UNIVERSITY OF MEDICINE AND PHARMACY
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GHEORGHE NEAȚĂ

CURRENT DIAGNOSIS AND THERAPY STRATEGIES
IN THE NON-VARICEAL UPPER DIGESTIVE HAEMORRHAGES

DOCTORAL THESIS ABSTRACT

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MATERIAL AND METHOD

MOTIVATION AND OBJECTIVES

The acute UPPER DIGESTIVE HAEMORRHAGE is still a medico-surgical emergency commonly met with an estimated incidence of 100 to 100,000 adults. In the 80's, approximately 75 - 80% of patients with upper digestive haemorrhages caused by peptic ulcers needed surgical intervention, with a mortality rate of approximately 10% and those having variceal ulcers of up to 50%. There is more and more evidence indicating that the progress in the medical practice of the latest decades has also influenced the Upper Digestive Haemorrhages aetiology. The progress includes the introduction of the proton channels inhibitors, Helicobacter pylori removal with patients having peptic ulcer, prophylactic therapy for patients taking anti-inflammatory, non-steroidal (AINS) medication, more efficient treatments for patients having portal high blood pressure and use of endoscopy both for diagnosis and therapy purposes. Despite all that, their impact in the Upper Digestive Haemorrhages related incidence and mortality is still unclear.

At the same time with the introduction into the medical practice of the diagnosis and treatment currently using the upper digestive endoscopy, it was passed from the stage of the medicine based on the clinical and diagnosis sense of probability in upper digestive haemorrhage emergency cases to “the medicine based on evidence”, especially endoscopic ones. This assertion is perfectly valid in nonvariceal upper digestive haemorrhage cases.

The endoscopic era has indisputably achieved remarkable progress in putting an accurate aetiological diagnosis of certainty during the first 24 hours and at the same time it offers the possibility of an immediate conclusive or temporary haemostasis, depending upon the aetiology on over 90% of the cases, thus avoiding high risk unexpected and
unwanted surgical interventions and allowing the required time to prepare certain patients for whom the surgical intervention is required and advisable.

It is also difficult to believe that in a near future high performance diagnosis putting techniques should be developed or new therapeutic methods which might fundamentally change the prognosis of patients with upper digestive haemorrhage.

Therefore, mortality rate is to be lowered mainly by the existing means optimisation. For this current diagnosis and therapy strategy, there must be an indisputable scientific justification and the action sequencing must be based on the most logical, efficient and quick algorithm.

The thesis has in view the following objectives:
- overall research of the main causes of upper digestive haemorrhages, their morbidity and evolution incidence over the last twenty years, as well as of alteration spread of different therapeutic means, be it conservatory or surgical;
- morbidity alterations correlation through upper digestive haemorrhages with different demographic factors (gender, age groups, origin);
- structuring of patients with upper digestive haemorrhages by batches of research belonging to the preendoscopy period (batch A and B) and to the endoscopy period (batch C);
- research on the current strategies of diagnosis and treatment of nonvariceal upper digestive haemorrhages, on the batch of patients belonging to the endoscopy period, of its results by applying an algorithm accepted by the Surgery Clinics I and gastroenterology;
- influence of modern strategies of diagnosis and treatment over morbidity and mortality because of upper digestive haemorrhages;
- discussions regarding the own results as compared to the data in the literature;
- conclusions based on own research.

**CLINICAL MATERIAL**

There were submitted to research adult patients, over 20 years old and with upper digestive haemorrhage and grouped by different periods between 1991 and 2009, the proposed objectives being followed and compared.

The upper digestive haemorrhage was permanent the same with haematemesis, maelena or other doubtless evidence (rectal touch) proving blood loss at the level of the upper digestive tract from the level of the pharynx-oesophagus to the duodenal-jejunal angle (Treitz). All patients were hospitalized, were put a diagnosis and were treated in the Surgery Clinics I and Gastroenterology, Anaesthesia and Critical Care of Craiova.

The decision to hospitalise patients with upper digestive haemorrhage was made by the doctors’ teams doing rounds in the emergency ward after conferring with a surgeon specialist without using a risk stratification method, patients being hospitalised in the Surgery and Anaesthesia and critical Care ward for severe forms.

