WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES
SJIF Impact Factor 7.632
Volume 8, Issue 12, 28-37 Research Article ISSN 2278 – 4357

AWARENESS OF INTERACTIONS OF NSAIDS WITH SOME DISEASES AMONG PHARMACISTS IN KHARTOUM STATE

[1]*Fahad Gasim Alsiddig Alabass, [2,3]Ahmed Mustafa Khidir and [3]Ali Awad Allah Ali Moh. Saeed

[1]College of Post Graduate Study, University of Medical Sciences and Technology.
[2]Pharmaceutics Department Graduate Study Omdurman Islamic University.
[3]Faculty of Pharmacy, National University.

Article Received on
25 Sept. 2019,
Revised on 15 Oct. 2019,
Accepted on 05 Nov. 2019
DOI: 10.20959/wjpps201912-14881

***Corresponding Author**
Fahad Gasim Alsiddig Alabass
College of Post Graduate Study, University of Medical Sciences and Technology.

ABSTRACT

Introduction: Drug- Disease interactions may cause deterioration in the patient's clinical status, resulting in additional treatment, hospitalization, and/ or an extended hospital stay. NSAIDs inhibit the enzymatic production of prostaglandins. In Sudan and prescribing are more than other drugs or may be used routinely by more patient by them self without sufficient know –how the effect of (NSAIDs) if they have other diseases e.g., Asthma, gastrointestinal upset (peptic ulcer). **Objectives:** To assess the extent of awareness of drug-diseases interactions of NSAIDs among Pharmacists and Doctors in Khartoum state pharmacies and hospitals. **Materials and methods** this study was conducted in Khartoum state pharmacies and hospitals during the period of May to 15Th October 2011, it is cross-sectional study. **Sample size** 120 of pharmacists and 50 doctors working in Khartoum state hospitals will be selected randomly. Structured pre tested questionnaire will be developed to collect the data. Moreover, the information was collected from books, international journals. BNF and scientific websites. The analyzing of data using SPSS program. **Results:** 76% of doctor expected that there will be drug-drug or drug-disease interaction between asthmatic patients and NSAIDs. 75.5% from the pharmacists stated that NSAIDs may interact with asthmatic patients by worsening the asthma. 91.67% of doctors expected that there will be drug-disease interaction between ulcerative patients and NSAIDs. 88% stated that the interaction by increasing gastric acid secretion and worsening of the ulcer in these patients. 55.5% from the doctors did not ask the patients about the period of using NSAIDs when they come to take NSAIDs. **Conclusion:** More than half of the practicing

pharmacists and medical doctors are aware about the interaction between NSAIDs and asthma, hypertension and patients having ulcer. Unfortunately in spit of that, they dispense and prescribe NSAIDs to these patients respectively. Half of the doctors did not ask the patients about the period of using NSAIDs when they come for treatment. Half of the pharmacists are reluctant to ask the patients about the medical history when they are taking NSAIDs.

KEYWORDS: Interactions, NSAIDS with Diseases.

INTRODUCTION

Drug interaction occurs when the actions of one drug (victim, object, and substrate) are altered by the presence of another drug (perpetrator, precipitant, interacting drug). The alteration can result in decreased efficacy (even therapeutic failure) or increased pharmacodynamics effects causing adverse drug events (ADE). Clinicians and pharmacists must be aware of Drug- Disease interactions possibility and use their best judgment when prescribing or assessing drug therapy. The effects of moderate interaction may cause deterioration in the patient's clinical status, resulting in additional treatment, hospitalization, and/ or an extended hospital stay. The effect of a major interaction are potentially life threatening or can lead to permanent damage. In addition to be clinically significant, the interaction must be reasonably documented in the literature (suspected, probable or established). Pharmacodynamics interactions include those that result in additive or antagonistic pharmacological effects. Pharmacokinetic interactions include induction or inhibition of metabolizing enzymes in the liver or elsewhere, displacement of drug from plasma protein binding sites, alterations in gastrointestinal tract absorption, or competition for active renal secretion. The frequency or prevalence of interactions is dependent upon the number of concomitant medication and the complexity of the regimens. The prevalence is also dependent upon other variables such as patient adherence, hydration and nutritional status, degree of renal or hepatic impairment, smoking, and alcohol use, genetics and drug dosing. Additionally some patients may exhibit evidence of a particular drug interaction, while others with the same drug combination do not.[1] As far as we know this is the first study that was conducted in Sudan to evaluate the interaction between NSAIDs with some diseases' and the awareness of pharmacist and medical doctors about this interaction because of the importance of these interactions.

