectively [14]. Also, other study agreed with us [15, 16, 20]. Other research found that Ibuprofen (23.5%) was the most frequently prescribed drug, followed by celecoxib (20%) and naproxen (14.1%) [21]. Previous study found that 3.2% of participants received aspirin more than 6 tablets per day, while 1.5% & 6.1% used 6 tablets for per day and less than 6 tablets per day respectively. Also, they showed that 19.9% of participants received ibuprofen less than 4 tablets per day, while 6.8% & 1.3% used 1-2 tablets for every 4-6 hours and more than 4 tablets per day respectively [14]. In KSA, about 39.8% used Panadol and voltaren 50mg, 11% used Panadol and brufen 400 mg and ponstan, 12% used Panadol and brufen 600 mg and voltaren 50 mg, 2% used Panadol and olfen 100 mg and celebrix 100 mg, 3% used Panadol and brufen 600mg and celebrix 100 mg, 4.4% used Tylenol and tramadol 50 mg and celbex 100 mg [18]. Other study in KSA found that 61.9%, 29.4% and 10.9% of participants used ibuprofen, diclofenac and aspirin high dose. Paracetamol was the first drug choice to relief the pain (86.9%) followed by ibuprofen (20.9%) and diclofenac (8.5%) [12].

In this study, most participants (67.1%) used analgesic for treatment of headache, followed by 45% used it in toothache & high temperature, followed by 31-37% used in treatment of Arthritis, Influenza & Sore Throat and about 25.8% used in menstruation pain (Figure 2). Other study said that NSAIDs were prescribed in 38.5% of patients [21].

In our study, some Side effects were happened upon chronic use of painkiller such as stomach pain (45%), Kidney (31.5%), stomach ulcer & pulse disturbance (17.9%), hypertension (8.1%) and foot edema (3.8%). About 28.2% prefer to use herbal medicine as analgesic and 23.6% sometimes used while 48.2% did not prefer to use as analgesic (Figure 3). Other study in United States demonstrated that among 18 studies showed that 8 studies regarding three NSAIDs (celecoxib, etoricoxib, and diclofenac) demonstrated hepatotoxic effect which is demonstrated by elevation of liver enzymes (ALT & AST). Diclofenac had the highest proportion followed by celecoxib and etoricoxib [22]. Recent study in KSA stated that 72% of participants thought that over use of paracetamol can lead to liver failure. Also, they said that 47.2% & 65.1% knew that paracetamol have side effects and had contraindications respectively [14]. Other study showed that patients had lower clinical manifestation who used aspirin either alone or combined with other NSAIDs. NSAIDs can cause morbidity in some patients such as changing of bowel motion, profuse diarrhea, inflammatory bowel disease, or chronic blood loss with iron deficiency anemia. The pathogenesis is thought to be related to inhibition of prostaglandin synthesis with direct effect of drugs or its metabolites. The high prevalence of aspirin and other NSAIDs use suggests that adverse effects on GIT [4]. About 41.7%, 63.7% & 46.1% had an idea about side effects of ibuprofen, thought of causing stomach ulcers & had contraindications respectively [14]. From 1-2% of patients who used NSAID had GIT complications. This might be due to other factors such as old age (>65 years), concomitant use of aspirin or anticoagulant, history of peptic ulcer in addition to the dose and type of NSAID. There was an evidence suggests that NSAIDs increase the risk of lower GI bleeding similar to upper GI tract. The use of selective cyclooxygenase-2 inhibitors gave the same favorite effects as nonselective NSAIDs but with less GI toxicity either in lower or upper GIT [23]. About 43.3%, 57.1% & 61.2% had an idea about side effects of aspirin, thought of causing bleeding & had contraindications respectively [14]. More than 50% claimed that information about side effects of NSAIDs might lead them to discontinue their medication. More than 33% of respondents stated that their healthcare setting provided them with insufficient knowledge about the side effects of painkillers [13]. About 40% of patients knew that that NSAIDs had side effects and 14.9% suffer from these side effects [12].

