Standards of diagnostics and treatment of ulcerative colitis (UC) in Ukraine are based on world generally accepted approaches and include differentiated stage prescription of preparations in dependence on:

- spreading of pathological process;
- character of the course of the disease.
The traditional tasks of treatment are:

- Reducing disease activity
- Diminishing of expressed clinical symptoms
- Improving patients’ quality of life
- Preventing relapses
It is important to estimate possibilities of therapy taking the following into account:
- localization and gravity of process;
- activity of process;
- presence of complications;
- response to the previously applied therapy.

To present the individual chart of patient’s treatment:
- 1-st line of therapy
- 2-nd line of therapy

To estimate the prospect of applied therapy
Aminosalicylates

Corticosteroids

Immunosuppresants (AZA/MTX)

Biological therapy (IFX)

Operation
DIAGNOSIS

5-ASA (mildly or moderate course)

Absence of effect

Supporting therapy

Absence of effect, increase of activity

CS

CS + immunomodulators (moderate, severe activity)

More aggressive therapy CS with/or without immunomodulators (severe activity)

Immunomodulators

Operative treatment

DISEASE ACTIVITY

TREATMENT ALGORITHMS

DIFFICULTIES OF THERAPY ARE:

- 25-30% patients are resistant to the basic therapy with standard doses
- the side effects of systemic glucocorticoids and immunosuppressant are forecasted
Detecting localization, activity and complications

Excluding intercurrent diseases

Evaluating the efficiency of the previously applied therapy

Prescribing preparations having well-proven efficiency and high safety level

T. Andus, 2003
THE ULTIMATE GOAL OF PATIENTS’ TREATMENT

NOWADAYS

Removing or improving complaints and symptoms

Prophylaxis or reducing complications

FUTURE

«Convalescence» of mucous membrane

Development of etiotropic therapy
DESIGN OF INVESTIGATION

25 pts with the moderate course of the active distal UC (the index of clinical activity 6-12; endoscopic index – 4 according to Rachmilewitz, 1989) divided into 3 groups depending on curative complexes:

- group I (n=9) – mesalazine (tablets) 3 g/day and budesonide 9 mg/day for three taking;
- group II (n=8) – mesalazine (granuls) 3 g/day and budesonide 9 mg/day for one taking;
- group III (n=8) – mesalazine (granuls) 3 g/day and budesonide 9 mg/day for one taking and rebamipide 300 mg/day
**CLINICAL AND ENDOSCOPIC REMISSION after 8-week treatment**

<table>
<thead>
<tr>
<th>Patients groups</th>
<th>Clinical remission</th>
<th>Endoscopic remission, number, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>number, %</td>
<td>duration, days</td>
</tr>
<tr>
<td>Group I</td>
<td>5 (55.6%)</td>
<td>23.7 ± 1.4</td>
</tr>
<tr>
<td>Group II</td>
<td>5 (62.5%)</td>
<td>27.5 ± 1.7</td>
</tr>
<tr>
<td>Group III</td>
<td>6 (75%)</td>
<td>30.7 ± 1.8</td>
</tr>
</tbody>
</table>
NANA concentration in UC pts

Blood

Urine

- normal
- before treatment
- after treatment
FUCOSE CONCENTRATION in UC pts

Blood

Fucose concentration in UC pts

Urine

mmol/l

mmol/24 hours

– normal
– before treatment
– after treatment
Rebamipide enema versus 5-ASA enema for distal UC: a randomized controlled trial

40 pts with mildly to moderately active distal UC:
- group I (n=20) – rebamipide enema;
- group II (n=20) – 5-ASA enema.

Once a day for 4 weeks.

<table>
<thead>
<tr>
<th></th>
<th>Rebamipide enema</th>
<th>5-ASA enema</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Disease activity index</strong></td>
<td>before treatment</td>
<td>10,65±0,87</td>
</tr>
<tr>
<td></td>
<td>after treatment</td>
<td>6,6±3,2*</td>
</tr>
<tr>
<td><strong>Endoscopic index score</strong></td>
<td>before treatment</td>
<td>8,05±2,01</td>
</tr>
<tr>
<td></td>
<td>after treatment</td>
<td>6,0±2,38</td>
</tr>
<tr>
<td><strong>Endoscopic grading scale</strong></td>
<td>before treatment</td>
<td>1,65±0,48</td>
</tr>
<tr>
<td></td>
<td>after treatment</td>
<td>1,15±0,48</td>
</tr>
<tr>
<td><strong>Biopsy score</strong></td>
<td>before treatment</td>
<td>7,8±1,73</td>
</tr>
<tr>
<td></td>
<td>after treatment</td>
<td>6,3±1,65</td>
</tr>
</tbody>
</table>

The efficacy of RE was similar to that of 5-ASA.

