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ORIGINAL ARTICLE

NSAIDS Induced Acute Gastric Perforation

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Abstract

Background: Acute gastric perforation (AGP) is a sudden and severe emergent condition with increased morbidity and mortality from associated peritonitis and systemic derangements. Non-steroidal anti-inflammatory drugs (NSAIDs) are known to cause of this disease. Most patients with AGP present late to hospital and require prompt correction of metabolic derangements and urgent surgical repair of the perforation and treatment of associated peritonitis.

Aim: To audit and characterize patients with a clinical and operative diagnosis of NSAIDs induced acute gastric perforation.

Methods: A prospective observational study of patients presenting in the emergency room with acute abdomen and a clinical diagnosis of NSAIDs induced gastric perforation, confirmed intra-operatively. Information was analysed with SPSS 17 (SPSS Statistics for Windows, Chicago, USA) using descriptive statistics and presented as percentages and tables.

Result: There were 16 patients diagnosed with NSAIDS induced gastric perforation, 14 males (87.5%) and 2 females (12.5%). Twelve (68%) cases occurred at 50 years and below. One patient underwent reoperation for failed repair. Six deaths (37.5% mortality) were recorded. All the patients presented in shock with deranged biochemical parameters. The perforations were in the gastric antrum. Peritonitis was common.

Conclusion: Gastric perforation from NSAIDs is an important differential of acute abdomen, affecting predominantly males in Uyo, with nearly 80% involving young and middle-aged individuals. Acute kidney injury is a common association.

Keywords: Acute gastric perforation, NSAIDs, Renal injury, High morbidity.

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Introduction:

Acute gastric perforation (AGP) is characterized by a sudden excruciating epigastric pain which is vividly described in time and severity by the patient. Leakage of gastric contents into the peritoneal cavity often sets in motion a spectrum of local and systemic pathological events leading to generalised abdominal pain from chemical peritonitis, shock from significant third space fluid loss, renal and respiratory insufficiency. Sepsis presents later. The morbidity and mortality could be aggravated in the scenario of delayed presentation for care, rapid physiological derangement, presence of concomitant morbidity and delayed treatment.[1, 2]

Gastric ulcers are a common cause of perforation, but with current potent proton pump inhibitors (PPI), the incidence of gastroduodenal complications like bleeding and perforated gastric ulcer is low,[3,4] while increasingly, the role of nonsteroidal anti-inflammatory drugs (NSAIDs) as an independent risk factor for gastric perforation is becoming pronounced.[5] NSAIDs are cheap, widely available over the counter, unregulated and may be dispensed by non-qualified persons in many low- and medium-income economies. It is common practice in Nigeria to request for “pain tablets mixture" from a drug seller as typified by the contents of a patient’s drug bag (Fig. 1). These drug combinations often contain different NSAIDs of same class resulting in these drugs being taken at higher doses. Acute gastric perforation may also occur in severe burns, oral herbal remedies[6], sepsis, chemotherapy, multiple injuries and malignancy.[7]

This study examines the characteristics of patients who developed gastric perforation after ingesting different types of non-steroidal anti-inflammatory agents.

Type of study: A cross-sectional observational study of patients presenting in the emergency room with acute abdomen with an intra-operative diagnosis of acute gastric perforation.

Setting: A general surgery and nephrology unit in a tertiary hospital in Nigeria.

Inclusion: All adult patients with a clinical diagnosis of NSAIDs induced acute gastric perforation confirmed at laparotomy.

Exclusion: Gastric and duodenal perforation in known peptic ulcer patients on therapy, perforations not related to NSAIDs and patients without operative diagnosis of gastric perforation.

Ethical approval: Approval was obtained from the local institutional health research ethical committee.

Methods: Records of patients diagnosed with gastric perforation (by clinical and radiological evaluation) in the emergency room were captured in a prepared format. Each patient had a minimum of full blood count (FBC), urea, electrolytes and creatinine (UEC) estimation, abdominal X-ray to include lower chest or chest X-ray to include the upper abdomen and grouping and cross matching of blood.