Then the submittal to research and grouping by batches criteria were:
- a doubtless diagnosis of upper digestive haemorrhage,
- the possibility of endoscopic diagnosis and treatment depending upon which batches were grouped by periods: preendoscopy and endoscopy.
The basic information about patients was retrospectively gathered from the monitoring charts of the U.P.U. (Emergency Ward), of surgery clinics, Anaesthesia and Critical Care unit and the endoscopic explorations register.

The methods of information gathering were similar for the 2 stages, except about endoscopy referring only to batch C.

The gathered data revealed information related to the time elapsed from diagnosis putting to hospital discharge or death, issues of the haemorrhage episode, associated diseases, use of non-steroidal medication or aspirin in the week before haemorrhage triggering.

Medical background, laboratory and endoscopic data, medical treatments, transfusions, persistent haemorrhage or its regress, surgical interventions or cause of death. For batch C (endoscopic) there were recorded the following additional data: use of other medication before haemorrhage triggering (corticoids anticoagulants, antisecretory and blocking medication for portal high blood pressure), varied comorbidities for ranking on the Rockall score, endoscopic interventions, hospitalisation duration, shock presence or absence, haemorrhage classification according to Forrest criteria.

The results of the haemorrhagic episodes were analysed in accordance with the haemorrhage persistence or its regress requiring transfusion and surgical intervention, hospitalisation duration and mortality within the hospital. Persistent and regressing haemorrhages were defined in accordance with the established criteria.

Over the preendoscopy period (1991 – 2001) the emergency surgical intervention caused a shock to patients with associated haemorrhage, while over the endoscopy period (2006 – 2009) the endoscopic therapy was applied from the very beginning, even if a new haemorrhage occurred. Blood transfusions were carried out when Hb cut-offs were decreasing under 8 – 9gr%.

Causes of death were major bleeding or other events in severe forms of upper digestive haemorrhage, old age and comorbidities.

**STATISTICAL RESULTS**

The incidence rates were calculated by applying a direct method in accordance with the analysed batch of patients.

Over the period 1991 – 2009 there were submitted to research (Table no. 5.1.) 1167 patients who in relation with the main causes were:

- **variceal upper digestive haemorrhages** 301 (25,74%) and
- **nonvariceal upper digestive haemorrhages** 866 (74,26%). Of this patients’ category the main causes were represented by duodenal and postoperative gastric peptic ulcers approximately 62%, as well as other causes 19,41% among which postmedication hemorrhagically erosive gastritis had a significant incidence of 9%.

<table>
<thead>
<tr>
<th>CAUSE</th>
<th>MONITORED PATIENTS’ NO.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper digestive haemorrhages</td>
<td>nonvariceal</td>
<td>866</td>
</tr>
<tr>
<td></td>
<td>variceal</td>
<td>301</td>
</tr>
</tbody>
</table>

**Table no. 5.1. Upper Digestive Haemorrhages Clinical Material 1991 – 2009**
Therefore, it is still obvious the nonvariceal upper digestive haemorrhages prevalence by peptic ulcers and other newer causes such as postmedication ulcer-haemorrhagic gastritis.

For a better pursuance of the proposed objectives – the large patients’ batch, depending upon the practice possibilities for diagnosis and therapy purpose of endoscopy, was assigned by two periods:
- the preendoscopy period which includes batches A and B (1991 – 2001);

By this patients’ grouping depending upon the diagnosis and therapy possibilities of the moment, we wished to highlight:
- the trend of the dynamic evolution of morbidity of the main causes triggering upper digestive haemorrhages, U.G.D. (Gastro-duodenal Ulcer) respectively and oesophageal varices. In ulcer cases, it has a decrease curve from 41,92% in 1995 to 33,72% in 2001 and then to 24,34% in 2009.

