Are Non-steroidal anti-inflammatory drugs prescribed wisely?
(A study on Non-steroidal anti-inflammatory drugs (NSAIDs) misuse in health care setting)

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Abstract: Non-steroidal anti-inflammatory drugs (NSAIDs) a class of drug that prescribed extensively throughout the world to relieve or reduce pain, and their safety profile became of increased concern for a number of years, they have been shown to be associated with increased risk of cardiovascular events and gastrointestinal bleeding, therefore, in 2015, the FDA strengthened the warnings regarding cardiovascular risk with non-aspirin NSAID use based on data collected over the last 10 years.

Aim:
The study is aimed to:

- Study the prevalence of NSAID consumption by Almoosa Specialist Hospital patients and evaluate their awareness about their adverse effects and precautions.
- Identify physician’s major barriers to choose NSAIDs wisely, and accordingly suggest developing a structured evident based pathway to properly prescribe them, and to reduce the demand of risky ones in patients with potential factors to develop adverse events.
- Assess the impact of choosing NSAIDs wisely on patient safety in healthcare setting

Methods:
Cross-sectional survey was distributed to a random sample of adult patients ranging from 35 – 65 years old to assess their knowledge about NSAIDs, and a retrospective, before and after study was conducted to evaluate prescribing pattern of NSAIDs and their related adverse events. Physicians received educations on a standardized evident based pathway to properly prescribe NSAIDs. Prescriptions were collected and analyzed during April to June in 2019 (pre-intervention) and during the July to August in 2019 (post-intervention). The intervention required adherence to the agreed pathway for prescribing. Compliance to that pathway was measured and compared between pre- and post-intervention periods.

Results:
The standardized evident based pathway intervention was associated with a decrease in the proportion of Diclofenac prescriptions (Risky NSAIDs) by 20%, (P= 0.0001). The proportion of Naproxen prescriptions (safe NSAIDs) increased by 500%, (P= 0.35). Admissions due to Kidney related adverse event and gastrointestinal adverse events was decrease from 941 to 593 (37%) and from 1022 to 751 (26.5%), respectively. The result was significant at P= 0.0001 level.

Conclusions:
Standardizing NSAIDs prescribing pattern by formulation of an evident based pathway or flow chart for physicians to properly prescribe NSAIDs, in addition to continues education and monitoring was associated with reduction in consumption of risky NSAIDs (Diclofenac) and increasing the prescriptions of the more safe NSAIDs (Naproxen), consequently, reducing kidney and gastrointestinal related adverse events.

Keywords: NSAIDs is Non-steroidal anti-inflammatory drugs.
1. INTRODUCTION

It is becoming increasingly alarming to ignore over prescribing and misuse of Non-steroidal anti-inflammatory drugs that has been widely observed as a common prescribing behavior in healthcare setting.

NSAIDs are one of the most frequently prescribed drugs globally as a pain reliever management in variety of Disease especially in Rheumatoid Arthritis (RA) and Osteoarthritis (OA) (4-5)

They inhibit cyclooxygenases enzyme pathway to decrease pain, fever, and inflammatory reactions (1-2)

NSAIDs can be the source of harm for patients. As the inhibition of these enzymes affects gastrointestinal, cardiovascular and renal function, additionally, they can cause other problems such as hepatotoxicity (6).

Noting that the safety profile of NSAIDs becomes questionable since rofecoxib and valdecoxib were removed from market earlier 2005 because of the cardiovascular related adverse effects (7-8).

In fact, a lot of studies and researches showed these drugs are the highest reason for patient’s hospitalizations due to side adverse effects.

NSAIDs related adverse events have been explored in several studies, such as that conducted by American Geriatric Society, American College of Rheumatology, and the European League Against Rheumatism, showed that they recommend using NSAIDs with caution and limit their use to the lowest effective dose and shortest duration. They recommend that, when used, gastrointestinal, renal and cardiovascular side effects should be routinely monitored. (9-10-11)

The adverse events rate among Diclofenac initiators increased by 50% compared with non-initiators (12). And COX-2-selective inhibitors and ibuprofen usage are associated with the highest risk of congestive heart failure, whereas naproxen was associated with a lower risk (13).

So far, little attention has been paid to improve physician’s awareness about what appropriate NSAIDs to choose for their patients (3-4).

It is not yet clear for the prescribers what is the safest NSAIDs for their patients, as not all NSAIDs carry the same risk.

It is still challenging for the prescribers to know how to co relate the appropriate NSAIDs versus patient risk factors, for instance and not limited to, gastrointestinal, cardiovascular, kidney and hepatic.

This indicate the need to develop a structured evident based pathway to guide physicians in choosing NSAIDs wisely.

This study provide an exciting opportunity to advance physicians knowledge to link risk levels of different NSAIDs with patient risk factors. However, community awareness in regard NSAIDs safety concerns is still an opportunity for improvement, as they assume that because these drugs are sold over the counter that they are completely safe, therefore, authors recommended a doubled effort at education regarding NSAIDs safety concerns to community population.