Table 2 showed that the knowledge of participants about their painkiller usages in KSA. Approximately 88% of participants did not use other drugs to treat other diseases in addition to analgesics or anti-inflammatories. While, 78.5% who used only one analgesic drug and the rest of participants used 2 or 3 drugs. The rate of using analgesics was varied, 3.8% used analgesic daily, 14.3% used it weekly and

81.9% used it monthly. Study done in KSA found that 50% of participants received 1-2 tablet every 4-6 hours while 2.3% receive more than 8 tablets within 24 hours [14]. Other study also in KSA showed that 54% did not use painkillers daily, whereas 43.3% took painkillers daily; 2.26% did not use at all. About 87% used analgesic from 1-3 tablets daily & 11.4% used from 4-7 tablets daily [18].

Some of our participants have chronic diseases such as diabetes (5.6%), hypertension (3.8%), kidney & heart diseases (1%), liver diseases (0.6%), while 84.1% did not have any disease. In our study we found that 17.1% of participants had bone disease and they used analgesics and anti-inflammatory, while 3% who had bone problems but not used analgesics. Other recent study in Saudi Arabia said that 57.8% of participants suffering from chronic diseases [18]. Our study demonstrated that female participants have menstruation pain and they used from 1-3 tablets /day (10%), and others used from 1-4 tablets/week (17.2), while others who had pain but not used analgesics (23.3%). About 50% did not have menstruation pain and so, did not use analgesics.

Table 1: Numbers and percentages of participants knowledge about analgesics and NSAIDs in KSA. (n= 496).

Questions	n (%)					n (%)				
	Do you know what are analgesic and anti-inflammatory ?	YES 463 (93.3)					NO 33 (6.7)			
Source of knowledge's	physician 244 (49.2)	pharmacist 144 (29)	School or university 162 (32.7)	Home 91 (18.3)	leaflet 182 (36.7)	advertisements 107 (21.6)	Others 83 (16.7)			
Do you have enough information about analgesics?	YES 119 (24)			NO 311 (62.7)			Don't know 66 (13.3)			
	YES 206 (41.5)			NO 40(8.1)			Sometimes 250 (50.4)			
Do you read leaflet about usage of analgesic?	YES 204 (41.1)			NO 98 (19.8)			Sometimes 194 (39.1)			
	Aspirin 30 (6)	Brufen 124 (25)	Panadol 352 (71)	Panadol Plus 112 (22.6)	Diclofenac 61 (12.3)	Ketofan 1 (0.2)	Others 68 (13.7)			
Do you know these Side effects upon chronic use of Painkiller?	Stomach pain 223 (45)	Stomach Ulcer 89 (17.9)	Kidney 156 (31.5)	Foot Edema 19 (3.8)	Hypertension 40 (8.1)	Pulse disturbance 89(17.9)	None 183 (36.9)			
	Headache 333 (67.1)	Arthritis 154 (31)	Sore throat 184 (37.1)	Influenza 186 (37.5)	High temp. 223 (45)	Toothache 224 (45.2)	Menstruation pain 128 (25.8)	Kidney 23 (4.6)	Bile pain 13 (2.6)	
Do you prefer herbal medicine as analgesic?	YES 140 (28.2)			NO 239 (48.2)			SOMETIMES 117 (23.6)			

Values expressed as numbers (n) and percentage (%)

Table 3 showed that very small number of participants with simple liver disease (0.6%), 4.2% with simple kidney diseases and 1.8% with simple heart diseases. The rate of using analgesic in patients with liver, kidney, heart diseases were 7.2% , 6.2%, 5.4% (1-2 tablets/day) respectively and 5.4% , 3.8%, 3.8% (1-2 tablets/week) respectively, 18% , 12.1%, 8.8% (1-2 tablets/month) respectively and 6% , 4.4%, 4.6% (>3 tablets/month) respectively (Figure 4). Recent study done in KSA, said that they use paracetamol 1-2 tablets every 4 to 6 h daily which is safe dose is safe according to the NHS

recommendations. The same usage was for the aspirin and ibuprofen daily doses [14]. Other study in Saudi Arabia said only 45% of the participants used NSAIDs daily, while others (38%) only used NSAIDs as needed. About 36.5%, 34.5% and 15.5% of patients took NSAIDs once daily, twice daily or three times per day respectively and only 21% of patients received NSAIDs before meal [13]. Receiving any dose of NSAIDs for one week, one month, or more than a month was associated with an increased risk of myocardial infarction. The use of NSAIDs for 1-7 days might increase the risk of myocardial infarction (92% for celecoxib, 97% for ibuprofen, and 99% for diclofenac, naproxen, and rofecoxib) [24]. Using of NSAIDs such as diclofenac, ibuprofen, indomethacin, ketorolac, naproxen, nimesulide, piroxicam and two COX 2 inhibitors (rofecoxib & etoricoxib in preceding 14 days was found to increase of risk of hospital admission for heart failure with a 19%, while there was no evidence that celecoxib at commonly used doses cause heart failure. [25].

