AstraZeneca

Non-interventional study report Synopsis

Study code	NIS-GRU-NEX-2009/2
Version No:	1.0
Date:	February 24, 2012

Study of incidence of drug-induced upper gastrointestinal (GI) bleeding

Time of study:
From June 21, 2010 to June 06, 2011

First patient enrollment: June 21, 2010

Last patient completion: June 06, 2011

AstraZeneca

REPORT SYNOPSIS

Study of incidence of drug-induced upper gastrointestinal (GI) bleeding

TIME OF STUDY

First patient enrollment: June 21, 2010

Last patient completion: June 06, 2011

STUDY SITES

This study was conducted in the Russian Federation. Six study sites participated in the study. Three hundred patients were enrolled.

STUDY OBJECTIVES

Primary objective

The primary objective is to determine the incidence of drug-induced acute upper GI bleeding in Russian patients.

Secondary objectives

1. To evaluate the severity of drug-induced upper GI bleeding in Russian patients
2. To collect information about the treatment of drug-induced upper GI bleeding in the setting of routine clinical practice in Russia
3. To evaluate the prevalence of gastroprotector therapy use in patients with upper GI bleeding and different risk factors who required this therapy
4. To evaluate the overall risk of fatal outcomes induced by upper GI bleeding in patients with different risk factors

STUDY DESIGN

This study was a non-interventional study, i.e., patients were not subjected to additional diagnostic or monitoring procedures exceeding the bounds of routine practice.

This is a multicenter, observational, prospective study designed for evaluation of the incidence of drug-induced upper GI bleeding in Russian patients, and for obtaining representative information about the treatment of this condition in routine clinical practice.

This observational, prospective study was based on collection of data from two examinations of each inpatient. The study physician collected data for all patients diagnosed with acute upper GI bleeding. Patients were eligible to be included in the study only if they gave their consent and signed the informed consent document after discussing objectives and methods of the study with the investigator.

From the beginning and until the end of the study, the study physician included admitted patients diagnosed with upper GI bleeding, who had been examined by him/her and met appropriate inclusion criteria.

Data collection was performed on admission of a patient diagnosed with acute upper GI bleeding and before the patient discharge from the hospital, after a course of routine therapy for this condition with medications or a surgical or endoscopic intervention.

CRITERIA FOR SELECTION OF PATIENTS

Participants of the study were patients admitted to a hospital with symptoms of upper GI bleeding and inpatients who developed GI bleeding during the period of hospitalization for another disease.

Inclusion criteria

Study participants met the following criteria:

1. Had established diagnosis of acute upper GI bleeding documented by symptoms, such as blood vomiting / “coffee ground” vomiting, melena and clinical or laboratory signs of acute hemorrhage.

2. Had given written informed consent before the onset of participation in this study.

Exclusion criteria

Patients were not included in the study if they met any of the following criteria:

1. Were unable or unwilling to sign the informed consent document.

CRITERIA FOR EVALUATION

Primary outcome measures

1. Number (n) and percentage (%) of patients with drug-induced upper GI bleeding.

Secondary outcome measures

1. Number (n) and percentage (%) of patients with each Forrest class of upper GI bleeding.

2. Number (n) and percentage (%) of patients with each symptom of gastro-intestinal bleeding (for example, “coffee ground” vomiting, melena, etc.)

3. Number (n) and percentage (%) of patients with each bleeding outcome (successful arrest of bleeding, recurrent bleeding, death)

4. Number (n) and percentage (%) of patients currently receiving or having received within one month prior to inclusion in the study different NSAIDs, antiplatelet agents, anticoagulants, combination therapy with NSAID plus antiplatelet agents/anticoagulants, NSAID plus corticosteroids, or antiplatelet agents/anticoagulants plus corticosteroids.

5. Number (n) and percentage (%) of patients currently taking gastroprotectors.

6. Number (n) and percentage (%) of patients with each concomitant disease contributing to upper GI bleeding (such as IHD, rheumatic diseases, etc.).

7. Number (n) and percentage (%) of patients receiving each type of haemostatic therapy for GI bleeding including endoscopic hemostasis, surgery, conservative therapy (antisecretory agents, plasma or packed red cell transfusion, etc.).

Secondary outcome measures included regression analysis of the interaction between outcomes of upper GI bleeding and the following demographic characteristics / risk factors: age; sex; concomitant diseases, therapy with NSAIDs, anticoagulants, antiplatelet agents and corticosteroids; gastroprotector therapy; patient status (admitted for GI bleeding or inpatient having developed GI bleeding during his/her stay in the hospital for another disease); endoscopic Forrest class of bleeding; bleeding severity.

PATIENT POPULATIONS FOR ANALYSIS

Three hundred patients were included in statistical analyses.

.

SOCIAL AND DEMOGRAPHIC CHARACTERISTICS AND BASELINE VARIABLES

Most patients participating in the study were males (66.00%). Mean age was 54±18 years (from 20 to 98). 295 patients (98.33%) were caucasian. Most patients (36.00%) worked; 22.33% of patients were retirees, and 18.33% of patients were jobless. The least percentage of patients (2.00%) was students.

More than a half of study participants had pernicious habits that might promote upper GI bleeding [3]: 52.67% of patients were smokers (or stopped smoking less that one year ago);

59.33% consumed alcohol (14.33% abused alcohol); 19.73% of patients had more than 1 cup of coffee daily (median 3 cups daily).

SUMMARY OF RESULTS

1. Primary outcome measure. 123 patients (41.00% of study population) had upper GI bleeding induced by drugs including NSAIDs (acetylsalicylic acid, ketorolac, metamizole sodium, nimesulide, diclofenac, paracetamol, meloxicam, ketoprofen), prednisolone, and metotrexate.

