SAS Journal of Medicine
Abbreviated Key Title: SAS J Med
ISSN 2454-5112
Journal homepage: https://saspublishers.com

OPEN ACCESS

Hepato Gastroenterology

Gastrointestinal Bleeding and Non-Steroidal Anti-Inflammatory Drugs in Hospitals in Bamako, Mali

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DOI: 10.36347/sasjm.2022.v08i04.024 | **Received:** 19.03.2022 | **Accepted:** 21.04.2022 | **Published:** 26.04.2022

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Abstract **Original Research Article**

The main aim of this study was to investigate the role of non-steroidal anti-inflammatory drugs in digestive bleeding in a hospital setting and in a context of social and security instability. ***Patients and methods:*** This was a prospective and analytical study that took place in the Hepato-Gastroenterology Department of the Gabriel TOURE University Hospital over a period of two years and included all patients hospitalized for digestive hemorrhage. These patients had benefited from the research of sociodemographic characteristics, the notion of taking non-steroidal anti-inflammatory drugs (dose and duration), a physical examination and a digestive endoscopy. ***Results:*** At the end of this study, 78 cases of non-steroidal anti-inflammatory drug use out of 210 patients hospitalized for digestive hemorrhage were recorded, i.e. a frequency of 37.1%. The mean age of our patients was 47.01±19.3 years with a sex ratio of 2.9. Housewives and farmers represented 28.2% and 20.5% respectively. Hematemesis was the reason for consultation in 71.8%. Digestive hemorrhage and smoking were the most common antecedents. Diclofenac was the most commonly used drug in 53.9% of cases, with bleeding occurring in the first week after taking the non-steroidal anti-inflammatory drug in 53.9% of cases. Signs of hypovolemic shock were frequently found. The GD ulcer was the cause found in 66.2% of cases. Hemorrhage occurred significantly (p=10-8) in the first week of taking non-steroidal anti-inflammatory drugs and was significantly associated with NSAID use. There was no statistically significant difference in the occurrence of death between the molecules. ***Conclusion:*** NSAID-induced GI bleeding in adults is one of the major GI emergencies and remains an important cause of morbidity and mortality.

Keywords: Digestive hemorrhage, Non-steroidal anti-inflammatory drug, Emergency-Mali.

1. INTRODUCTION

Digestive hemorrhage (HD) in adults is one of the main digestive emergencies and remains an important cause of morbidity and mortality. The action of non-steroidal anti-inflammatory drugs (NSAIDs) on the intestinal mucosa is mainly through the inhibition of cyclooxygenase, thus reducing the synthesis of prostaglandins [1]. It is a frequent reason for emergency room visits and the most frequent causes are peptic ulcer and rupture of esophageal varices [2]. One third of patients hospitalized for upper GI bleeding in France were taking NSAIDs [3]. Intestinal complications of NSAIDs account for 10 to 40% of all severe digestive complications associated with the use of these drugs [1]. In Great Britain and France, NSAID-related gastroduodenal bleeding is responsible for 500 to 2000 deaths per year [3]. In an African multicenter study in 2010 on upper GI bleeding, aspirin and NSAIDs accounted for 12.5% and 11.7% of the factors promoting this bleeding, respectively [4]. In Togo and Morocco in 2012, NSAID use was found in 17% and 25.9% of patients with upper GI bleeding, respectively [2]. In a previous study in Mali, a notion of taking NSAIDs was reported in 6.3% of cases of upper GI bleeding [5]. Self-medication and the failure of drug control measures in our country prompted us to undertake this work with the objective of studying the role of NSAIDs in the occurrence of GI bleeding in the

hepato-gastroenterology department in a context of social instability.

2. PATIENTS AND METHODS

This was a prospective and analytical study over two years (from July 2019 to July 2021) that took place in a Hepato-Gastro-Enterology service in Bamako. It focused on patients hospitalized for digestive hemorrhage confirmed by the presence of blood in feces (vomit or stool) and or by the finding of blood in the digestive tract during endoscopy in patients who took NSAIDs. Patients with GI bleeding who had not taken NSAIDs in the three months preceding the occurrence of the bleeding were not included in the study. The interview sought the patient's sociodemographic characteristics (age, sex, occupation, marital status), the patient's history, the circumstances of the bleeding, risk factors such as the use of NSAIDs, tobacco, alcohol and other drugs, the dose and duration of NSAID use. Physical examination looked for altered general condition, signs of hemodynamic shock (decreased blood pressure, increased heart rate, cold sweats, state of consciousness), hepatosplenomegaly, collateral venous circulation (CVC), ascites, red blood and melanin stools, and pathology of other organs. A complete blood count (CBC), rhesus typing, blood ionogram, and creatinine to assess the impact of the hemorrhage; a transaminasemia to assess liver damage; and a prothrombin level (PT) to assess hepatocellular function were performed. Digestive endoscopy was performed to search for the cause of the hemorrhage and an abdominal ultrasound to search for associated or underlying pathology.