Table 2: Numbers and percentages of participant knowledges about the use of analgesics and NSAIDs in KSA. (n= 496).

Questions	n (%)					n (%)	
Do you use other drugs with analgesic or anti-inflammatory?	YES					NO	
	57 (11.5)					439 (88.5)	
2- Do you use more than one analgesic?	YES (2-3 drugs)					NO (only one)	
	107 (21.6)					389 (78.4)	
3-The rate of using analgesic	Daily		Weekly			Monthly	
	19 (3.8)		71 (14.3)			406 (81.9)	
Do you have chronic diseases?	Diabetes	Kidney	Liver diseases	Hypertension	Heart diseases	Other diseases	None
	28 (5.6)	5 (1.0)	3 (0.6)	19 (3.8)	4 (1.0)	40 (8.1)	417 (84.1)
Do you have bone problems? Do you use analgesic?	YES, I use analgesic			YES, I don't use analgesic		NO, I don't use analgesic	
	85 (17.1)			15 (3.0)		396 (79.8)	
Do you have menstruation pain? Do you use analgesic?	YES, 1-3 or > 3 tab / day		YES, 1-3 or > 3 tab / week		YES, I don't use analgesic		NO, I don't use analgesic
	41 (10)		71 (17.2)		96 (23.3)		204 (49.5)

Values expressed as numbers (n) and percentage (%)

Table 3: Numbers and percentages of participants knowledge about the rate of using analgesics and NSAIDs in patients with liver, heart or kidney diseases in KSA. (n= 496).

Questions	n (%)						n (%)			
	YES, Simple			YES, Acute			YES, Chronic			NONE
Do you have liver diseases? What is the degree of infection?	3 (0.6)			0 (0.0)			0 (0.0)			493 (99.4)
Do you have kidney diseases? What is the degree of infection?	21 (4.2)			0 (0.0)			5 (1.0)			470 (94.8)
Do you have heart diseases? What is the degree of infection?	9 (1.8)			0 (0.0)			0 (0.0)			485 (97.8)
The rate of using analgesic in patients with: A-B-C	1-2 tab / day	3tab / day	> 3 tab / day	1-2 tab / week	3tab / week	> 3 tab / week	1-2 tab / month	3 tab / month	> 3 tab / month	None
Liver diseases	36 (7.2)	8 (1.6)	3 (3.6)	27 (5.4)	10 (2.0)	7 (1.4)	89 (18.0)	15 (3.0)	30 (6.0)	271 (54.6)
Kidney diseases	31 (6.2)	6 (1.2)	3 (0.6)	19 (3.8)	10 (2.0)	4 (0.8)	60 (12.1)	13 (2.6)	22 (4.4)	328 (66.1)
Heart Diseases	27 (5.4)	4 (0.8)	4 (0.8)	19 (3.8)	7 (1.4)	4 (0.8)	44 (8.8)	11 (2.2)	23 (4.6)	353 (71.2)

Values expressed as numbers (n) and percentage (%)

Figure 1: Answers of patients (%) about is the most analgesic you used.

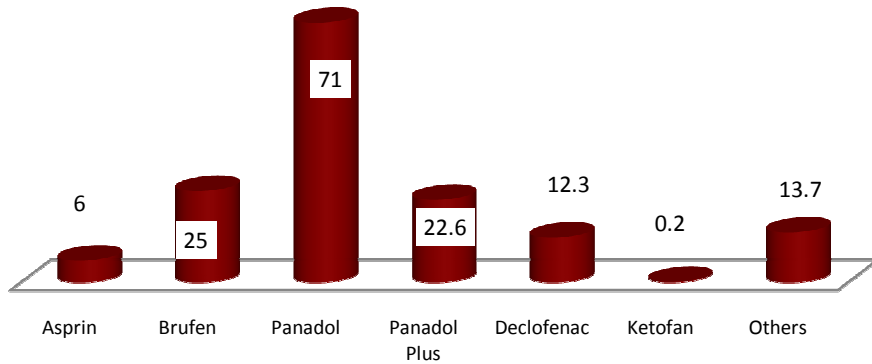


Figure 2: Answers of patients (%) about uses of analgesics.