<table>
<thead>
<tr>
<th>Nonvariceal upper digestive haemorrhages</th>
<th>Total</th>
<th>1167</th>
<th>100</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.G. (Gastric Ulcer)</td>
<td>344</td>
<td>39.72</td>
<td></td>
</tr>
<tr>
<td>U.D. (Duodenal Ulcer)</td>
<td>340</td>
<td>39.26</td>
<td></td>
</tr>
<tr>
<td>Postoperative U.P. (Peptic Ulcer)</td>
<td>11</td>
<td>1.27</td>
<td></td>
</tr>
<tr>
<td>Other causes</td>
<td>171</td>
<td>19.74</td>
<td></td>
</tr>
<tr>
<td>Different haemorrhagically erosive gastritis</td>
<td>56</td>
<td>6.46</td>
<td></td>
</tr>
<tr>
<td>Medication haemorrhagically erosive gastritis (AINS, a.s.o.)</td>
<td>65</td>
<td>7.50</td>
<td></td>
</tr>
<tr>
<td>Gastric cancer</td>
<td>13</td>
<td>1.50</td>
<td></td>
</tr>
<tr>
<td>Mallory Weiss Syndrome</td>
<td>10</td>
<td>1.15</td>
<td></td>
</tr>
<tr>
<td>Gastric polyp</td>
<td>3</td>
<td>0.34</td>
<td></td>
</tr>
<tr>
<td>Iatrogenous</td>
<td>4</td>
<td>0.46</td>
<td></td>
</tr>
<tr>
<td>No case known</td>
<td>30</td>
<td>3.46</td>
<td></td>
</tr>
</tbody>
</table>

Table no. 5.2. Morbidity Evolution because of U.G. (Gastric Ulcer) and U.D. (Duodenal Ulcer)

<table>
<thead>
<tr>
<th>BATCH</th>
<th>U.G. (Gastric Ulcer)</th>
<th>U.D. (Duodenal Ulcer)</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Monitored patients’ no.</td>
<td>%</td>
<td>Monitored patients’ no.</td>
</tr>
<tr>
<td>Batch A 1991 - 1995</td>
<td>301</td>
<td>40,51</td>
<td>676</td>
</tr>
<tr>
<td>Batch B 1996 - 2001</td>
<td>235</td>
<td>31,62</td>
<td>559</td>
</tr>
<tr>
<td>Batch C 2006 - 2009</td>
<td>207</td>
<td>27,86</td>
<td>325</td>
</tr>
<tr>
<td>Total</td>
<td>743</td>
<td>100</td>
<td>1560</td>
</tr>
</tbody>
</table>
In exchange, **oesophageal varices** have an increase trend from 28.23% in 1991 to 45.18% in 2009.

![Chart](image.png)

**Chart no. 5.3. Morbidity – Nonvariceal Upper Digestive Haemorrhages as compared to Variceal Upper Digestive Haemorrhages**

**Table no. 5.3. Upper Digestive Haemorrhages Research Batches – Main Causes**

<table>
<thead>
<tr>
<th>RESEARCH BATCH</th>
<th>CAUSE</th>
<th>U.G. (Gastric Ulcer)</th>
<th>U.D. (Duodenal Ulcer)</th>
<th>U.P.P.O. (Postoperative Peptic Ulcer)</th>
<th>Other causes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Monitored patients’ no.</td>
<td>%</td>
<td>Monitored patients’ no.</td>
<td>%</td>
</tr>
<tr>
<td><strong>NONVARICEAL UPPER DIGESTIVE HAEMORRHAGES</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preendoscopy period (1991 – 2001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BATCH A (1991 – 1995)</td>
<td></td>
<td>115</td>
<td>33.43</td>
<td>122</td>
<td>35.88</td>
</tr>
<tr>
<td>BATCH B (1996 – 2001)</td>
<td></td>
<td>114</td>
<td>33.13</td>
<td>110</td>
<td>32.35</td>
</tr>
<tr>
<td><strong>Endoscopy period (2006 – 2009)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>VARICEAL UPPER DIGESTIVE HAEMORRHAGES</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Monitored patients’ no.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BATCH A</td>
<td></td>
<td>85</td>
<td></td>
<td></td>
<td>28.23</td>
</tr>
<tr>
<td>BATCH B</td>
<td></td>
<td>80</td>
<td></td>
<td></td>
<td>26.50</td>
</tr>
<tr>
<td>BATCH C</td>
<td></td>
<td>136</td>
<td></td>
<td></td>
<td>45.18</td>
</tr>
</tbody>
</table>

These dynamic issues regarding mortality can be explained by the introduction of antiulcerous modern medication beginning with the 90’s in U.G.D. (Gastro-duodenal Ulcer) cases and by the increase of alcohol consumption in variceal upper digestive haemorrhages.
The monitoring of the therapeutic methods evolution finds a decrease of the surgical interventions spread from 76.89% for haemorrhagic UGD (Gastro-duodenal Ulcer) over the preendoscopy period to 27.46 (2009).