Nonsteroidal Anti-Inflammatory Drugs

Salicylates and other similar agents used to treat rheumatic disease share the capacity to suppress the signs and symptoms of inflammation. Although all NSAIDs are not approved by the Food and Drug Administration (FDA) for the whole range of rheumatic diseases, all are probably effective in rheumatoid arthritis, seronegative spondyloarthropathies (e.g., psoriatic arthritis and arthritis associated with inflammatory bowel disease), osteoarthritis, localized musculoskeletal syndromes (e.g., sprains and strains, low back pain), and gout (except tolmetin, which appears to be ineffective in gout). Since aspirin, the original NSAID, has a number of adverse effects, many other NSAIDs have been developed in attempts to improve upon aspirin's efficacy and decrease its toxicity.[30]

Gastrointestinal and peptic ulcer

The most common symptoms associated with these drugs are gastrointestinal, including anorexia, nausea, dyspepsia, abdominal pain, and diarrhea. These symptoms may be related to the induction of gastric or intestinal ulcers, which is estimated to occur in 15% to 30% of regular users. Ulceration may range from small superficial erosions to full-thickness perforation of the muscularismucosa. All of the selective COX-2 inhibitors have been shown to be less prone than equally efficacious doses of traditional NSAIDs to induce endoscopically visualized gastric ulcers and this has provided the basis of FDA approval of valdecoxib and celecoxib. Gastric damage by NSAIDs can be brought about by at least two distinct mechanisms. Inhibition of COX-1 in gastric epithelial cells depresses mucosal cytoprotective prostaglandins, especially PGI_2 and PGE_2. These eicosanoids inhibit acid secretion by the stomach, enhance mucosal blood flow, and promote the secretion of cytoprotective mucous in the intestine. Inhibition of PGI_2 and PGE_2 synthesis may render the stomach more susceptible to damage and can occur with oral, parenteral, or transdermal administration of aspirin or NSAIDs. There is some evidence that COX-2 also contributes to constitutive formation of these prostaglandins by human gastric epithelium; products of COX-2 certainly contribute to ulcer healing in rodents. Another mechanism by which NSAIDs or aspirin may cause ulceration is by local irritation from contact of orally administered drug with the gastric mucosa. Local irritation allows back diffusion of acid into the gastric mucosa and induces tissue damage. It is also possible that enhanced generation of lipoxygenase products (*e.g.*, LTs) contributes to ulcerogenicity in patients treated with NSAIDs.[2]

Blood Pressure, Renal, and Renovascular Adverse Events

Traditional NSAIDs and COX-2 inhibitors have been associated with renal and renovascular adverse events. NSAIDs have little effect on renal function or blood pressure in normal human subjects. However, in patients with congestive heart failure, hepatic cirrhosis, chronic kidney disease, hypovolemia, and other states of activation of the sympatho-adrenal or renin-angiotensin systems, prostaglandin formation becomes crucial in model systems and in humans. NSAIDs are associated with loss of the prostaglandin-induced inhibition of both the reabsorption of Cl^- and the action of antidiuretic hormone, leading to the retention of salt and water. NSAIDs promote reabsorption of K^+ because of decreased availability of Na^+ at distal tubular sites and suppression of the prostaglandin-induced secretion of renin. The latter effect may account in part for the usefulness of NSAIDs in the treatment of Bartter's syndrome.[2]