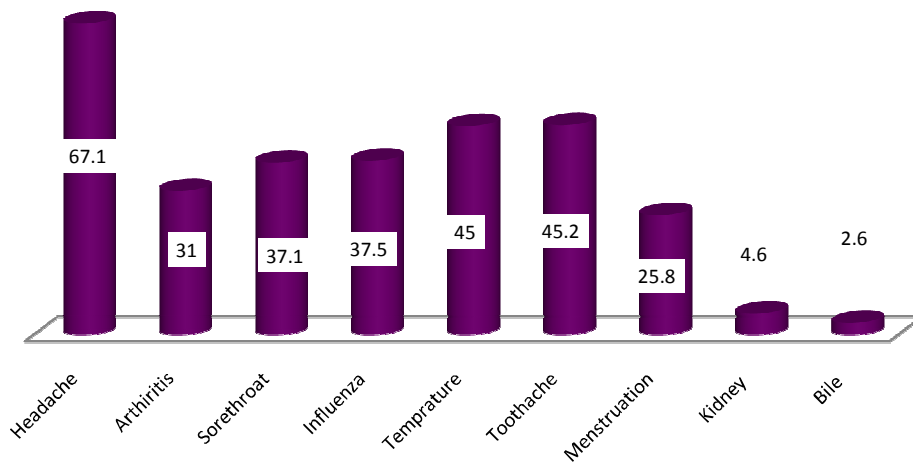
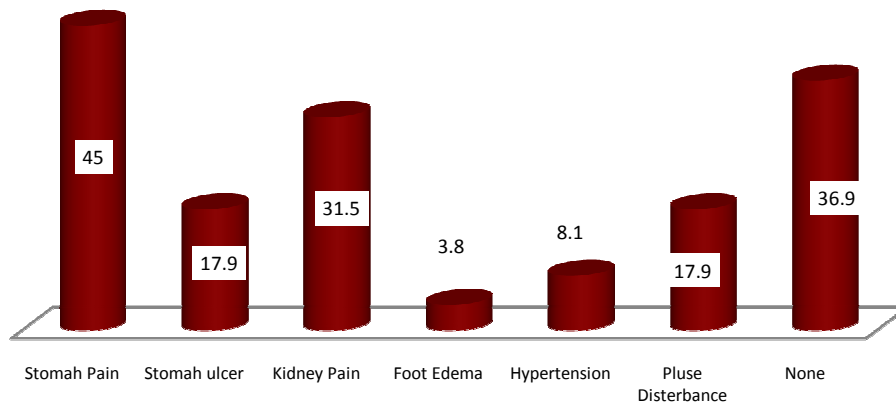
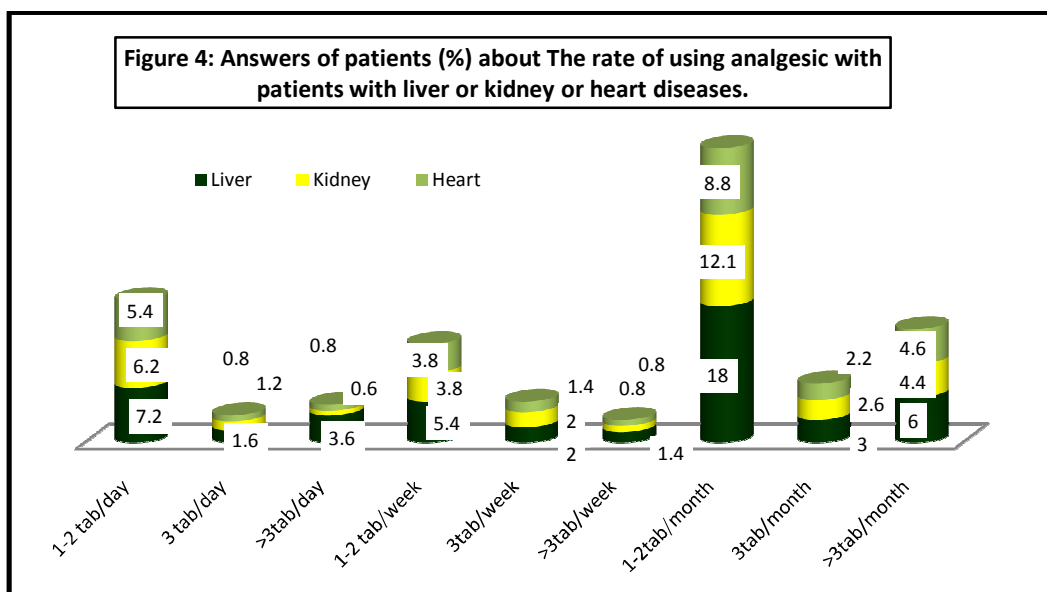


