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Abstracts

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HISTORY OF THE INTERNATIONAL SYMPOSIUM OF GASTROENTEROLOGY

Jan Kotrlík

I'm pleased to greet you all to the 10th International Symposium of Gastroenterology (ISG). I would also like to take this opportunity to tell you about how the symposium was established and provide you with a brief history of the symposium.

While the 10th World Congress of Gastroenterology was being held in Los Angeles in 1994, Dr. Rudolf Bares, the director general and owner of PRO.MED.CS, was achieving success with his pharmaceutical company. Dr. Bares was a charismatic businessman, excellent linguist and strong supporter of Czech and Slovak gastroenterology, hepatology and pharmacology. His wish was for Czech gastroenterology to penetrate European medicine.

Dr. Bares' diplomatic skills allowed him to forge strong contacts and become familiar with European gastroenterology. In 1994 he contacted Professor J. R. Armengol Miró, the internationally recognised president of the ESGE, and another member of the ESGE committee, Professor Nowak from Katowice (Poland). I was president of the Czech Gastroenterological Society (CGS) at the time.

We were asked to work with CGS to prepare the scientific programme of the first ISG. As Dr. Bares lived in Andorra at the time, the first symposium was logically held in Andorra La Vella in 1995. Programme topics included illnesses of oesophagus, stomach and duodenum. Speakers and moderators came from the Czech Republic, Spain, Poland, Slovakia and Andorra. The auditorium was filled with 236 gastroenterologists from these countries.

The 2nd ISG in Prague in 1997 discussed illness of the small and large intestines with 226 participants attending. The 3rd ISG was hosted in Palma de Mallorca and the main topics for the 224 attendees were acute and chronic pancreatitis and duodenal cancer. Gastroenterological emergencies were discussed at the 4th symposium, which was attended by 400 people.

During the first symposia we had the opportunity to compare literature published in Spain and Central Europe. English was used as the official language from the very beginning. This was a learning period for both speakers and audiences alike. A social programme with visits to interesting sites has always been an integral part of ISG, as this allowed all of the participants to make new contacts and start friendships with people from faraway countries.

The 5th ISG in 2003 was again hosted in Andorra. All topics focused on the gallbladder, the biliary tract and liver. As many new buildings had been constructed in Andorra since the last ISG, the social programme was moved to the town of La Seu d'Urgell on the Spanish border. This was a pleasant and unforgettable meeting.

In the new millennium, PRO.MED.CS has successfully penetrated the pharmaceutical markets of Eastern Europe and Central Asia, and as a result, the composition of the audience has changed. New attendees to the symposia were gastroenterologists from the Balkans, the Baltic States, the Russian Federation, Ukraine, Belarus and Central Asia. The audience became truly international. Symposium venues also moved eastward.

The 6th ISG on the topic of emergencies in gastroenterology hosted 303 attendees in Cracow, with the gala evening held in Niepołomice, the former summer residence of the Polish kings.

The 7th ISG was held in Tallinn and the main objective of the programme was to answer the question: How to diminish the mortality from cancer in gastroenterology. Again over 300 people from 15 countries registered to attend. The 8th ISG was organised in Kiev for 298 gastroenterologists from 19 countries. Lectures focused on emergencies in gastroenterology.

The last, 9th ISG held in 2012 took place in the capital of Uzbekistan, Tashkent. A total of 381 physicians heard lectures on IBD, autoimmune diseases, and endoscopic approaches in the therapy of emergent GIT diseases and conditions. This was the first ISG to feature speakers from Eastern Europe and Central Asia. The attendance of Dr. Adkham Ikramov, the Minister of Health of Uzbekistan, fostered international cooperation and friendship. Everyone was fascinated by the extensive media coverage the symposium enjoyed.

Last but certainly not least, I would like to emphasise that without the financial support of PRO.MED.CS, and specifically Thomas Bares, it would not have been possible to organise the ISG events. I must say that like his father Dr. Rudolf Bares, he, too, is an extraordinary man.

Kotrlík J. History of the International Symposium of Gastroenterology. In: *10th International Symposium of Gastroenterology, Prague, Czech Republic, 12–14 June, 2014*. [online].

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ENDOSCOPIC TREATMENT OF RELATED COMPLICATIONS DURING THERAPEUTICAL ENDOSCOPY

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Miró J.A. Endoscopic treatment of related complications during therapeutical endoscopy. In: *10th International Symposium of Gastroenterology, Prague, Czech Republic, 12–14 June, 2014*. [online].