The final analysis highlights the medical treatment 21.79% for all nonvariceal upper digestive haemorrhages over the endoscopy period.

Chart no. 5.4. Nonvariceal Upper Digestive Haemorrhages Treatment Evolution in U.G.D. (Gastro-duodenal Ulcer)

For the ulcerous disease 15.59%, other causes 5.94%.

The explanation can be again the effect of the good results of the modern treatment by gastric antisecretory agents (antagonists of H₂ receptors, proton pump inhibitors or gastro-duodenal mucous membrane protecting drugs) as well as of the current implementation of endoscopy in our activity after the year 2004.

CONCLUSIONS

3. Upper digestive haemorrhages causes are extremely numerous. In practice, we meet two large cause groups:
   a. Nonvariceal upper digestive haemorrhages
   b. Variceal upper digestive haemorrhages

   Overall, the most frequently met upper digestive haemorrhages are caused by the gastro-duodenal ulcers which represented 57.67% of the monitored patients.

4. From 1980 to 2010 great changes have occurred. The incidence and mortality caused by the upper digestive haemorrhages and by the haemorrhage in UGD (Gastro-duodenal Ulcer) has significantly decreased, in spite of that, incidence decreased only at people younger than 65 years old, while a decreased mortality occurred at all ages.

5. In the first preendoscopy period of research (for us) (1991 – 2001) endoscopy would serve only sporadically to put a diagnosis, the proton pump inhibitors were not administrated as a routine, and surgery was the standard criterion for UGD (Gastro-duodenal Ulcer) treatment.

   In the second period (2006 – 2009) the selected casuistry was subjected to Helicobacter pillory removal, the endoscopic therapy became standardised, and the
proton pump inhibitors proved to be able to prevent the occurrence of a new ulcer haemorrhage, thus improving the overall results.

6. The impressive progress nowadays with regard to the incidence and the results can be greatly owned to the evolution of clinics and the modern methods of putting a diagnosis and administrating a treatment implemented in the medical practice over the last 20 years.

A further decrease of the upper digestive haemorrhage incidence would require an implementation within the clinic of the prevention strategies with elderly people and hospitalised patients. Such efforts should be focused on preventing haemorrhages with patients of risk factors containing nonsteroidal anti-inflammatory drugs that can be also found in our research.

7. Morbidity by U.G. (Gastric Ulcer) and U.D. (Duodenal Ulcer) under the influence of modern medical treatments has permanently decreased especially for U.D. (Duodenal Ulcer) from 43,33% to 20,83%, in exchange the incidence has increased with elderly people;

- the evolution of the therapeutic methods highlights the percentage increase of the conservatory treatment (medical – endoscopic) from 23% in 1995 to 78,21% in 2009, as compared to the surgical treatment decrease from 75% to 21,59%;
- even if the morbidity of nonvariceal upper digestive haemorrhages main causes has decreased, the annual average of haemorrhagic complications is still constant;
- mortality decreased from 10% in the 80’s to 4,5% in 2009.

8. The diagnosis and therapy strategy on the batches submitted to research (Batch C) was based on an algorithm that pursued:

- initial and quick evaluation in order to determine haemorrhage severity, evolution and prognosis factors;
- haemodynamic stabilisation;
- E.D.S. (Upper Digestive Endoscopy) practice in the first 24 hours by localising the source, the aetiological diagnosis and the endoscopic haemostasis;
- case reevaluation;
- establishing the permanent therapeutic conduct;
  - conservatory treatment (endoscopic and medical)
  - surgical treatment

9. By the causal diagnosis (clinical, endoscopic and laboratory) it has been found that the spread of the different aetiologies of nonvariceal upper digestive haemorrhages changed over the research period of time. Thus, the ulcerous disease under its different anatomo-clinical forms had an incidence of 57,67% at the end of the research period (Batch C).

   U.G. (Gastric Ulcer) – 26,73%; U.D. (Duodenal Ulcer) – 28,46%

10. The therapeutic strategy was in accordance with the established algorithm, the results being as follows:
- medical and endoscopic conservatory treatment 310 – 76,70%
- surgical treatment 94 – 23,26%
  - Ulcerous disease 63 – 15,59%
  - Other lesions 24 – 5,94%