Original Article

Improper Use of Antisecretory Drugs in a Tertiary Care Teaching Hospital: An Observational Study

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ABSTRACT

Background: Antisecretory drugs (ASDs) are prescribed for preventing and treating nonsteriodal, antiinflammatory drug (NSAID)-induced gastrointestinal adverse effects and for stress ulcer prophylaxis (SUP). The suitability of long-term use of ASDs has been evaluated elsewhere but not in the Kingdom of Saudi Arabia (KSA). **Objectives**: To evaluate the improper use of pantoprazole, a proton pump inhibitor (PPI) and ranitidine, a histamine 2 (H2) receptor antagonist (H2RA); and to identify the associated factors for misuse of these two drugs at a referral hospital. **Materials and Methods**: In 2006, a study was carried out at a tertiary care teaching hospital in Riyadh, where patients' medical charts were evaluated for two months. All hospitalized patients on ASDs drugs, aged 18 and above were identified. A standard criterion for proper use of ASDs was applied during evaluation. **Results**: Of the 661 patients studied, the use of ASDs was more significant among males (57.9%) as compared to females. Proper use of ASDs show a significant increasing trend with patients' age. The use of ranitidine (56%) was significantly higher than that of pantoprazole (44%). The unjustified use of the drugs was observed in 282 (43%) patients. Improper use of the drugs decreased as duration of hospital stay lengthened. Two departments, namely medicine and surgery, were significantly associated with the prescription of the two drugs. Higher numbers of improper prescriptions of these drugs were associated with the surgery department (49.3%) than with the medicine department (38.2%). **Conclusion**: Improper use of ASDs was observed in 43% of the patients. Based on the results of this study, correct measures need to be implemented in order reduce the misuse of ASDs.

Key Words: Antisecretory drugs, improper use

Received 02.03.2007, Accepted 21.04.2007
The Saudi Journal of Gastroenterology 2007 13(3):124-128

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Antisecretory drugs (ASDs), mainly proton pump inhibitors (PPIs), have rapidly become one of the world's most widely prescribed medicines for treating and preventing nonsteroidal antiinflammatory drug (NSAID)-induced gastrointestinal adverse effects. NSAIDs are responsible for more than 100,000 hospitalizations and 16,000 deaths each year in the United States alone due to upper gastrointestinal bleeding, ulceration and perforation. Some reports say up to 60% of patients suffering from dyspepsia are on ASDs, namely PPIs or H2RAs, without proper investigation.[1-5]

Their exceptional symptom control in acid peptic disorders has led to the indiscriminate use of ASDs for nonspecific, upper gastrointestinal symptoms without proper investigation.[6] ASDs form the cornerstone in the management of upper gastrointestinal bleeding and stress ulcer prophylaxis (SUP) in intensive care units (ICU). But many patients admitted to general medical wards (nonICU units) are also routinely placed on these drugs for SUP when neither their admission nor the comorbid diagnoses support their use for either treatment or prophylaxis.[7]

A recent study showed that SUP is overutilized in the nonICU setting and patients are often prescribed ASDs unnecessarily, resulting in significant increase in expenditure.[8] Another hospital-based study revealed that 63% of the patients had no valid indication for PPIs.[9] Thus, the initiation and the continuous use of these drugs without correct indications will result in significant costs. Numerous studies have evaluated the appropriateness of long-term use of ASDs in general practice.[10-12] The extent of misuse of ASDs in Saudi Arabia's hospitals is unknown. While there are various formulations of these classes of drugs (H2RA and PPI) available in the country, ranitidine and pantoprazole are the only available formulary drugs in our hospital.

Thus, this study was carried out with the following objectives:

i. To evaluate the improper use of pantoprazole and ranitidine in terms of their initiation and continuation in our tertiary care teaching hospital.
ii. To observe the characteristics of patients, hospital stay, reason of prescription and place of prescription

(department), which are associated with the improper use of pantoprazole and ranitidine.