Analgesic Nephropathy

Analgesic nephropathy is a condition of slowly progressive renal failure, decreased concentrating capacity of the renal tubule, and sterile pyuria. Risk factors are the chronic use of high doses of combinations of NSAIDs and frequent urinary tract infections. If recognized early, discontinuation of NSAIDs permits recovery of renal function.[2]

Pregnancy and Lactation

Prolongation of gestation by NSAIDs has been demonstrated in model systems and in humans. Some NSAIDs, particularly indomethacin, have been used off-label to terminate preterm labor. However, this use is associated with closure of the ductus arteriosus and impaired fetal circulation in utero, particularly in fetuses older than 32 weeks' gestation. COX-2-selective inhibitors have been used as tocolytic agents; this use has been associated with stenosis of the ductusarteriosus and oligohydramnios.[2]

Anti-asthma drugs interaction with NSAIDs

Anti-asthma drugs + NSAIDs

Aspirin and many other NSAIDs can cause bronchoconstriction in some asthmatic patients. Celecoxib, etoricoxib and meloxicam do not usually cause bronchospasm in aspirin or NSAID-sensitive patients. Aspirin, nimesulide and piroxicam appear not to alter theophylline pharmacokinetics.[31]

Zafirlukast + Aspirin

Aspirin 650 mg four times daily is reported to have resulted in a mean increase in the plasma levels of zafirlukast 40 mg daily of 45%. No further details are available. The clinical importance of this interaction awaits assessment but the manufacturers do not suggest any alteration in the zafirlukast dosage.[31]

Aspirin or other Salicylates + Corticosteroids or Corticotropin

Serum salicylate levels are reduced by corticosteroids and therefore salicylate levels may rise, possibly to toxic concentrations, if the corticosteroid is withdrawn without first reducing the salicylate dosage. Concurrent use increases the risk of gastrointestinal bleeding and ulceration.

MATERIALS AND METHODS

This study was conducted in Khartoum state pharmacies and hospitals during the period of May to 15 Th October 2011, It is cross-sectional study. **The Inclusion criteria:** Pharmacist working in Khartoum State responsible for dispensing medication **and** Doctors working in Hospitals of Khartoum state. **The Exclusion criteria:** All pharmacists are not responsible for dispensing medications, Medical representatives, Industrial pharmacists, Doctors not responsible for prescribing and Teaching staff.

Sample size 120 of pharmacists working in Khartoum state pharmacies will be selected randomly **and** 50 doctors who are working in Khartoum state hospitals will be selected randomly. Structured pre tested questionnaire will be developed to collect the data. Moreover, the information was collected from books, international journals. BNF and scientific websites. The data will be coded and analyzed using SPSS 16 program and presented in tables and figures and test of significance will be carried for each data.

RESULTS

8% from the doctors prescribe NSAIDs for asthmatic patients, 95.24% from them prescribe NSAIDs to 1 – 5 asthmatic patients for every 10 asthmatic patients. 76% of doctor expected that there would be drug-drug or drug-disease interaction between asthmatic patients and NSAIDs. 37.50% have seen failure of treatment due to interaction between NSAIDs and asthmatic. 55.5% from the pharmacists dispense NSAIDs to 10 asthmatic patients per day, while 13.3% from the sample dispense NSAIDs to 20 asthmatic patients per day and 31.1% from the sample collected said no patients. 75.5% from the pharmacists stated that NSAIDs

might interact with asthmatic patients. 73.3% from the pharmacists stated that NSAIDs worsen the asthma.