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TAILORED APPROACH TO CHEMOTHERAPY OF GI MALIGNANCIES

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Petruželka L. Tailored approach to chemotherapy of GI malignancies. In: *10th International Symposium of Gastroenterology, Prague, Czech Republic, 12–14 June, 2014*. [online].

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TOWARDS OPTIMAL SCREENING OF COLORECTAL CANCER

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Abstract: Colorectal cancer (CRC) poses serious health risks to the European population, mainly in the Central European region where it is the second most common cancer and at the same time, the second most common cause of cancer deaths.

CRC prevention includes two modalities: screening (early diagnosis of a disease in asymptomatic individuals) and surveillance (long-term follow-up of high-risk individuals).

The development of CRC screening can be attributed to two main processes: fecal occult blood testing evolution and the transition from opportunistic to population based program setting.

Initially, the gFOBTs were used widely, mostly because of the favorable results of randomized controlled study (year 1993) confirming the 15–33% CRC mortality reduction, low test cost and easy handling. In the last decade many trials showing the superiority of FIT were published. Higher sensitivity for colorectal neoplasia and higher target population compliance were detected. The main issue is to find an appropriate cut-off level to balance the sensitivity and cost-effectiveness. Most studies prefer the cut-off level in the range of 75–100 ng/mL.

Colonoscopy is considered as a gold standard for CRC screening, but there has not been any randomized controlled trial confirming reduction in CRC mortality by using this method. Therefore, an extensive international study (the NordICC Study) has started to prove this fact in the long term perspective. In contrast, recent data from England points to 43% reduction in CRC mortality with flexible sigmoidoscopy screening. Other methods have not been implemented yet as a regular part of the screening programs and are still under development (CT colonography, capsule colonoscopy, molecular tests).

In 2010, the European Guidelines for Quality Assurance in Colorectal Cancer Screening and Diagnosis were published. It is based on the recent and evidence based data focused on CRC secondary prevention and diagnosis. Concerning the program organization, it prefers the population based setting that can lead to adequate target population compliance (acceptable level of 45%, recommended level of 65%). Programs including personal invitations were successfully tested or implemented in many European countries and generally achieved very promising results regarding the participation rate of the target population.

In the Czech Republic, the switch from opportunistic to population based program has begun on January 2014 and is still ongoing.

Conclusion: Trends in colorectal cancer screening are heading towards particular methods involvement and program organization evolution. The CRC mortality reduction can be achieved only by the implementation of population based programs with increase of the target population participation.

Zavoral M., Suchánek Š. Towards optimal screening of colorectal cancer. In: *10th International Symposium of Gastroenterology, Prague, Czech Republic, 12–14 June, 2014*. [online].

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REFLUX ESOPHAGITIS: BARRETT, ONE OF ITS COMPLICATIONS, DIAGNOSIS, THERAPY & FOLLOW UP

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We will discuss the following topics:

Symptoms & complications of gastroesophageal reflux disease

Esophageal symptoms: Heart burn, upper abdominal pain

Extraesophageal symptoms: Cough, hoarseness, laryngitis (posterior), granuloma of vocal cords, larynx carcinoma, asthma, bronchitis, non-cardiac-chest-pain, dental erosions, sleeping apnea

Complications: Bleeding, strictures, *Barrett (intestinal metaplasia)*, ulcerations, *adenocarcinoma of the esophagus*

Diagnosis of reflux disease

Endoscopy (*High Definition*, magnification, chromoendoscopy), NBI (Narrow Band Imaging; Olympus), FICE (Flexible spectral Imaging Colour Enhancement, Fuji), pH-metry, Bilitec, therapy test, manometry, X-ray: esophagus, CT, endosonography, impedance measurement, experimental procedures: optical coherence tomography, light scattering, laser endomicroscopy.

Endoscopic classifications

Savary & Miller (grade 0; endoscopy negative – grade IV; stricture, *Barrett*); MUSE (metaplasia, ulcer, stricture, erosions); Los Angeles (A–D).

Associations between different forms of gastro-esophageal reflux disease

No regular progression from mild to severe reflux disease. Older age, male sex, and white ethnicity: risk factors in the development of severe forms of GERD. Most severe grade of GERD reached at the onset of the disease (El-Serag & Sonnenberg. *Gut* 1997; 41: 594–599).

Prevalence of Barrett's esophagus in the general population: An endoscopic study

Prevalence of BE: with reflux symptoms: 2.3%; without reflux symptoms: 1.2% ($P = 0.8$); with esophagitis: 2.6%; without: 1.4% ($P = 0.32$); alcohol ($P = 0.04$) & smoking ($P = 0.047$): independent risk factors for BE (Ronkainen, *et al.* *Gastroenterology* 2005; 129: 1825–1831).