2. Secondary outcome measure. Number and percentage of patients with different Forrest classes:

    - 7 patients (2.33% of study population) had Forrest IA class upper GI bleeding;
    - 18 patients (6.00% of study population) had Forrest IB class upper GI bleeding;
    - 18 patients (6.00% of study population) had Forrest IIA class upper GI bleeding;
    - 20 patients (6.67% of study population) had Forrest IIB class upper GI bleeding;
    - 66 patients (22.00% of study population) had Forrest IIC class upper GI bleeding;
    - 6 patients (2.00% of study population) had Forrest III class upper GI bleeding;
    - 165 patients (22.00% of study population) had unidentified Forrest class upper GI bleeding.

3. Secondary outcome measure. Number and percentage of patients with different symptoms of gastrointestinal bleeding:

    - 89 patients (29.67% of study population) had a GI bleeding symptom of “blood vomiting”;
    - 86 patients (28.67% of study population) had a GI bleeding symptom of “coffee grounds” vomiting;
    - 122 patients (40.67% of study population) had a GI bleeding symptom of “black stools”;
    - 66 patients (22.00% of study population) had a GI bleeding symptom of “melena”;
    - 6 patients (2.00% of study population) had a GI bleeding symptom of “blood in stool”;
    - 54 patients (18.00% of study population) had GI bleeding with signs of hypovolemia (shortness of breath, tachycardia, pale skin);

- 144 patients (48.00% of study population) had other GI bleeding symptoms.

4. Secondary outcome measure. Number and percentage of patients with different outcomes of GI bleeding:

    - 274 patients (92.26% of population for statistical analyses) had successful bleeding arrest;
    - 16 patients (5.38% of population for statistical analyses) had fatal outcomes of bleeding;
    - 7 patients (2.36% of population for statistical analyses) had rebleeding;

5. Secondary measure. Number and percentage of patients who received drugs contributing to upper GI bleeding:

    - 76 patients (25.33% of study population) received NSAIDs;
    - 49 patients (16.33% of study population) received antiplatelet agents;
    - 18 patients (6.00% of study population) received anticoagulants;
    - 4 patients (1.33% of study population) received a combination therapy (NSAIDs plus antiplatelet agents/anticoagulants;
    - 1 patient (0.33% of study population) received a combination therapy with NSAIDs plus corticosteroids;
    - None of patients received combination therapy with antiplatelet agents / anticoagulants plus corticosteroids).

6. Secondary outcome measure. Number and percentage of patients currently receiving gastroprotectors:

    - 28 patients (9.33% of study population) were taking gastroprotectors at the time of inclusion;
    - 284 patients (94.67% of study population) took gastroprotectors as a therapy for upper GI bleeding.

7. Secondary outcome measure. Number and percentage of patients with different co-morbidities promoting upper GI bleeding:

    GI co-morbidities

    - 108 patients (36.00% of study population) were diagnosed with gastric / duodenal ulcer;
    - 24 patients (8.00% of study population) were diagnosed with varix dilatation;

- 8 patients (2.67% of study population) were diagnosed with GI tumor/polyp;
- 39 patients (13% of study population) were diagnosed with GI bleeding;
- 6 patients (2.00% of study population) were diagnosed with mucosal tear (Mallory-Weiss syndrome);
- No patients were diagnosed with nonspecific ulcerative colitis or Crohn's disease.
- 42 patients (14.00% of study population) had other GI co-morbidities.

Joint and spine co-morbidities

- 27 patients (9.00% of study population) were diagnosed with osteoarthritis;
- 6 patients (2.00% of study population) were diagnosed with rheumatoid arthritis;
- 5 patients (1.67% of study population) were diagnosed with gout;
- 3 patients (1.00% of study population) were diagnosed with reactive arthritis;
- 55 patients (18.33% of study population) were diagnosed with dorsopathy;
- 10 patients (3.33% of study population) were diagnosed with other joint and spine diseases;
- No patients were diagnosed with ankylosing spondylitis.

Circulatory co-morbidities

- 63 patients (21.00% of study population) were diagnosed with IHD (exertional angina; history of myocardial infarction; post-infarction cardiac sclerosis);
- 22 patients (7.33% of study population) were diagnosed with cerebrovascular disease (acute/chronic cerebral ischemia; acute impairment of cerebral circulation; ischemic stroke.

Urogenital co-morbidities

- 1 patient (0.33% of study population) was diagnosed with chronic glomerulonephritis;
- 13 patients (4.33% of study population) were diagnosed with urolithiasis.

8. Secondary outcome measure. Number and percentage of patients who received different types of therapy for upper GI bleeding

    - 90 patients (30.00% of study population) received endoscopic hemostasis; infiltration of the bleeding area was performed in 53 patients (17.5% of study population). Coagulation was performed in 45 patients (15.00% of study

population). Clipping was not performed in any study patients. 31 patients (10.33% of study population) received other types of endoscopic hemostasis;

- Surgery was performed in 23 patients (7.67% of study population);

- 296 patients (98.67% of study population) received conservative therapy. 295 patients (98.33% of study population) received therapy with antisecretory agents. 90 patients (30.00% of study population) received fresh frozen plasma transfusion (median dose, 820 ml). 99 patients (33.00% of study population) received packed red cell transfusion (median dose, 2.85 units). 139 patients (46.33% of study population) received other types of conservative therapy.

9. Dependence of the upper GI bleeding outcome on different factors determined by the binary logistic regression analysis:

    - Age was a negative predictor for successful arrest of bleeding (p=0.046, OR = 0.966; 95% CI 0.934 – 0.999);

    - Presence of hypotension was a negative predictor for successful arrest of bleeding (p=0.004; OR = 0.123; 95% CI 0.029 – 0.519).