All patients were informed of the nature of the study and their verbal consents were required for inclusion. Data were collected on a survey form and analyzed with Epi info 7.2 software. The chi-square test was used to compare our results, which were significant at a probability of $p < 0.05$.

3. RESULTS

At the end of this study, 1526 patients were hospitalized, including 210 patients for digestive hemorrhage, i.e., a frequency of 13.8%, among whom 78 (37.1%) had taken NSAIDs. The mean age of our patients was 47.01± 19.3 years with extremes of 12 and 86 years and a sex ratio of 2.9. Housewives, Farmers and Workers were the most affected socio-professional strata with respectively 22/78 (28.2%), 16/78 (20.5%) and 15/78 (19.2%). The majority of these patients (71.8%) had consulted for haematemesis within a mean period of 4.69 ± 6.7 days (extreme from 1 to 30 days) and this haemorrhage occurred significantly within the first week (p= 10-8) and after the third week (p= 0.001) of taking the NSAID. A history of GI bleeding and smoking was found in 15.4% and 12.8% of patients respectively. More than half (53.9%) of our patients had taken diclofenac (see Table 1). The reason for taking NSAIDs was dental pain and aches in 35.9% and 21.8% of cases respectively (see Table 2). Pallor, melena and signs of hypovolemic shock were the most common (73.1%, 61.5% and 61.5%). Hepatic cytolysis and increased creatinine levels were found associated with anemia in 28.1% and 37.1% of our patients respectively. Gastrointestinal bleeding occurred in the same week as drug intake in 53.9% of cases and was significantly associated with diclofenac and aspirin intake (p= 4 10-7 and 2 10-6) (Cf. Table 3). Peptic ulcer disease (PUD) was found in 66.2% of cases (see Table 4) and was significantly associated with the use of diclofenac, aspirin and ibuprofen (p= 10-8, 0.0003 and 0.0015 respectively). The use of all NSAIDs was significantly associated with the occurrence of hematemesis. Bleeding was stopped in 64 patients, i.e. 82.1% of cases. The overall mortality was 12.8%. We found cases of death by hemorrhagic shock in patients who took diclofenac and ibuprofen without any statistically significant difference (p= 0.23).

Table 1: The molecules

molecules	Workforce	Percentage%
Diclofenac	**42**	**53,9**
Acetylsalicylic acid (aspirin)	18	23,1
Ibuprofen	11	14,1
Piroxican	4	5,1
Ketoprofen (profenid)	3	3,8
total	78	100

Table 2: Reason for NSAID use

Reason for taking NSAIDs	Workforce	Percentage (%)
Dental pain	**28**	**35,9**
Curvature	**17**	**21,8**
Abdominal pain	11	14,1
Lumbar pain	7	8,9
Hemorrhoidal crisis	5	6,4
Influenza	3	3,8
Panaris	2	2,6

Reason for taking NSAIDs	Workforce	Percentage (%)
Arthrose	1	1,3
High blood pressure	1	1,3
L1, L2, L3 fracture	1	1,3
Appendicitis	1	1,3
Trauma to left knee	1	1,3
Total	78	100

Table 3: Occurrence of hemorrhage in relation to the molecule

Delays (days)	≤7j	8-14	15-21	>21	Total	*Statistical test*
molecules	Workforce (%)	Workforce (%)	Workforce (%)	Workforce (%)	Workforce (%)	*P*
Diclofenac	22 (28,2%)	05 (6,4%)	0 -	15 (19,2%)	42 (53,8%)	*0,0000004*
Acetylsalicylic acid (aspirin)	14 (17,9%)	02 (2,6%)	0 -	02 (2,6%)	18 (23,1%)	*0,000002*
Ibuprofen	06 (7,7%)	01 (1,3%)	01 (1,3%)	03 (1,3%)	11 (14,1%)	*0,0973*
Piroxican	0 -	0 -	03 (3,8%)	01 (1,3%)	04 (6,4%)	
Ketoprofen (profenid)	0 -	0 -	02 (2,6%)	01 (1,3%)	03 (3,8%)	

Table 4: FOGD results

FOGD results	Workforce	Percentage (%)
GD Ulcer	**45/68**	**66,2**
VO/VCT	10/68	14,7
Erythematous Gastritis	06/68	8,8
Esophagitis	03/68	4,4
No lesions	04/68	5,9

* Esogastroduodenal endoscopy was not performed in 10 patients. VO: esophageal varicose vein. VCT; cardio-tubercular varicose vein

4. DISCUSSION

This study, prospective and analytical over two years, allowed us to collect 78 cases of NSAID use out of 210 patients hospitalized for HD, i.e. a frequency of 37.1%. This result is underestimated because some patients could consult traditional practitioners before referring to our structure. Our patients did not benefit from the search for Helicobacterpylori in the acute context of GI bleeding, nor did some of our patients benefit from endoscopy. However, this sample allowed us to analyze the characteristics of HD in the context of NSAID use.