Each patient received fluid resuscitation to achieve a urine output ≥50ml/hour and normal UEC values. Cases where the creatinine, urea and potassium levels were above 700 mmol, 7mmol, and 5.0 mmol respectively (AKI) were reviewed by a nephrologist and underwent haemodialysis prior to surgery. Intravenous antibiotics were administered. Each patient underwent

a midline exploratory laparotomy with excision of the ulcer margins and simple closure of the gastric perforation. Peritoneal lavage with warm saline was done.

Information obtained were age, sex, intraoperative oxygen saturation and diagnosis, volume of intra-abdominal fluid collection, deranged UEC, oxygen saturation and final disposition of patients. The contents of patient's drug bags (where available) and radiographs were also documented. All patients were followed till discharge, death or second postoperative clinic visit.

Data analysis was done with SPSS 17 (SPSS Statistics for Windows, Chicago, USA) using descriptive statistics and presented as tables.

Result:

Sixteen cases of NSAIDs induced gastric perforation were recorded over twelve months. There were 14 males (87.5%) and 2 females (12.5%) [Table 1.] Twelve (68%) cases occurred at 50 years and below. Five (31.3%) cases occurred in the 41– 50 age group, 3 (18.1%) in 31 - 40 age group, 3 (18.1%) in 20-30 group. The reason for ingesting these medications was to treat musculo-skeletal pain.

All patients presented in shock (Table 2) and had deranged initial UEC values; three underwent two to three sessions of haemodialysis before surgery. Free air underneath the diaphragm was a common radiological finding. The perforations were located anteriorly in the gastric antrum. The average free peritoneal fluid volume was 2.4L. Histology of the ulcers were benign with inflammatory changes. One patient underwent reoperation for failed repair. Six deaths (37.5% mortality) were recorded.

Discussion

Acute gastric perforation is a severe surgical emergency requiring urgent intervention.[8] The presence of acid in the peritoneal cavity elicits a brisk chemical peritonitis leading to markedly deranged fluid and electrolytes status. Systemic inflammatory responses are also triggered with implications on respiratory function. Failure to institute early and appropriate resuscitation and treatment worsens the outcome and increases the probability of mortality. This study shows NSAIDs induced gastric perforation to be a disease of males in our practice, with a peak in the 41-50 years age group. Similar findings are reported by researchers working on peritonitis complicating gastro-intestinal perforations in India.[9, 10] We observed an association with either alcohol or cigarette use among the young.

NSAIDs are a class of drugs commonly taken by the general population because of

their analgesic, anti-inflammatory and antipyretic effects.[11] They include aspirin, diclofenac, ibuprofen and piroxicam. They are cheap, freely available over the counter and easily subject to abuse. All patients in this study obtained the drugs without prescription or continued refilling an original prescription in a drug store and were unaware of the active agents in the drugs and often took a combination of agents containing the same active molecule (Figure 1), culminating in overdose. The primary reasons they took these drugs was for musculoskeletal pain relief.

Complications of NSAIDs on the gastrointestinal system include bleeding gastric and duodenal ulcers, and to a lesser degree, perforation and obstruction; these events occurring irrespective of the drugs being obtained through prescription or over the counter. NSAIDS act by inhibiting cyclooxygenase-1(COX-1) in the gastric mucosa resulting in the suppression of prostaglandin (PG) synthesis resulting in PG mediated hypersecretion of acid, decreased mucus and bicarbonate secretion, and decreased mucosal blood flow.[12] The risk of gastric perforation is dose dependent; ingestion of high doses of the drug over a short time period increases the risk of gastric perforation.[13] Our patients invariably ingested an overdose of a combination of different NSAIDs over a short duration and so easily developed gastric perforation and acute kidney injury (AKI)[14, 15]

The diagnosis of gastric perforation from NSAIDs can be made from the history and examination.[16] Our patients presented with a sudden excruciating epigastric pain which subsequently became generalised and doubled up the patients with guarding, tenderness and subsequently all developed abdominal distension. Usually, patient is in shock and this was characteristic of our patients (Table 2). Urinary output may gradually decrease with time. An upright chest radiograph to include the upper abdomen will show free air under the diaphragm (Figure 2) in approximately 70% of cases.[17] In this study, all the X-rays showed variable amounts of air under the diaphragm. Abdominal CT scan[18] or upper gastrografin series may be indicated in cases where the diagnosis is difficult to make.