M. Miyata et al., 2006
Efficacy and safety of rebamipide enemas for active UC pts
(a randomized, multicentre pilot study)

19 pts with mild to moderate active distal US
4-week once a day treatment

I group (n=9)
1 g of mesalazine enema + baseline treatment

II group (n=10)
150 mg of rebamipide enema + baseline treatment

The efficacy and safety of RE treatment appears to be equal to ME for active distal UC.

R. increase regeneration by enhancing expression of intercellular claudin-1 in colonic epithelial cells.

H. Ogata et al., 2006
MECHANISMS OF CITOPROTECTIVE EFFECT OF REBAMIPID IN UC pts

- Increase of PgE₂ in IMM
- Induction of the COG-2 expression
- Improvement of microcirculation in IMM
- Stimulation of regeneration of intestine mucous membrane
- Improvement of EGF and EGF-receptor expression
- ↓ POL in IMM
- Improvement of claudin-1 expression
- Suppression of neutrophil functions

↑ resistance of IMM (citoprotection)
BUDESONIDE FOR THE TREATMENT OF ACTIVE DISTAL UC

**Study design** – open, randomized, multicenter

**Duration** – 8 weeks

**Dosage**

- **group I**: 3 caps. 3 mg 3 times a day (n=7)
- **group II**: 3 caps. (9 mg) 1 time a day (n=8)

<table>
<thead>
<tr>
<th>Group</th>
<th>28-th day</th>
<th>56-th day</th>
<th>Remission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>0</td>
<td>3 (38%)</td>
<td>0</td>
</tr>
<tr>
<td>Group II</td>
<td>4 (57%)</td>
<td>4 (57%)</td>
<td>7 (57%)</td>
</tr>
<tr>
<td>P</td>
<td>0.026*</td>
<td>0.619</td>
<td>0.026</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Improve of clinical activity index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
</tr>
<tr>
<td>3 (38%)</td>
</tr>
<tr>
<td>Group II</td>
</tr>
<tr>
<td>5 (71%)</td>
</tr>
<tr>
<td>P</td>
</tr>
<tr>
<td>0.315</td>
</tr>
</tbody>
</table>

Prescribing B. in a dose of 9 mg one-time has an advantage in comparison with taking 1 caps. 3 times a day.

* - statistic reliable

Kolkman et al., 2004
PROTECTIVE EFFECT OF MELATONININE IN COLITIS

A. Akcan et al., 2008

- **Antioxidant effect**
- **Improving the microcirculation**
- **Stimulating the repair of intestinal epithelium**

Graphs showing:
- **TNF-α and endotoxine, blood serum**
- **Caspase-3 activity**
- **Myeloperoxidase activity**
BASIC FUNCTIONS OF ESSENTIAL PHOSPHOLIPIDS

- Antioxydative effect
- Desagregational effect
- Immunomodulation in a cellular level
- Restore of the damaged membrane structures of the cell
- Increase of prostaglandins synthesis

- Hepatoprotective effect
- Stimulation of endogenic phospholipids synthesis
DEPROTEINATED HEMODERIVATE—removal of tissue hypoxia and improvement of circulation of blood into the mucous membrane of intestine

- Increase of energetic potential of cells (increase in 5 times of cell consumption of glucose)
- Diminishes inflammatory-cellular infiltration, anabolism action
- Improves blood supply, removes tissue hypoxia
CONCLUSION

1. Optimization of the curative complexes with the substitution of the Mesalazine in tablets on granules, especially with additional Rebamipide prescription, in one time daily taking of Budesonide leads to rising of the effectiveness of treatment and improvement of life spending quality in UC patients.
MODERN APPROACHES TO UC TREATMENT

Basic therapy

↑ resistance mucous barrier of intestine

«Convalescence» of mucous membrane

citoprotector (Rebamipide)
bilious acids (Ursodeoxycholic acid)
endogenous matters (Melatonin)
stabilization of membranes (phosphatidilcholine)
antihypoxants (deproteinated hemoderivate)
correction of microbiocenosis disorders