

Drug Induced Bleeding Gastroenteropathy

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Abstract

Aim: Adverse Drug Reactions are one of the leading cause of hospitalization and mortality in health systems (in developed and developing countries), and the relevance is increasing year to year. The aim of this study was to determine the incidence of drug induced gastrointestinal bleeding and drugs most frequently involved in a tertiary care hospital.

Study: We performed a retrospective study working on a pharmacovigilance database from a tertiary care Hospital (Hospital General de Agudos Dr. Cosme Argerich) with information of the last five years.

Results: We detected 48 events of drug induced gastrointestinal bleeding. 45 cases of upper gastrointestinal bleeding and 3 cases of lower gastrointestinal bleeding. Almost all events were serious and three of them were lethal. NSAIDs, anticoagulant and acetylsalicylic acid were the drugs most frequently involved.

Conclusions: In concordance with international bibliography, drug induced gastrointestinal bleeding is a common event and usually because of auto medication or medical prescribing errors. Some of these events lead to prescribing cascades.

Keywords: *Drug Induced Gastrointestinal Bleeding; Anticoagulant; NSAIDs; Acetylsalicylic Acid*

Introduction

Adverse Drug Reactions are nowadays one of the four main causes of death in developed countries [1-6] and represents between 0.5 and 20 per cent of all general hospital admissions all over the world.

Although continuous medical education and pharmacovigilance plans (from industry and from regulatory entities), this percentage is increasing in the last years, and there are some different explanations for this, including the aging of the population and multiple new therapeutics lines.

But, according to multiples articles in the last ten years [7-10] something can be appreciated: the drugs most frequently involved in Adverse Drug Reactions – related admissions are ever the same and are the most traditionally and “secure” drugs (aspirin, NSAIDs, corticoids, antidiabetic drugs, etc).

Drug induced bleeding can be in stomach (the most frequent) but also in small intestine (drug induced enteropathy) and in colon (drug induced colopathy).

In this article, we want to show how often Drug Induced – gastrointestinal bleeding occurs, which are the drugs most frequently involved and how serious are these events. Also, estimate the percentage of this events that end in Prescribing Cascade [11,12].

Methods

We performed the work based on a pharmacovigilance database from a tertiary care hospital in Buenos Aires City, in Argentina. This database has information of the last five years. To determine if a medical adverse event was an Adverse Drug Reaction, we applied the Naranjo Score [13] and include for this work only the certain ADR or the probable ones.

Then, Adverse Drug Reaction were classified according to seriousness (we considered serious when it was lethal, it compromised life, lead to hospital admission or prolonged it, caused teratogenicity or permanent disability). All this ADR were reported to the Argentinian Regulatory Agency (ANMAT).

We also evaluated if this drug induced Gastrointestinal Bleeding were part of prescribing cascade, according to a recent algorithm [11].

Results

Upon a total of 2990 Adverse Drug Reaction in the Pharmacovigilance Database, we detected a total of 48 (1.6 per cent of all ADR of the database - CI 95%: 1.15 - 2.05 %) events of drug induced gastrointestinal bleeding (certain or probable according to Naranjo algorithm), 45 events of upper gastrointestinal bleeding and 3 events of lower gastrointestinal bleeding. Of these 48 events, 46 (95.86 per cent; CI 95%: 90.18 - 100 per cent) were serious and the cause of seriousness was hospitalization in 36 events, prolongation of hospitalization in 7 events and there were 3 cases of death related gastrointestinal bleeding (all of these three were Upper Gastrointestinal Bleeding). Six cases were hospitalized in critical care unit, including the three fatal cases.

Female sex was affected in 29 cases (60.41 per cent of all; CI 95%: 46.58 - 74.25 per cent) and male sex in 19 cases (39.58 per cent of all; CI 95%: 25.74 - 53.41 per cent). The average age was 70.27 years (CI 95%: 66.10 - 74.43 years).

Considering the drugs, NSAIDs were involved in 21 cases (43.75 per cent; CI 95%: 29.71 - 57.78 %), acetylsalicylic acid in 9 cases (18.75%; CI 95%: 7.70 - 29.79 %), acenocoumarin or warfarin were involved in 10 cases (20.83%; CI 95%: 9.34 - 32.32 %), other anti-coagulants in 2 cases, and then combinations of drugs. The three cases of lower gastrointestinal bleeding were drug induced colopathy (confirmed with endoscopy and histology), two cases by NSAIDs and one case by acetylsalicylic acid.

When we evaluated combinations of medications, there was one case of combination of fluoxetine with NSAIDs (this combination has a pharmacovigilance alert because of the increased risk of gastrointestinal bleeding and other bleedings) and one of acenocoumarin and amiodarone (amiodarone is a drug highly used in Argentina but it has the potential of inhibition of cytochromes and the metabolism of multiple drugs including oral anticoagulants).

Drugs	Number of cases
NSAIDs	21
Warfarin and other oral anticoagulants	10
Acetylsalicylic Acid	9
Other drugs and combinations	8

Table 1: Drugs involved in drug – induced gastrointestinal bleeding.

	Yes	No	Do not know
Are there previous conclusive reports on the reaction?	1	0	0
Did the adverse event appear after the suspected drug was given?	2	-1	0
Did the adverse reaction improve when the drug was discontinued or a specific antagonist was given?	1	0	0
Did the adverse reaction appear when the drug was re-administered?	2	-2	0
Are there alternative causes that could have caused the reaction?	-1	2	0
Did the reaction reappear when a placebo was given?	-1	1	0
Was the drug detected in any body fluid in toxic concentrations?	1	0	0
Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	1	0	0

Did the patient have a similar reaction to the same drug or similar drugs in any previous exposure?	1	0	0
Was the adverse effects confirmed by any objective evidence?	1	0	0

Table 2: Naranjo Algorithm for assessing drug causality in a medical adverse event. The scoring is: 9, certain ADR; 5-8, probable ADR; 1-4, possible ADR; 0, doubtful.

Discussion

As other articles from other authors [14,15], NSAIDs, acetylsalicylic acid, and oral anticoagulants were the drugs most frequently involved in gastrointestinal bleeding. NSAIDs appeared frequently because of auto medication. We did not estimate exactly in this work the clinical and economic burden of this complications but we can infer that is very relevant because of the high frequency of hospitalization of this ADR and the average time of hospitalization of gastrointestinal bleeding.

People suffering drug induced gastrointestinal bleeding was elderly population. Considering the standard treatment of gastrointestinal bleeding the use of omeprazole, and considering that approximately 20% of patients receiving parenteral omeprazole will suffer some Adverse Drug Reaction, this percentage will end in a two steps cascade.

Conflict of Interests

None of the authors has conflict of interest.

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