Biochemical and haematological parameters (excepting leucocytosis) were normal in the early period post perforation but become deranged as a response to systemic inflammatory reaction and acute kidney injury. Electrolytes abnormalities and varying degrees of acute kidney injury were common. The patients required fluid replacement to correct biochemical deficits while three were unresponsive to these measures and underwent sessions of haemodialysis and the definitive procedure done immediately after dialysis. One patient required postoperative haemodialysis. There were no known peculiarities in those who required dialysis excepting the abnormally raised serum creatinine, urea and potassium.

We relied on the World Society for Emergency Surgery (WSES) guidelines on perforated and bleeding peptic ulcer.[19] All of the perforations occurred anteriorly in the gastric antrum (Fig 3) and the defects

did not exceed 2cm. We routinely adopt the operative approach because our patients had peritonitis and required lavage of the infective materials from the peritoneum. We excised the margins of the perforation and sent same for histological assessment followed by simple closure of the defect (Fig. 4); application of omental patch was not routine. Proton pump inhibitors were started in the emergency room and continued upon discharge and patient dissuaded from further patronage of over-the-counter pain medicines. Definitive procedures like truncal vagotomy and drainage or gastric resection may be considered for physiologically stable patients[20] but are not in common practice.[21]

The mortality of 37.5% we had was considered high when compared to 11% reported by Dakubo et al.[22] The common reasons for the high mortality in our patients were delayed surgery, low saturation (< 92% on 100% oxygen), creatinine levels higher than 700mmol/l, and re-operation after a failed closure. Only one patient underwent laparotomy and closure of the perforation within 24 hours of symptoms; the delays to operation were due to wrong diagnosis and/ or late referrals from the primary hospitals of presentation or difficulties with transportation especially from communities with poor access. The patient with persistently low oxygen saturation was a smoker and his initial repair failed necessitating a second repair.

Limitations: We did not investigate concomitant ingestion of herbal remedies by the patients; these remedies are very popular in the locality of study. Most herbal remedies for pain contain alcohol and other gastric irritants which can contribute to gastric perforation. Also, the small number of patients in this study makes our conclusion not generally applicable.

Conclusion: NSAIDs induced gastric perforation predominantly affects males and requires prompt operative management. Severe biochemical derangements, low oxygen saturation and re-operation are associated with mortality.

Figure 1: Typical contents of a patient's drug bag containing multiple brands of NSAIDS.

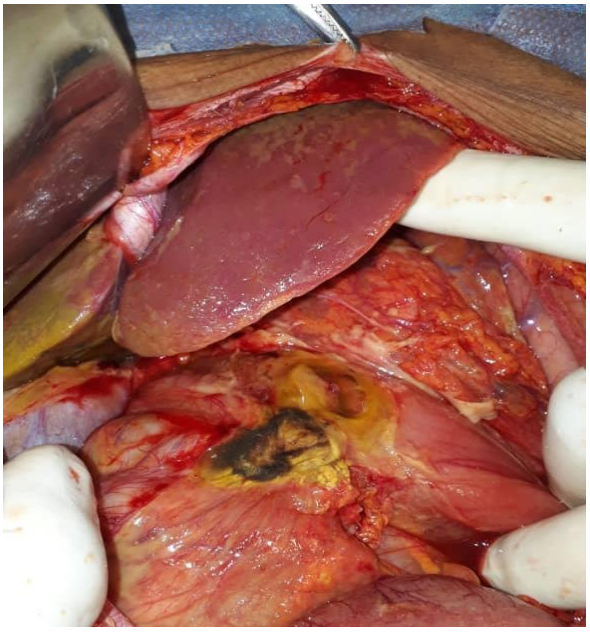

Figure 3: Bile-stained tissue around the site of perforation in the anterior aspect of the gastric antrum. There was approximately 3L of infected fluid in the peritoneum.