MATERIALS AND METHODS

This is an observational study conducted at a tertiary teaching hospital in Riyadh, Saudi Arabia. All hospitalized patients on ASDs, aged 18 and above, were identified on a daily basis for a period of two months, from March to April 2006, with the help of inpatient pharmacy records. The medical records of these patients were reviewed and the data was collected regarding the type of drugs, dosage, indication and duration of treatment, endoscopy findings, gender, age and department affiliation of the prescribing physician.

The following indications were considered to be appropriate for initiation of ASD therapy:

1. primary prophylaxis for preventing stress ulcer
2. active gastric ulcer or duodenal ulcer disease confirmed at endoscopy
3. gastro-esophageal reflux disease confirmed at endoscopy
4. *H. pylori* eradication regimen
5. coprescription with two or more NSAIDs, including aspirin
6. coprescription with even small doses of aspirin in elderly patients or patients with history of peptic ulcer disease
7. coprescription with NSAIDs or with small doses of aspirin together with warfarin or heparin
8. coprescription with small doses of aspirin together with large doses of glucocorticoid
9. patients with the diagnosis of Zollinger-Ellison syndrome[2,4,13-17]

Statistical analysis

Data was coded and entered into Statistical Package for the Social Sciences (SPSS version 14) to perform analysis. The chi-square test was used to observe the association between two categorical variables (characteristics of patients and two types of drugs) and to observe the significant trend across the four levels of study variables (age and hospital stay) in relation to the outcome variables (type of drug and indication for use). Z-tests for proportions were used to test significance of single proportion and to compare the two proportions.

RESULTS

Files of 661 patients admitted during the two months of the study were reviewed. Of these, 340 (51.4%) were from the medical department, 227 (34.4%) from the surgical department and 94 (14.2%) from other departments. It was found that a significantly higher proportion of male patients (57.9%) were on ASDs than female patients (42.1%) ($Z = 4.17$, $P < 0.0001$). But no association was observed between gender and type of ASDs used ($X^2 = 3.08$, $P = 0.079$) [Table 1]

The age distribution in relation to type of ASDs showed a significantly higher trend ($X^2 = 14.69$, $P < 0.0001$), that is, the proportion of use of ASDs was found to be higher with increasing age. However, no significance was found across the days of patients' hospital stay in relation to the type of ASD used ($X^2 = 0.30$, $P = 0.58$) [Table 1]. Of the 661 patients observed for ASD use, 372 (56%) were on ranitidine and 289 (44%) on pantoprazole, which reveals the significantly higher use of ranitidine in these patients ($Z = 3.11$, $P = 0.002$).

There was also a significant difference between the type of the drug used (ranitidine and pantoprazole) across four different age groups. The use of ranitidine is higher in the age group ≤ 40 years whereas the use of pantoprazole was higher in the age group > 41 years ($X^2 = 13.24$, $P < 0.001$). The difference in the type of drug used was also significant across the type of specialty department (medicine and surgery) where these patients were treated and the type of ASD (pantoprazole and ranitidine) used ($X^2 = 36.69$, $P < 0.0001$).

The use of pantoprazole was higher (72.6%) in the medicine department than in the surgery department (47.1%) whereas the use of ranitidine in these two departments was 27.4% and 52.9%, respectively [Table 1]. The proper use of ASDs (risk factor and prophylaxis) was observed in 379 (57.3%) patients, which was significantly higher than the 282 patients (42.7%) who received it inappropriately ($Z = 3.8$, $P < 0.001$). Among the patients who received ASDs appropriately, 203 patients (30.7%) had a risk factor, while 176 patients (26.6%) had them for SUP [Table 2].