Figure 3: Answers of patients (%) about adverse effects of using analgesics.





CONCLUSION

From our results we can conclude that there was a high utilization of NSAIDs with Saudi population especially paracetamol. We should target public awareness health education campaign about the use of analgesics. and future studies should be conducted. Activation of an electronic tracking system will help in observation of an inappropriate medications prescription and dispensing by health professionals which can be a major factor in the over and misuse of those medications. Future studies should focus on improving the people awareness of self-medication and proper use of medications.

REFERENCES

- Ascherio A, Schwarzschild MA. The epidemiology of Parkinson's disease: risk factors and prevention. *Lancet Neurol*2016; 15:1257-72.
- Shin S, Noh C, Lim S, et al. Non-steroidal anti-inflammatory drug-induced enteropathy. *Intest Res* 2017; 15:446-55.
- Ungprasert P, Cheungpasitporn W, Crowson CS, Matteson EL. Individual non-steroidal anti-inflammatory drugs and risk of acute kidney injury: a systematic review and meta-analysis of observational studies. *Eur J Internal Med.* 2015;26(4):285-91.
- Nimmim AT. Effects of Non-Steroid Anti-Inflammatory Drugs on the Lower Gastrointestinal Tract. *AL-Qadisiyah Medical Journal.*2018;14:60-70.
- Wongrakpanich S, Wongrakpanich A, Melhado K, Rangaswami J. A Comprehensive Review of Non-Steroidal Anti-Inflammatory Drug Use in The Elderly Aging and disease.2018;9:143-150.
- Asghar W, Jamali F. The effect of COX-2-selective meloxicam on the myocardial, vascular and renal risks: a systematic review. *Inflammo-pharmacology.* 2015;23(1):1-16.
- Zhang X, Donnan PT, Bell S and Guthrie B. Non-steroidal anti-inflammatory drug induced acute kidney injury in the community dwelling general population and people with chronic kidney disease: systematic review and meta-analysis *BMC Nephrology.* 2017 volume 18, Article number: 256
- Sondergaard KB, Weeke P, Wissenberg M, Olsen A-MS, Fosbol EL, Lippert FKTorp-Pedersen, C, Gislason, GH & Folke, F. Non-steroidal anti-inflammatory drug use is associated with increased risk of out-of-hospital cardiac arrest: a nationwide case-time-control study. *European Heart Journal - Cardiovascular Pharmacotherapy.* 2017;3(2):100-107. <https://doi.org/10.1093/ehjcvp/pvw041>
- Imani F, Motavaf M, Safari S, Alavian SM. The Therapeutic Use of Analgesics in Patients with Liver Cirrhosis: A Literature Review and Evidence-Based Recommendations. *International monthly journal in the field of hepatology.* 2014 .14(10)
- Wong, R.S.Y. (2019). Role of Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) in Cancer Prevention and Cancer Promotion. *Advances in Pharmacological Sciences* Volume 2019, Article ID 3418975, 10 pages, <https://doi.org/10.1155/2019/3418975>
- AlKhamees O.A., AlNemer, K.A., Maneea, M.W. Faisal A. AlSugair F.A., AlEnizi, B.H., Alharf, A.A. (2018). Top 10 most used drugs in the Kingdom of Saudi Arabia 2010-2015. *Saudi Pharmaceutical Journal* 26 : 211-216
- Abougambou S.S.*, Abdoun, S.A., and Alharbi N.S. (2019). Awareness of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) use among population in Saudi Arabia *OJPSR:* April-2019: Page No: 40-52
- Babelghaith SD, Alarifi MN, Wajid S, Alhawassi TM, Alqahtani SK, Alghadeer SM.(2019). Knowledge of patients on safe medication use in relation to nonsteroidal anti-inflammatory drugs. *Saudi J Anaesth.* 13:106-11.

