ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES Knowledge to Innovation

Vol 7, Issue 3, 2014

ISSN - 0974-2441

Original Article

ADVERSE DRUG REACTIONS AND INTERACTIONS OF NSAIDs IN GENERAL CARE HOSPITAL

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Received: 3 April 2014, Revised and Accepted: 2 May 2014

ABSTRACT

Objective: The main aim is to evaluate the Pharmacological aspects of theusage of NSAIDs in a multi-specialty tertiary care hospital. The secondary objectives are to obtain the extent of usage of NSAIDs in the hospital, to prevent inappropriate use of NSAIDs, to analyze Cost effectiveness as continuity of work done by Maheshwariet.al[1].

Methods: The study was carried out in multi-specialty hospital. Specially prepared proforma were been designed for the collection of the data. NSAIDs are most commonly prescribed as twice daily dosing.

Results: The most commonly prescribed was ketorolac with twice daily dosing followed by diclofenac with twice daily dosing. 264 prescriptions(58.53) had shown potential drug interactions with NSAIDs. The gastroprotective agents that are given along with NSAIDs are H_2 blockers were the most commonly prescribed drugs given in 299 patients (66.2%).

Conclusion: Drug use problems are common and have significant clinical and economic implications.It is important to remember that most adverse drug reactions would subside once the offending agent was discontinued or its dose reduced.

Key Words: NSAIDs, Drug interactions, analgesics

INTRODUCTION

Adverse drug reactions: Any response to a drug which is noxious and unintended, and which occurs at doses normally used in man for prophylaxis, diagnosis or therapy of disease or for the modification of the physiological function[2].

Drugs will always be associated with ADRs. Health care professionals, including physician, nurses, and pharmacists, have always tried to avoid ADRs in their patients. The pharmaceutical industry attempts to develop new drugs with low incidence of ADRs and to discover serious ADRs during drug development and as early as possible with post marketing surveillance programs. Applying the knowledge about the risk factors, causes, and ways of an ADR occurrence to individual patients, the ADR incidence and the cost can be reduced and thus can improve health care. It is difficult for the physicians to be knowledgeable about the ADR that can occur with the number of new drugs available in the market, the who generally possess the most pharmaceutical knowledge on the health care team must prepare themselves to take on this role.

Drug interactions: it refers to an adverse drug response produced by the administration of a drug or co exposure of the drug with other substance, which modifies the patient response to the drug[2].

Cost effective analysis: It is the measure of the incremental cost of achieving an incremental health benefit expressed as a particular health outcome that varies according to indication of the drug[3].

Typical criteria reviewed in prospective studies include the following

Indications, Drug selection, Doses prescribed, Dosage form and route of administration, Duration of therapy, Costs, Therapeutic duplication, Quantity dispensed, Contraindications, Therapeutic outcome, Adverse drug reactions and Drug interactions.

MATERIALS AND METHODS:

All inpatient profiles of patients who were admitted for various reasons in different wards of the hospital and who were prescribed NSAIDs were taken for the study.

The drugs prescribed were classified according to the WHO ATC classification system. Ibuprofen and diclofenac have been classified as low risk; Aspirin, sulindac, naproxen and indomethacin were classified as moderate risk; and ketoprofen and piroxicam as high risk for GI adverse events. These categories were used to calculate the percentage of each classification over the total non selective NSAIDs prescribed[4].

Prescribing data obtained were analyzed for statistical significance.

The results were tabulated. Logistic regression analysis was done to see if there was any association between two NSAIDs which were largely prescribed. The student t test was performed to see if there was any significance in the ADRs reported

RESULTS

Table 1: Frequency of dosing of NSAIDS

Drugs	No of patients(n=451)
Once daily	35
Twice daily	355
Thrice daily	73

Table1 indicates NSAIDs are most commonly prescribed as twice daily dosing.