Amongst the patients who correctly received ASDs, the distribution of pantoprazole and ranitidine was 138 (36.4%) and 241 (63.6%) respectively. Of the 282 patients who received ASDs inappropriately, the numbers of patients receiving pantoprazole and ranitidine were 151 (53.5%) and 131 (46.5%) respectively, showing a significant association between the indication (and appropriateness) of use and type of drug ($X^2 = 18.6$, $P < 0.0001$) [Table 3]. It was found that improper prescriptions for these two ASDs were issued for 130/340 (38.2%) and 112/227 (49.3%) by the medicine and surgery departments respectively. This indicates a significant difference between the two departments ($Z = 2.61$, $P = 0.01$).

There was no association between the indication for the use of ASDs (proper or improper use) and the gender of the patients ($X^2 = 0.213$, $P = 0.64$). However, a significant trend across the four age levels of patients in relation to the indication of use was observed ($X^2 = 225.22$, $P < 0.0001$) suggesting that appropriate use increased with increasing

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Table 1: Association between study variables and the antisecretory drug

Study variables	Type of antisectory drug (%)		Total (*n* = 661)	X^2 - value	*P* - value
	Pantoprazole *n* = 289 (44)	Ranitidine *n* = 372 (56)			
Age Group (years)					
< 20	10 (3.4)	32 (8.6)	42 (6.4)	14.69	0.0001
21-40	39 (13.5)	79 (21.2)	118 (17.9)		
41-59	102 (35.3)	119 (32.0)	221 (33.4)		
> 60	138 (47.8)	142 (38.2)	280 (42.3)		
Gender					
Male	179 (61.9)	204 (54.8)	383 (57.9)	3.08	0.079
Female 110 (38.1)	168 (45.2)	278 (42.1)			
Hospital stay (days)					
< 8	100 (34.6)	125 (33.6)	225 (34.0)	0.30	0.58
8-14	52 (18.0)	88 (23.6)	140 (21.2)		
15-21	50 (17.3)	53 (14.2)	103 (15.6)		
> 21	87 (30.1)	106 (28.6)	193 (29.2)		
Department					
Medicine	247 (72.6)	93 (27.4)	340 (51.4)	36.69	< 0.0001
Surgery	107 (47.1)	120 (52.9)	227 (34.4)		
Other	42 (44.7)	52 (55.3)	94 (14.2)		

Table 2: Association between the reason for prescribing antisecretory drugs and various departments

Reason	Department			Total *n* = 661 (%)	X^2-value	*P*-value
	Medicine *n* = 340	Surgery *n* = 227	Others *n* = 94			
For risk factor group (RF)*	122	58	23	203 (30.7)	11.74	0.019
Prophylaxis (P)*	88	57	31	176 (26.6)		
Improper use	130 (38.2)	112 (49.3)	40	282 (42.7)		

*(*P* + RF = proper use)

Table 3: Association between the indications of use of antisecretory drugs and the study variables

Study variables	Indication of use		Total (*n* = 661)	X^2 - value	*P* - value
	Proper use (P + RF)* (*n* = 282)	Improper use (*n* = 379)			
Age (in years)					
< 20	12	30	42	225.22	< 0.0001
21-40	35	83	118	0.213	0.64
41-59	53	168	221	6.77	0.009
> 60	279	1	280	18.60	< 0.0001
Gender					
Male	223	160	383		
Female	156	122	278		
Hospital stay (days)					
< 8	117	108	225		
8-14	78	62	140		
15-21	59	44	103		
> 21	125	68	193		
Type of drug					
Pantoprazole	138 (36.4)	151 (53.5)	289		
Ranitidine	241 (63.6)	131 (46.5)	372		

*(*P* = prophylaxis. RF = Risk factor)

age of the patients [Table 3]. It was found that as duration of the hospital stay increased, the proportion of proper use of ASDs increased while improper use decreased ($X^2 = 6.77$, $P = 0.009$) [Table 3].

There was a significant association between specialty

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(medicine, surgery, others) and reason for prescribing ASDs ($X^2 = 11.74$, $P = 0.019$) [Table 2]. Whereas the medicine department prescribed ASDs for 122 out of 340 (35.9%) patients for a risk factor, only 58 out of 227 (25.5%) patients of the surgery department who were prescribed ASDs actually had a risk factor for a risk factor ($Z = 2.61$, $P = 0.012$).