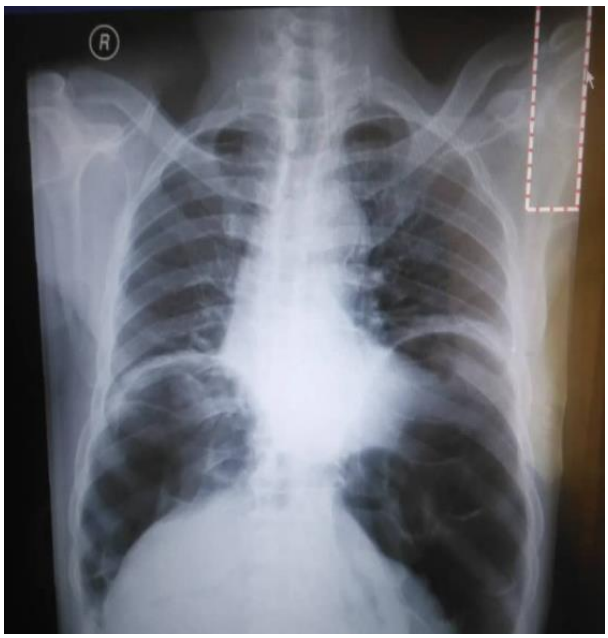

Figure 2: X-ray showing massive bilateral air under the diaphragm in a patient with gastric perforation.

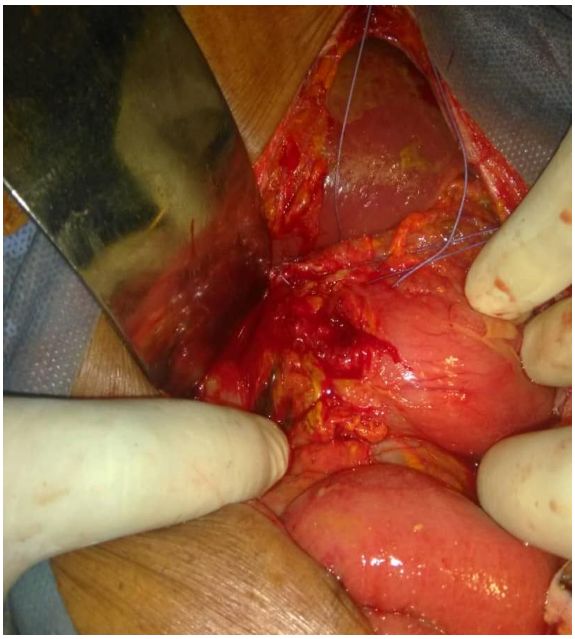

Figure 4: Simple closure of an anterior perforation in the gastric antrum being done after excising the margin.

Table 1: Characteristics of patients with clinical and operative diagnosis of NSAIDs induced gastric perforation.

Characteristics	Number (%) n=16
Gender	
Male	14 (87.5)
Female	2 (12.5)
Age group	
20-30	3 (18.1)
31-40	3 (18.1)
41-50	5 (31.3)
51-60	2 (12.5)
61-70	1 (6.3)
71-80	0 (0)
≥81	2 (12.5)
Other factors	
Alcohol	6 (37.5)
Cigarette smoking	4 (25.0)
Presentation	
Shock	16 (100)
Creatinine ≥ 700mmol/L	3 (18.1)
Oxygen saturation <92%	1 (6.3)
Duration (hours)	
24	1
25 - 48	4
49 - 72	2
> 72	7
Re-operation	1 (6.3)
Final outcome	
Alive & discharged	10 (62.5)
Dead	6 (37.5)

Table 2: Vital signs of patients diagnosed with NSAID induced gastric perforation.

Parameter	Frequency (%)
Pulse (beats/minute)	
< 80	2 (12.5)
81 – 100	2 (12.5)
101-120	5 (31.3)
> 120	7 (43.7)
Blood Pressure (mmHg)	
<100/60	6 (37.5)
100/60 – 120/80	9 (56.3)
> 120/80	1 (6.2)

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