Table 2: frequency of dosing of all NSAIDS received for study population

Drug	OD	BD	TDS
Ibuprofen + para	1	5	21
Diclofenac	4	73	17
Ketorolac	0	88	10
Ibuprofen	0	5	10
Piroxicam	9	22	7
Aceclofenac	0	12	4
ASP	0	17	3
Aceclofenac + para	2	62	1
Indomethacin	0	2	0
Etodolac	1	1	0

Table2 indicates frequency of dosing for each NSAID. The most

commonly prescribed was ketorolac with twice daily dosing followed by diclofenac with twice daily dosing.

Table 3: Number of therapeutic duplications of nsaids

Drugs	No of duplications(n=451)	% of Duplications
Ketorolac + (Ibuprofen + para)	3	0.66
Ketorolac + Diclofenac	1	0.22
Inj. Diclofenac + Tab. Diclofenac	1	0.22
Ibuprofen + Aceclofenac	1	0.22
Ketorolac + (Aceclofenac + para)	1	0.22

Table 3 indicates that only 6 therapeutic duplications were present out of total 451 prescriptions.

Table 4: Potential drug – drug interactions in study population

Interactions	No of patients(n=451)	% of interactions
No interactions	187	41.46
Mild	169	37.4
Moderate	94	21.06
Severe	1	0.22

Table 4 indicates that 264 prescriptions(58.53) had shown potential drug interactions with NSAIDs.

Table 5: Routes of administration of NSAIDs

Routes	No of patients(n=451)	%
P/O	231	51.2
IM	156	34.5
P/O + IM	55	12.1
L/A	7	1.55
L/A + P/O	2	0.44

Table5 Indicates that NSAIDs were more commonly prescribed orally (n=231, 51.2%) followed by IM route (n=156, 34.5%).

Table: 6 distribution of gastroprotective agents in patients receiving NSAIDs

Drugs	No of patients(n=451)	%
H2 blockers	299	66.2
PPIs	95	21.06
H2 blockers + PPIs	27	5.98
None	30	6.65

Table 6 indicate the gastroprotective agents that are given along with NSAIDs. H2 blockers were the most commonly prescribed drugs given in 299 patients (66.2%).

Table 7: Potential drug-drug interactions with nsaids

NSAID	Mild	No	Moderate	No	Severe	No
Ketorolac	Ranitidine	72	Gentamicin	26	Indomethacin	1
			Dexamethasone	1		
			Phenytoin	2		
Ibuprofen	Ranitidine	52	Furosemide	9		
	$Mg(OH)_2$	1	Phenytoin	10		
			Glipizide	3		
			Clopidogrel	2		
			Amlodepine	1		
			Spironolactone	3		
			Prednisolone	2		
			Ofloxacin	4		
			Dexamethasone	1		
			Digoxin	2		
			Ketorolac	1		
			Gentamicin	3		
			Losartan	2		
Aceclofenac	Ranitidine	3	Losartan	1		
			Glibenclamide	2		
			Levofloxacin	1		
			Gentamicin	1		
			Metoprolol	1		
			Ramipril	1		
Diclofenac	Ranitidine	44	Gentamicin	11		
	Ceftriaxone	1	Atorvastatin	5		
	Clopidogrel	1	Aspirin	1		
	$Mg(OH)_2$	1	Furosemide	1		
			Glipizide	2		
			Losartan	2		
			Phenytoin	1		
			Clopidogrel	1		
			Amlodepine	1		
Aspirin	Pantoprazole	3	Insulin	7		
	Rabeprazole	1	Losartan	1		
			Clopidogrel	2		
			Prazocin	1		
			Glipizide	1		

Table 7 Indicates various drug interactions with NSAIDs which shows among mild interactions NSAIDs with ranitidine is the most common, in moderate with gentamycin and in case of severe it is indomethac

Table 8: Cost utilization of combination of NSAIDS

Drugs	No of patients	Cost (Rs)
Ibuprofen + para	96	147
Aceclofenac +para	66	398.64
Aceclofenac + seratopeptidase + para	20	240.8

Table8 Indicate the number of patients receiving combination of NSAIDs during the study period and the cost incurred per day.