4% from the doctors prescribed NSAIDs a history of ulcer patients 100% from the doctors prescribed NSAIDs to 1 – 5 ulcerative patients every 10 ulcerative patient. 91.67% of doctor expected that there would be drug-drug or drug-disease interaction between ulcerative patients and NSAIDs. 75% have seen failure of treatment due to interaction between NSAIDs and ulcerative patients.

44.4% from the pharmacists dispense NSAIDs to 1 – 10 ulcerative patients per day, while 26.6% from the sample dispense NSAIDs to 11- 20 ulcerative patients per day and 26.6% from the sample collected said no patients. 97% from the pharmacists in the study stated that NSAIDs might affect ulcerative patients. 88% stated that the interaction by increasing gastric acid secretion and worsening of the ulcer in these patients.

34% from the pharmacists did not ask patients about the medical history when they ask to give them NSAIDs, while 66% from them they ask the patients about the medical history. 48% from the pharmacists which ask patients about the medical history they ask about if they have asthma or not while 37.78% not ask and 13.33% missing 71.11% from the pharmacists which ask patients about the medical history they ask about if they have ulcer or not 15.56% not ask and 13.33% missing. 37% from the pharmacists which ask patients about the medical history they ask about if they have renal problems or not. 48.89% not ask and 13.33% missing. 55.5% from the doctors did not ask the patients about the period of using NSAIDs when they come to take NSAIDs. 40% asks and 4.44% missing.

DISCUSSION

As far as we know this is the first study was conducted in Sudan to evaluate the interaction between NSAIDs with some diseases among pharmacists and doctors and the awareness of pharmacist and medical doctors about this interactions because of the importance of these interactions.

8% from the doctors prescribe NSAIDs for asthmatic patients, 95.24% from them prescribe NSAIDs to 1 – 5 asthmatic patients for every 10 asthmatic patients. 76% of doctor expected that there would be drug-drug or drug-disease interaction between asthmatic patients and NSAIDs. 37.50% have seen failure of treatment due to interaction between NSAIDs and

asthmatic. 55.5% from the pharmacists dispense NSAIDs to 10 asthmatic patients per day, while 13.3% from the sample dispense NSAIDs to 20 asthmatic patients per day and 31.1% from the sample collected said no patients. 75.5% from the pharmacists stated that NSAIDs might interact with asthmatic patients. 73.3% from the pharmacists stated that NSAIDs worsen the asthma.

4% from the doctors prescribed NSAIDs a history of ulcer patients 100% from the doctors prescribed NSAIDs to 1 – 5 ulcerative patients every 10 ulcerative patient. Szczeklik A et al stated that to prevent life-threatening reactions, patients with AIA should avoid aspirin and other analgesics that inhibit COX-1.[23] 91.67% of doctor expected that there would be drug-drug or drug-disease interaction between ulcerative patients and NSAIDs. 75% have seen failure of treatment due to interaction between NSAIDs and ulcerative patients. 44.4% from the pharmacists dispense NSAIDs to 1 – 10 ulcerative patients per day, while 26.6% from the sample dispense NSAIDs to 11- 20 ulcerative patients per day and 26.6% from the sample collected said no patients. 97% from the pharmacists in the study stated that NSAIDs might affect ulcerative patients. 88% stated that the interaction by increasing gastric acid secretion and worsening of the ulcer in these patients. Pilotto A, et al stated that the risk of upper GI bleeding is significantly higher in elderly acute vs chronic users of NSAIDs or regular-dose aspirin. In acute NSAID or aspirin users, co-treatment with proton pump inhibitors, but not with H2-blockers, may reduce the risk of bleeding compared with non-users.[29]

34% from the pharmacists did not ask patients about the medical history when they ask to give them NSAIDs, while 66% from them they ask the patients about the medical history. 48% from the pharmacists which ask patients about the medical history they ask about if they have asthma or not while 37.78% not ask and 13.33% missing 71.11% from the pharmacists which ask patients about the medical history they ask about if they have ulcer or not 15.56% not ask and 13.33 missing. 37% from the pharmacists which ask patients about the medical history they ask about if they have renal problems or not. 48.89% not ask and 13.33 missing. 55.5% from the doctors did not ask the patients about the period of using NSAIDs when they come to take NSAIDs. 40% asks and 4.44 missing.