The aim of this project is to:

✔ Study the prevalence of NSAID consumption by Almoosa Specialist Hospital patients and evaluate their awareness about their adverse effects and precautions.

✔ Identify physician’s major barriers to choose NSAIDs wisely, and accordingly suggest developing a structured evident based pathway to properly prescribe them, and to reduce the demand of risky ones in patients with potential factors to develop adverse events.

✔ Assess the impact of choosing NSAIDs wisely on patient safety in healthcare setting

2. METHOD

A retrospective, before and after study was conducted in which the prescribing pattern of NSAIDs and their related adverse events was compared in periods before and after implementing the intervention.

The study was carried out in out-patient pharmacy in Almoosa specialist hospital, Saudi Arabia, 240 beds, data were collected from April to September 2019.
NSAIDs prescriptions were observed, measured and analyzed from the clinics where the trend of prescribing NSAIDs is usually high and for long period of time, there for those clinics were selected for this purpose, clinics that prescribe NSAIDs for ≤ one week were not included in the study.

To assess patient prevalence on NSAIDs and their awareness about its adverse effects, a cross sectional survey was distributed to a random sample of adult patients ranging from 35 – 65 years old , survey was done by chief medical officer and chief pharmaceutical officer and was conducted by our colleague in pharmacy department, the questionnaire is designed to answer 10 questions regarding knowledge of patients about NSAIDs, its side effects, duration, source of acquiring (over the counter- OTC versus prescription), the reason behind use, and the frequency.

Face to face Interviews were conducted for physicians where they have been asked to explain their rational behind prescribing NSAIDs inappropriately. Then they have been engaged to agree on a structured evident based pathway or flow chart that guide all prescribers in selecting the appropriate NSAIDs.

Ultimately, a Flow chart has been developed to facilitate and optimize NSAIDs prescribing (figure 1) and has been communicated to all prescribers through several educational sessions conducted by both chief medical officer and chief pharmaceutical officer.

A dashboard has been created to facilitate data collection in order to monitor any changes in physician's prescribing pattern.

Prescriptions were evaluated and analyzed along with the agreed evident based flow chart (figure 1).

However, there are challenges that necessitate additional efforts in order to achieve and sustained the optimum outcome such as:

The new hired physicians won’t be aware about the standardized hospital pathway in prescribing NSAIDs which requires continuous educational activities.

NSAIDs being an over the counter drugs without any level of restriction necessitates extra efforts for community education.

In addition to that, supportive Information technologies with advanced capabilities for data collection is very essential.

Statistical analysis:

Data were analyzed using SPSS version 26.0 and t-test result was significant as described in result section.

3. RESULT

One hundred percent of those surveyed patients indicate that they use NSAIDS as shown in graph 1.

The pie chart (graph 2) below shows that 57% of patient gets their NSAIDS from doctor office. The majority of participants indicates that they are using NSAIDs either daily or weekly (43% and 37% respectively), graph 3.

Almost two-third of the participants (60%) using it continuously more than 2 months (graph 4).

When participants were asked about the reason behind their use of NSAIDs, almost more than one third indicates that they are using it for occasional headache (44%), graph 5.

Participants are familiar only with two types of NSAIDs Diclofenac and Coxib (60% and 40% respectively) which considered risky NSAIDs as shown in graph 6.

It is apparent from graph 7 that low percent of the participants are aware about side effects (27%).

Graph 8 showed that most of them are taking NSAIDs without food (60%).

The overall response to this questionnaire indicate lack of awareness about NSAIDs safety profile.
Graph 1: NSAIDs Consumption
- 93% Active Pain
- 7% Prophylactically

Graph 2: SOURCE OF PAINKILLER
- 43% OTC
- 57% Physician

Graph 3: Frequency
- 10% PRN
- 43% Daily
- 37% Weekly
- 10% Monthly

Graph 4: Duration
- 40% Continuously
- 60% Intermittently

Graph 5: Reason of Consumption
- 44% Headache
- 37% Knee pain
- 13% Back pain
- 3% Neck pain
- 3% Post surgery

Graph 6: Most Commonly Used
- 40% Diclofenac
- 60% Coxib
After Physicians interview, it was clear that some felt that they are not aware about risk differences among NSAIDs, while other considered that it is patient preference, but all agreed that NSAIDs has been misused and a structured flow chart will help optimizing the prescribing pattern.

The results obtained from the preliminary analysis are shown in the graph below.

During the period of first quarter of the study, before implementing the standardized pathway that guides NSAIDs prescribing, 23% of all prescriptions in Almoosa Specialist Hospital containing one or more NSAIDs. Among this, Diclofenac prescriptions contribute to 30% and Naproxen prescriptions contribute to one percent.

After the intervention, education on the agreed pathway of NSAID prescribing, implementing it and monitoring, results shows,

Significant \( p = 0.0001 \) reduction (20%) in Diclofenac prescribing as shown in graph 9, graph 10 shows clear significant trend \( p = 0.35 \) of increasing (500%) in Naproxen prescribing (the more safe NSAIDs).