DISCUSSION

The effects of potential drug interactions are,

NSAIDS with Ulcer healing agents: Plasma concentration of NSAIDs is increased by ulcer healing agents.

NSAIDs with anti platelet agents: Increased risk of haemorrhage might be present.

NSAIDs with antibiotics: Plasma concentrations of antibiotics are increased and there will increased risk of convulsions when given with NSAIDs

NSAIDS with corticosteroids: Increased risk of gastrointestinal bleeding and ulceration when given with corticosteroids

NSAIDS with anti epileptics: NSAIDS enhances the effects of anti epileptic drugs by increasing the plasma concentration.

NSAIDS with Diuretics: Risk of nephrotoxicity of NSAIDs will be increased when given with Diuretics

NSAIDs with Anti Diabetics: NSAIDs enhance the effect of sulphonylureas.

NSAIDs with ACE inhibitors: Increased risk of renal impairement when given with NSAIDs

NSAIDs with lipid lowering agents: Excretion of NSAIDs is increased by lipid regulating agents

NSAIDs with NSAIDs: Increased side effects and bleeding

NSAIDs with Cardiac glycosides: NSAIDs possibly increase the plasma concentration of cardiac glycosides and also possible exacerbation of heart failure and reduction in renal function.

NSAIDs with Beta blockers: NSAIDS antagonise the hypotensive effect of beta blockers.

NSAIDs with Calcium channel blockers: NSAIDs antagonize hypotensive effect of calcium channel blockers[7].

ADVERSE EFFECTS

Salicylates: Nausea, vomiting, epigastric distress, increased occult blood loss in stools, gastric mucosal damage and peptic ulceration.

Propionic acid derivatives: Side effects are milder. Gastric discomfort, nausea and vomiting. Gastric erosion and occult blood loss are rare.

Anthranilic acid derivative: Diarrhoea, epigastric distress, skin rashes, dizziness and other CNS manifestations. Haemolytic anaemia is rare.

Aryl-acetic acid derivatives: Epigastric pain, nausea, headache, dizziness, rashes. Gastric ulcer and bleeding are less common. Reversible elevation of serum amino transferases has been reported more commonly, kidney damage is rare.

Oxicam derivatives: Gi side effects are more than Ibuprofen. Rashes and pruritis are seen. Edema and reversible azotaemia have been observed.

Pyrrolo-pyrrole derivatives: Nausea, abdominal pain, dyspepsia, ulceration, loose stools, drowsiness, headache, dizziness, nervousness, pruritis, pain at injection site, raise in serum transaminase and fluid retention have been noted.

Indole derivatives: Gastric irritation, nausea, anorexia, gastric bleeding and diarrhoea are prominent. Frontal headache, dizziness, ataxia, mental confusion, hallucination, depression and psychosis can occur. Leukopenia, rashes and other hypersensitivity reactions are also reported. Increased risk of bleeding due to decreased platelet aggregability.

It is contraindicated in machinery operators, drivers, psychiatric patients, epileptics, kidney disease, pregnant women and in children.

Pyrazolones: Few cases of agranulocytosis were reported.

Selective COX-2 inhibitors: Nausea and rashes occur occasionally, leukopenia is rare[5].

CONCLUSION

This study highlights the need for a greater awareness of the potential for drug-related admissions, perhaps provided by inter professional working and regular medication review of patients thought to be at high-risk of drug-related admissions. It is important to remember that most adverse drug reactions would subside once the offending agent was discontinued or its dose reduced. The simplest way to prevent most adverse drug reaction is to use the minimum dose of drugs. The simple principle of 'start low and go slow' should be followed. For this, health care professionals need to be trained in drug safety and a habit of rational drug use should be inculcated in them from the beginning.

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