CONCLUSION

1. More than half of the practicing pharmacists and medical doctors are aware about the interaction between NSAIDs and asthma, and patients having ulcer. Unfortunately, in spite of that, they dispense and prescribe NSAIDs to these patients respectively.

2. Half of the doctors did not ask the patients about the period of using NSAIDs when they come for treatment.
3. Half of the pharmacists are reluctant to ask the patients about the medical history when they are taking NSAIDs.

Recommendations

1. Most of doctors and pharmacists are aware about these interactions and they are still dispensing NSAIDs so there must be a notification from the health authority about the interactions of NSAIDs to all doctors and pharmacists
2. Half of pharmacists and doctors did not ask the patients about the medical history when they dispense NSAIDs.

REFERENCES

1. Leon Shargel, et al. (2004), Comprehensive Pharmacy Review. 5th edition.
2. Busse WW, Calhoun WF, Sedgwick JD. Mechanism of airway inflammation in asthma. Am Rev Respir Dis., Jun, 1993; 147(6 Pt 2): S20-4.
3. Horwitz RJ, Busse WW. Inflammation and asthma.Clin Chest Med., Dec, 1995; 16(4): 583-602.
4. Rowe BH, Keller JL, Oxman AD. Effectiveness of steroid therapy in acute exacerbations of asthma: a meta-analysis. Am J Emerg Med., Jul, 1992; 10(4): 301-10.
5. Rowe BH, Edmonds ML, Spooner CH, Diner B, Camargo CA Jr. Corticosteroid therapy for acute asthma. RespirMed., Apr, 2004; 98(4): 275-84.
6. Peters SP, Kunselman SJ, Icitovic N, Moore WC, Pascual R, Ameredes BT, et al. Tiotropium bromide step-up therapy for adults with uncontrolled asthma. N Engl J Med., Oct 28, 2010; 363(18): 1715-26.
7. Camargo CA Jr, Weiss ST, Zhang S, Willett WC, Speizer FE. Prospective study of body mass index, weight change, and risk of adult-onset asthma in women. Arch Intern Med., Nov 22 1999; 159(21): 2582-8.
8. DiPiro.J, Talbert.R,etl, Pharmacotherapy A Pathophysiologic Approach, Seventh Edition, 2008; 569.
9. Snowden S, Nelson R. The effects of nonsteroidal anti-inflammatory drugs on blood pressure in hypertensive patients. Cardiol Rev., Jul-Aug, 2011; 19(4): 184-91.