Risk factors for adenocarcinoma:

Symptomatic gastroesophageal reflux as a risk factor for esophageal adenocarcinoma

Methods: Case-control study, adenocarcinomas of esophagus 189, cardia 262, squamous-cell ca 167, controls 820.

Results: reflux symptoms: odds ratio for Barrett 7.7; frequent, severe, long standing symptoms: odds ratio 43.5.

Conclusion: Strong & probably causal relation between gastroesophageal reflux and esophageal adenocarcinoma (Lagergren, *et al.* N Engl J Med 1999; 340: 825–831).

Barrett > 2 cm

Case-control study: smoking: OR 3,7; BMI Index at 20 years > 25: OR 2.6; sitting job: OR 2.0; male; rare reflux symptoms: OR 0.3; rare therapy with PPIs: OR 0.1.

These risk factors very common: Identification of a group at risk not possible (De Jonge, *et al.* Am J Gastroenterol 2006; 101: 1421–1429).

Pathogenesis of adenocarcinoma of the esophagus

Acid reflux ± bile acids; reflux induced inflammation; recruitment of stem cells out of bone marrow (or esophagus?); intestinal metaplasia = “healing”; oxidative stress; Cox-2-expression elevated; prostaglandin E2; stimulation of proliferation; reduction of apoptosis; DNA-damage.

Barrett’s esophagus: strong risk factor for esophageal adenocarcinoma, but the absolute annual risk, 0.12%, is much lower than the assumed risk of 0.5%, which is the basis for current surveillance guidelines. Thus data from the current study call into question the rationale for ongoing surveillance in patients who have Barrett’s esophagus without dysplasia (Hvid-Jensen F., *et al.* N Engl J Med 2011; 365: 1375–1383).

Diagnosis and risk stratification of Barrett

Prague Classification: C: circumferential; M: maximal extent (Sharma P., *et al.* The development and validation of an endoscopic grading system for Barrett’s esophagus: the Prague C & M criteria. Gastroenterology 2006; 131: 1392–1399).

Chromoendoscopy or NBI in routine diagnostic work up: No proof for an earlier detection of neoplasia as compared to HD magnifying endoscopy.

Surveillance & therapy of Barrett

High grade dysplasia/neoplasia: endoscopic mucosectomy.

Low grade dysplasia: annual control; endoscopic therapy?

No dysplasia: control every 2–3 years, endoscopic therapy (BARRX): Radiofrequency ablation in Barrett’s esophagus with dysplasia: In patients with dysplastic Barrett’s esophagus: radiofrequency ablation associated with high rate of complete eradication of both dysplasia and intestinal metaplasia and reduced risk of disease progression (Shaheen, *et al.* N Engl J Med 2009; 360: 2277–2288).

For further reading: Bennett, *et al.* Consensus statements for management of Barrett’s dysplasia and early-stage esophageal adenocarcinoma, based on a Delphi process. Gastroenterology 2012; 143: 336–346. 81 of the 91 statements achieved consensus despite generally low quality of evidence.

- 1) Specimens from endoscopic resection are better than biopsies for staging lesions.
- 2) It is important to carefully map the size of the dysplastic areas.
- 3) Patients that receive ablative or surgical therapy require endoscopic follow-up.

- 4) High-resolution endoscopy is necessary for accurate diagnosis.
- 5) Endoscopic therapy for HGD is preferred to surveillance.
- 6) Endoscopic therapy for HGD is preferred to surgery.
- 7) The combination of endoscopic resection and radiofrequency ablation is the most effective therapy.
- 8) After endoscopic removal of lesions from patients with HGD, all areas of BE should be ablated.

Mössner J. Reflux Esophagitis: Barrett, one of its complications, diagnosis, therapy & follow up. In: *10th International Symposium of Gastroenterology, Prague, Czech Republic, 12–14 June, 2014*. [online]. Available from URL: http://www.promedcs.eu/sites/default/files/abstractbook_2014_web_a4_19-06-2014.pdf

STILL DISMAL PROGNOSIS OF PANCREATIC CANCER

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Introduction: Pancreatic cancer is the fourth cause of cancer related mortality last years. Patients rarely present early and at time of diagnosis usually have advanced disease. Only 20% of patients present with resectable tumors. There are 2.201 new cases of pancreatic cancer with a projected mortality of 56.5% based on recent cancer statistics in Czech Republic in 2013 (data of IBA, Brno).