This indicate that there is increase in awareness about the safest NSAIDs between pre and after the intervention.

The more surprising part in this data is that kidney and GI related adverse event admissions is decreased as shown in the below graph 11.
The result is significant at \( P = 0.0001 \) level.

### Admission Related Events

<table>
<thead>
<tr>
<th></th>
<th>Kidney</th>
<th>GI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q 2 - 2019</td>
<td>941</td>
<td>1022</td>
</tr>
<tr>
<td>Q 3 - 2019</td>
<td>593</td>
<td>721</td>
</tr>
</tbody>
</table>

#### Graph 11

**Want to prescribe NSAID for > 1 week?**

**You must**

1. **Assess CV Risk**
   - Is patient on ASA 81mg?
     - **No**
       - Low CV risk patient
     - **Any doubt?**
       - Refer to cardiologist for risk assessment
     - **Yes**
       - High CV risk patient

2. **Assess GI Risk**
   - According to:
     - Age > 65 years
     - History of uncomplicated ulcer
     - Concomitant ASA (Not as cardiac protector)
     - Concomitant Clopidogrel
     - Concomitant Cortisone
     - Positive H. Pylori
   - **Low GI risk**
     - No Risk factor
   - **Medium GI risk**
     - \( \leq 2 \) Risk factors
   - **High GI risk**
     - 3 Risk factors
     - Or concomitant steroid
     - Or Anti-Coagulant
     - Or History of complicated ulcer
   - Any doubt?
     - Refer to cardiologist for risk assessment
3. Ensure:

- Baseline Scr. and every 3 months
- Consider Drug-Drug interaction e.g. if concomitant steroid, anti-coagulant
- If known CKD and/or concomitant ACEI, ARBs, Diuretics, use with caution only Naproxen or Ibuprofen
4. DISCUSSION

An initial objective of the project was to improve physician’s awareness and to optimize NSAIDs prescribing in health care setting.

The current study found that, focusing on improving physician’s awareness in regards safety profile of NSAIDS help in optimizing their prescribing pattern, and so cardiovascular, kidney and gastrointestinal related adverse events can be mitigated.

This fact was one of the most important clinically relevant finding in this study, even though, this result needs to be interpreted with caution, as it is important to bear in mind the possible other contributing factors in these responses.

However, this result agree with the finding of the study conducted by Gooch et al. which highlighted that NSAID’s effects during the progression of Chronic Kidney Disease(CKD) in geriatric population(4). The conclusion was that high cumulative NSAIDs taken by patients is linked to increase CKD progression.

Concerning the acute kidney injury (AKI) and the use of NSAIDs use in geriatric population, Kate et al. design an AKI hospitalization model where he discovered that NSAIDs and diuretics can predict acute kidney injury (6-7).

The American Geriatric Society updated the Beers Criteria in 2015. The recommendation was that the continuous us of all NSAIDs, including high dose aspirin, should be avoided because of the risk of gastrointestinal bleeding. High-risk groups include: age above 75 years, corticosteroid use, current use of anticoagulants or antiplatelet agents “quote” (14)

A case-control study was done by Page et al. In geriatric population that they were initially hospitalized due to congestive heart failure. The study addressed patients with NSAIDs (all NSAIDs other than low dose aspirin) and patients with no NSAIDs prescription. The patients under NSAIDs had increased risk of hospital admission due to congestive heart failure (OR 2.1, 95% CI 1.2-3.3) (4)

The scope of this study was limited to only prescribed NSAIDs by doctors and not over the counter demand by patients, future research should therefor concentrate on control the misuse of NSAIDs in absence of prescription, that dispensed over the counter.

5. CONCLUSION

There is limited knowledge about NSAIDs safety and side effects among Almoosa Specialist Hospital adult population, so healthcare professionals and patients should receive proper education regarding the benefits and risks of NSAIDs, particularly in individuals who are, or may be, susceptible to gastrointestinal, cardiovascular side effects or kidney impairment to be able to tailor a patient’s risk factors versus appropriate NSAIDs.

The present study proved that the effect of improving physician’s awareness improve appropriate NSAIDs prescriptions, and the results are significant in decreasing the prescriptions of the risky NSAIDs (Diclofenac) and increasing the prescriptions of the safe one (Naproxen), consequently, reducing kidney and gastrointestinal related adverse events.

The results of the study provide valuable information to scholars, practitioners, and policy makers.

More research needed to better improve awareness among the population in order to mitigate the high demand of over the counter NSAIDs.

ACKNOWLEDGEMENT

The authors are grateful for help from the pharmacists Rasha, Howeda, Bushara, hospital Pharmacists, Almoosa Specialist Hospital for collecting data during the course of this project, and for Mona, Head of physical therapy department Almoosa Specialist Hospital for her support in communication with journals and finalizing the paper.

Compliance with Ethics Guidelines

Not required, as this article does not contain any studies or interventions with human participants or animals performed by any of the authors.

Conflict of interest

There is no conflict of interest.
REFERENCES