14. Amal I. Siddig, Abdulhadi M. Alqahtani , Alia AlShalawi, Marwah Turkistani, Sarah Binbaz and Amal Altowairqi (2020). Awareness of analgesics complications in Saudi Arabia: a cross-sectional study. *Future Journal of Pharmaceutical Sciences* 6:6, 1-6. <https://doi.org/10.1186/s43094-020-0018-5>
15. Karami NA, Altebainawi AF, Alfarki SA et al (2018). Knowledge and attitude of analgesics use among Saudi population: a cross-sectional study. *Int J Med Sci Public Health* 7(2) <https://www.scopemed.org/?mno=1003629>
16. Dale O, Borchgrevink PC, Fredheim OM, Mahic M, Romundstad P, Skurtveit S et al (2015). Prevalence of use of non-prescription analgesics in the Norwegian HUNT3 population: impact of gender, age, exercise and prescription of opioids. *BMC Public Health* 15:461
17. Palos GR, Mendoza TR, Cantor SB, Aday LA, Cleeland CS (2004) Perceptions of analgesic use and side effects: what the public values in pain management. *J Pain Symptom Manag* 28:460–473
18. Bahdailah, A.A. (2019). Pattern use of Non-steroidal Anti-inflammatory Drugs among Saudi Community: Patients' Perspective. *PTB Reports*, Vol 5, Issue 2, May-Aug, 2019.
19. Gopal K, Rani V, Ganesh S, et al. 2010. Awareness of the adverse effects of NSAIDs among its buyers from community pharmacies. *Journal of pharmacy research*. 3:2890-2893.
20. Sarahroodi S, Maleki-Jamshid A, Sawalha AF, Mikaili P, Safaeian L (2012). Pattern of self-medication with analgesics among Iranian university students in Central Iran. *J Family Community Med* 19:125–129
21. Mazhar F, Haider N, Sultana J, Akram S, Ahmed Y.(2018). Prospective study of NSAIDs prescribing in Saudi Arabia: Cardiovascular and gastrointestinal risk in patients with diabetes mellitus. *Int J Clin Pharmacol Ther*. 56(2):64-71. Doi: 10.5414/CP203071.
22. Sriuttha, P Buntitabhon Sirichanchuen, and Unchalee Permsuwan (2018). Hepatotoxicity of Nonsteroidal Anti-Inflammatory Drugs: A Systematic Review of Randomized Controlled Trials *International Journal of Hepatology* Article ID 5253623, 13 pages <https://doi.org/10.1155/2018/5253623>
23. Sostres, C., Gargallo, C.J. and Lanás, A., Sostres *et al.* (2013). Nonsteroidal anti-inflammatory drugs and upper and lower gastrointestinal mucosal damage. *Arthritis Research & Therapy* 15(3):S3 <http://arthritis-research.com/content/15/S3/S3>
24. Bally, M., Dendukuri, N., Rich, B., Nadeau, L., Helin-Salmivaara, A., Garbe, E., Brophy, J.M. (2017). Risk of acute myocardial infarction with NSAIDs in real world use: 105 Bayesian meta-analysis of individual patient data. *BMJ*,357:j1909 <http://dx.doi.org/10.1136/bmj.j1909>
25. Arfè, A., Scotti, L., Varas-Lorenzo, C., Nicotra, F., Zambon, A., Kollhorst, B., Schink, T., Garbe, E., Herings, B., et al. (2016). Non-steroidal anti-inflammatory drugs and risk of heart failure in four European countries: nested case-control study. *BMJ* 2016;354:i4857 <http://dx.doi.org/10.1136/bmj.i4857>

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