10. Awofisayo O, Awofisayo O, IferiI and Akpan O, "The Pattern of Sale and Use of Non-Steroidal Anti-Inflammatory Drugs in Rural and Urban CentresinNigeria"., Tropical Journal of Pharmaceutical Research, September, 2008; 7(3): 1013-1018.
11. Gopal K*, Rani V, Ramji, Vidhya, Ganesh S, Shalini, Janardhan V, Reddy U" Awareness of the adverse effects of NSAIDS among its buyers from community pharmacies", Kannan Gopal et al. / Journal of Pharmacy Research, 2010; 3(12): 2890-2893.
12. Derle DV, Gujar K, Sagar B" Adverse effects associated with the use of nonsteroidalantiinflammatorydrugs" Indian journal of pharmaceutical sciences, 2006; 68(4): 409-414.
13. Aneja A, Farkouh ME. Adverse cardiovascular effects of NSAIDs: driven by blood pressure, or edema? Ther Adv Cardiovasc Dis., Feb, 2008; 2(1): 53-66.
14. Bavry AA, Khaliq A, Gong Y, Handberg EM, Cooper-Dehoff RM, Pepine CJ. Harmful effects of NSAIDs among patients with hypertension and coronary artery disease. Am J Med., Jul, 2011; 124(7): 614-20.
15. Schjerning Olsen AM, Fosbøl EL, Lindhardsen J, Folke F, Charlot M, Selmer C, Lamberts M, Bjerring Olesen J, Køber L, Hansen PR, Torp-Pedersen C, Gislason GH. Duration of treatment with nonsteroidal anti-inflammatory drugs and impact on risk of death and recurrent myocardial infarction in patients with prior myocardial infarction: a nationwide cohort study. Circulation, May 24, 2011; 123(20): 2226-35.
16. Brook RD, Kramer MB, Blaxall BC, Bisognano JD. Nonsteroidal Anti-Inflammatory Drugs and Hypertension. J Clin Hypertens (Greenwich), Oct, 2000; 2(5): 319-323.
17. Johnson AG.NSAIDs and increased blood pressure. What is the clinical significance? Drug Saf, Nov, 1997; 17(5): 277-89.
18. B. Nørgård; L. Pedersen; S.P. Johnsen; R.E. Tarone; J.K. McLaughlin; S. Friis; H.T. Sørensen "COX-2-Selective Inhibitors and the Risk of Upper Gastrointestinal Bleeding in High-Risk Patients With Previous Gastrointestinal Diseases" Alimentary Pharmacology & Therapeutics, 2004; 19(7).
19. Lanas A. A review of the gastrointestinal safety data--a gastroenterologist's perspective. Rheumatology (Oxford), May, 2010; 49(2): ii3-10.
20. Martin R. TrameÁr, R. Andrew Moore, D. John M. Reynolds, Henry J. McQuay "Quantitative estimation of rare adverse events which follow a biological progression: a new model applied to chronic NSAID use", Pain, 2000; 85: 169±182.
21. Siew C. Ng and Francis K.L. Chan" NSAID-induced gastrointestinal and cardiovascular injury", Gastroenterology, 2010; 26: 611–617.

22. Szczeklik A(Aspirin-induced asthma: a tribute to John Vane as a source of inspiration), pharmacological report, 2010; 62: 526-529.
23. Levy S, Volans G. The use of analgesics in patients with asthma. Drug Saf., 2001; 24(11): 829-41.
24. Nizankowska-Mogilnicka E. [Asthma with hypersensitivity to aspirin]. Pol Merkur Lekarski, Jun, 2003; 14(84): 561-5.
25. Szczeklik A, Nizankowska E, Mastalerz L, Szabo Z. Analgesics and asthma. Am J Ther., May-Jun, 2002; 9(3): 233-43.
26. Thomsen SF, Kyvik KO, Skadhauge LR, Steffensen I, Backer V. Regular use of non-steroidal anti-inflammatory drugs increases the risk of adult-onset asthma: a population-based follow-up study. ClinRespir J., Apr, 2009; 3(2): 82-4.
27. Simon RA. Adverse respiratory reactions to aspirin and nonsteroidal anti-inflammatory drugs. Curr Allergy Asthma Rep., Jan, 2004; 4(1): 17-24.
28. Rouff GE, the impact of NSAIDs on hypertension: alternative analgesics for patients at risk, May-June, 1998; 120(3): 376-87.
29. Pilotto A, Franceschi M, Leandro G, Paris F, Niro V, Longo MG, D'Ambrosio LP, Andriulli A, Di Mario F. The risk of upper gastrointestinal bleeding in elderly users of aspirin and other non-steroidal anti-inflammatory drugs: the role of gastroprotective drugs. Aging ClinExp Res., Dec, 2003; 15(6): 494-9.
30. Bertram G. Katzung, 2006, Basic & Clinical Pharmacology 10th edition, USA, McGraw-Hill.
31. Ivan H Stockley, 2005, Stockley's Drug Interactions, UK, Pharmaceutical Press.