DISCUSSION

There is a growing unease over the rapid increase in ASD prescriptions, mainly PPIs, both in hospital and general practice and the rising costs associated with this trend.[18] The present study shows that a total of 53% of all hospitalized patients were on ASDs during the study period and this percentage is even more than what has been published by others (30–40%).[9,19,20] It is not possible to compare the trend of PPI use in Saudi Arabia since there is no previous data available.

Although the use of PPIs has increased significantly over a period of time in Europe and North America,[20] this study shows that the overall use of H2RAs (such as ranitidine) is higher than that of PPIs (*e.g.*, pantoprazole), at least among our patients. A majority (43%) of patients studied were aged 60 years and above, a situation similar to what had been published by Carvajal *et al.* in 2004 in Spain.[15] The proportion of elderly patients was higher in this study because they harbor serious comorbid illnesses that bring them to the hospital and require admission for longer periods.

Our study showed that 43% of the prescriptions for ASDs were written without an appropriate indication. Similar studies in the past indicated that ASDs were misused in hospitals and in general practice. A study conducted for over one year in a single county hospital in the USA showed that only 22.5% of all outpatient prescriptions of pantoprazole had a proper indication.[21] A recent study revealed that 22% of hospitalized patients had received SUP in a nonICU setting, out of which 54% were discharged and given ASDs without proper indication, which had cost the hospital $111,791 annually.[8]

Similarly, studies published in Europe and Ireland showed that 51 and 57% of their patients respectively, were given PPIs improperly. Maclaren *et al.* had illustrated in their study that even after implementation of intravenous PPI guidelines, prescribing practices for SUP did not show any improvement.[22] Most of the patients who received SUP were on an H2RA (ranitidine). This is comparable to what had been reported by Daley *et al.* in their study where 63.9% of ICU clinicians chose an H2RA as their first-line drug while 23% chose PPIs, when asked for their preferred choice between H2RAs and PPIs. From the clinicians who chose PPIs, about 64.7% used them when H2RAs failed initially.[23]

The frequency of prescribing pantoprazole was found to be higher in patients with an existing risk factor and was mostly recommended by physicians. Cardiologists from the medical department issued the most prescriptions, followed by neurologists. The reason was that they had the highest number of patients, most of them elderly who were on aspirin or anticoagulants for either stroke prevention or cardiac ischemia. In the surgery department, most prescriptions were issued by orthopedic surgeons, followed by general surgeons. Their patients had major surgeries and were either on NSAIDs for pain management, anticoagulants for deep vein thrombosis prophylaxis or on both drugs.

Our study reveals that there is significant evidence that ASDs are being misused. Therefore, individual hospitals should develop their own strategies to overcome such misuse, notably for PPIs. Strategies that can be used include controlled policies like formulary restriction, PPI order sheets or stop-orders for specific indications. This practice has been successfully implemented in reducing antibiotic misuse.[24] The other strategy of immediate concurrent feedback, which involves providing instant feedback to doctors at the time of prescription, was deemed to be improper.

However, a study showed that this approach was associated with more rational prescribing of ASDs and was important in saving resources.[25] Writing and implementing guidelines for the uses of ASDs, mainly PPIs, by pharmacists can be another strategy to reduce misuse.[22,26] The study published by Skledar *et al.* showed pharmacists and physicians collaboratively developed evidence-based practice guidelines and adherence to it produced a 50% improvement in correct intravenous pantoprazole use.[16] Such a practice guideline can be in the form of a verbal, written or electronic communication.

CONCLUSION

Forty three percent of the patients in this study received ASDs improperly, indicating that Saudi Arabia, like other countries, suffers from widespread misuse of ASDs in hospital practice. The results of this study highlight the need for a monitoring mechanism to periodically study prescription patterns of ASDs in order to further reduce its misuse.

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Source of Support: Nil, **Conflict of Interest:** None declared.

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