Current treatment: The only known curative treatment for pancreatic cancer is surgical resection with negative margins (R0) for T1–3, N0–1, M0. Standard treatment for advanced pancreatic cancer (T3–4, N0–2, M0–1) has had minimal impact on natural course of the disease. Current standard chemotherapy for healthy, robust patients remains FOLFIRINOX chemotherapy which showed 4-month overall survival benefit compared to gemcitabine alone. Recently MPACT study showed that adding nabpaclitaxel to gemcitabine significantly improved overall survival compared to gemcitabine. However, the combination remains more toxic compared to gemcitabine. Erlotinib is the only targeted therapy drug which has shown statistically significant but only modest improvement in median survival. Both antiangiogenic agents and epidermal growth factor receptor (EGFR) antibodies have failed to improve survival in pancreatic cancer patients. Benefit of tumor ablation (RFA, IRE) for the prolongation of overall survival was not proved.

The rationale for delivering preoperative treatment to patients with borderline resectable tumors, as defined originally by Varadhachary, *et al.* in 2006, and subsequently endorsed by Americas Hepato-Pancreato-Biliary Association (AHPBA) and National Comprehensive Cancer Network (NCCN) guidelines, is based on potential downstaging to maximize R0 resections, selecting for surgery patients with stable or responding disease, early treatment of micrometastatic disease and giving therapy in a neoadjuvant setting, when it is expected to be better tolerated. Although this strategy has a sound rationale, its merits have not been demonstrated yet.

Conclusion: Resection is only one therapeutic procedures which (with adjuvant chemotherapy) prolongs survival significantly (T1–3, N0–1, M0), 2 – palliative treatment do not lead to significant prolongation of survival and results are comparable to non-treated patient (T3–4, N1, M0–1), 3 – patients survival is significantly better in high volume centres to compare to population data, 4 – radical resection versus palliative procedure in stage IIB leads to significant better survival in high volume centres, 5 – adjuvant CT increase survival significantly.

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Ryska M. Still dismal prognosis of pancreatic cancer. In: *10th International Symposium of Gastroenterology, Prague, Czech Republic, 12–14 June, 2014*. [online].

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ROLE OF LAPAROSCOPIC SURGERY IN GASTROINTESTINAL MALIGNANCIES

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Froněk J. Role of laparoscopic surgery in gastrointestinal malignancies. In: *10th International Symposium of Gastroenterology, Prague, Czech Republic, 12–14 June, 2014*. [online].

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PERIANAL CROHN'S DISEASE, DIAGNOSTIC AND THERAPEUTIC CONSIDERATIONS

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The perianal complications of Crohn's disease [CD] appear relatively frequently, mostly in patients with large bowel involvement who are affected in 30–50% of them. A clinical manifestations [complications] of perianal CD consist of perianal abscesses, various kinds of perianal fistulas, perianal skin tags and with broad spectrum of ulcerative lesions at the anal channel [from a small ulcerations to the deep fissural lesions or a huge cavitating ulcerations]. The most frequent condition which affected perianal region in CD patients are the skin tags. An accurate diagnosis of perianal CD is based on the results of three procedures. The highest importance has an investigation of perianal region and anal channel by experienced surgeon under general

anesthesia. The magnetic resonance of the pelvic floor or endosonography of the anal channel and distal rectum are imaging methods for diagnosis and disease activity evaluation.

Next therapeutic approach depends on the results of these procedures. In the case of simple fistula-in-ano the perianal surgery (e.g. fistulotomy) or long-term antimicrobial therapy are highly effective. In the case of complex fistula or in those patients with severe anal channel involvement the complex and combine therapy (medical and surgical together) is absolutely required. The medical therapy consists in biological therapy (infliximab, adalimumab) and (or) immunosuppressive treatment by thiopurins [azathioprine, 6-mercaptopurine]. In the acute disease phase with severe inflammation and [or] purulent complications a long-term therapy with antimicrobial drugs by metronidazole and [or] ciprofloxacin are also needed. The surgical therapy is focused on the placement of the permanent non-cutting setons and abscesses drainage. In the case of the clinical improvement the advancement flap [anoplasty] is strictly recommended to achieve the permanent occlusion of the inner orificium of fistulas tract. These approach is effective in 60–70% of CD patients with complex perianal fistulations. Minority of CD patients are indicated to proctectomy and colostomy due to anal sphincter devastation or tight ano-rectal strictures.

Lukáš M. Perianal Crohn's disease, diagnostic and therapeutic considerations. In: *10th International Symposium of Gastroenterology, Prague, Czech Republic, 12–14 June, 2014*. [online].