The frequency of HD by NSAID in our study was 37.1%. This result is higher than those of Diarra *et al*., [6], Bardou *et al*., [7] and Levy *et al*., [3] who reported respectively 27.2%, 9% and 30%. This difference could be explained by a difference in sampling.

The mean age of our patients was 47.01 ± 19.3 years, comparable to the results reported by Razafimahefa *et al*., in Madagascar [8], Samlani Sebbane *et al*., in Morocco [9], and Bagny et al in Togo [2], which were respectively 45 years; 48 years and 49 years.

In our study, men were more affected with a sex ratio of 2.9. This finding was made by Razafimahefa *et al*., in Madagascar [8], Samlani Sebbane *et al*., in Morocco [9] who reported respectively 3.42 and 1.8.

Housewives and farmers each accounted for 28.2% and 20.5%. Diarra *et al*., [6] also reported a predominance of farmers and housewives with respectively 43.2% and 25.6%. This finding of predominance in the disadvantaged socio-professional strata can be explained by the daily activities tending to favor the intake of NSAIDs.

In our study, hematemesis was the reason for consultation in the majority of cases (71.8%). This same finding was made by Hagège et al (75%) [4], El Mekkaoui *et al*., (79.6%) [16] and Doumbia *et al*., (92.2%) [11].

Patients were hospitalized within the first week of HD onset in 76.9% of cases. This early hospitalization was reported by Doumbia *et al*., [11].

More than half of our patients had taken Diclofenac. This finding confirms that of Menu *et al*., [12] in a study on the prescription of NSAIDs stating that 68% of prescriptions were for short-lasting NSAIDs. Crickx reported that acetylsalicylic acid is the most commonly used first-line drug, the antiaggregant effect being obtained with doses lower (75 to 325 mg/d) than those required for its anti-inflammatory activity (500mg to 3g/d) [13].

The HD in our study occurred within the first week of taking the NSAID. This may be explained by the nature of the NSAIDs (short shelf life), consumed by our patients.

In our study, 35.9% and 21.8% of patients took NSAIDs for dental pain and aches, respectively, whereas Menu *et al*., [12] reported that osteoarthritis was the first indication (52%) for the prescription of an NSAID.

Signs of hemodynamic shock such as pallor, arterial hypotension and tachycardia were found respectively in 73.1%, 61.5% and 53.8% of our patients. Dicko *et al*., [5] found dizziness, arterial hypotension and tachycardia in 54% of cases, 38.1% of cases and 47.6% of cases respectively. In these two studies, we note the frequency of signs of hemorrhagic shock.

In our study, GD ulcer accounted for 66.2% of the causes of hemorrhage. Our result is significantly higher than those of Razafimahe faetal [8] and Samlani Sebbane *et al*., [9] which were 35.6% and 16% respectively. The involvement of NSAIDs in the pathophysiology of GD ulcer and its bleeding complication could explain this finding.

The majority of our patients (80.8%) had been treated with PPI. This attitude is explained by the number of GD ulcer.

Hemorrhagic recurrence was found in 17.9% of cases, higher than the study of Hagège *et al*., [4] which was 5.4%.

Mortality was 12.8% in our study. This mortality is higher than that reported by Hagège *et al*., [4] which was 5.1% but lower than those reported by Samlani Sebbane *et al*., [9] and Doumbia *et al*., [11] which were respectively 22.4% and 23.4%. These differences can be explained by methodological differences.

In our study, we recorded 10 cases of death while taking Diclofenac and Ibuprofen without statistically significant difference (p=0.23).

Study limitations

- Frequency of digestive bleeding is underestimated by the fact that patients prefer to consult traditional healers before consulting a medical facility;
- Not all our patients had a digestive endoscopy;
- Our patients did not benefit from the search for helicobacter pylori.

CONCLUSION

Adult HD is one of the main digestive emergencies and remains an important cause of morbidity and mortality. The young age of our patients and the representative frequency of male gender are regularly reported in our setting. Hematemesis was the main reason for consultation. Diclofenac was the NSAID most responsible for hematemesis. Mortality was due in most cases to hemorrhagic shock. Preventive measures are necessary to reduce the impact of NSAIDs on the health of our populations.

Links of interest: The author and co-authors declare no links of interest in relation to this work.

Author contributions: the authors have all read this work and made contributions.

Acknowledgments: We thank all the patients who agreed to be included in this work and a pious thought to the deceased patients.

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