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ACUTE SEVERE ULCERATIVE COLITIS

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Ulcerative colitis (UC) is a chronic relapsing and remitting inflammatory large bowel disease of unknown origin. The inflammation is limited to the mucosal layer. Although majority of patients could be successfully managed with maintenance oral medication, up to 20% of patients will develop a severe course of inflammation and require hospitalization. Patients with a severe UC are suffering from loose bloody stools (more than 6) accompanied with abdominal cramps and systemic toxicity presenting as fever, anemia, tachycardia and weight loss. Subgroup of patients with severe UC could develop fulminant colitis with high risk of progressing to toxic megacolon and perforation. Majority of patients with severe UC will respond to i.v. glucocorticoids, some patients should receive antibiotics (e.g., ciprofloxacin and metronidazole). Administration of 5-aminosalicylic acid in those patients is questionable. At least one third will fail to improve after course of corticosteroids. Currently the treatment of choice in steroid-refractory colitis is an administration of i.v. cyclosporine, infliximab or surgery. This well-timed rescue medical therapy is considered to be safe when administered in well experienced units. Colectomy is a treatment of choice in medical refractory patients and within 4–7 days in patients with fulminant colitis who do not respond to corticosteroids, cyclosporine or infliximab with reasonable quality of life after the construction of ileal pouch-anal anastomosis.

Drastich P. Acute severe ulcerative colitis. In: *10th International Symposium of Gastroenterology, Prague, Czech Republic, 12–14 June, 2014*. [online].

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POSTOPERATIVE COMPLICATION IN CROHN'S DISEASE

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The goal of surgical treatment of IBD is the relief of symptoms, improving the quality of life of patients and reduction of postoperative complications. Better results are achieved in high volume hospitals (more than 145 hospitalisations/year) and when surgery is done by high volume surgeon. Results are affected by good timing of indications for surgery, which assumes a gastroenterologist oriented in IBD surgery and surgeon familiar with the options of conservative treatment.

Risk of complications after the surgery is necessary to be considered against the risk of adverse effects of conservative treatment, especially combined with immunosuppressive therapy. Relatively easy surgery like ileocecal resection is burdened with a minimal number of serious complications compared to a more complicated surgery, which is proctocolectomy with ileo-pouch-anal anastomosis. Combined immunosuppressive therapy with a higher risk of adverse events is not an alternative of simple operations but it should be considered before a complicated surgery.

The frequency of postoperative complications is higher within acute surgeries than the planned operations. Before elective surgery it is better to apply preventive measures.

Medication in preoperative period could influence the postoperative healing. Mesalazine, azathioprine and methotrexate is likely not to affect postoperative complications. Corticosteroids, especially doses above 20 mg prednisolone/day, biological therapy and combined immunosuppressive therapy increase the frequency of postoperative complications. For these reasons, it is advisable to reduce the dose of corticosteroid preoperatively. In case of combined immunosuppression, and biological therapy we lack dose adjustment data, but it is necessary to adapt the operation, for example, indicate a protective ileostomy creation.

Another factor increasing postoperative complications is malnutrition which mainly affects patients with Crohn's disease, suffering from chronic bowel obstruction. Preoperative preparation by artificial nutritional intervention especially by enteral rout is often necessary.

Surgical complications can be reduced by programs based on the basis of EBM type Enhanced recovery after surgery (ERAS), which includes preconditioning, reduction of perioperative fasting, no bowel preparation, minimally invasive surgical techniques.

Early postoperative septic complications range between 5–20%. Early detection and intervention is very important in immunosuppressed patients.

Long term complications in patients with Crohn's disease are short bowel syndrome, which is rare complication in hands of experienced surgeon, and anastomotic stenosis, which could be a consequence of small anastomotic leak. Stenosis could be solved by endoscopic dilation or strictureplasty and should be distinguished from early recurrence of the disease.

Within the surgical treatment of perianal Crohn's disease it is important to preserve sphincters and continence.

Proctocolectomy and ileopouchanal-anastomosis is gold standard of surgical treatment of ulcerative colitis. Early septic complications occur in 15–33%, but 95% of patients have a good quality of life with good long-term pouch function after this procedure. Late complications (pouchitis, cuffitis, fistulas...) are mostly conservatively solvable, but could be cause of pouch failure in Crohn's disease.

Surgical treatment of IBD requires specialized approach lies not only on the technique, but also on good operation's timing, which leads to a reduction of postoperative complications and mortality rate under 1%.

Šerclová Z. Postoperative complication in Crohn's disease. In: *10th International Symposium of Gastroenterology, Prague, Czech Republic, 12–14 June, 2014*. [online].

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PREDICTIVE FACTORS FOR TREATMENT FAILURE AND SURVIVAL IN OVERLAP SYNDROME OF PRIMARY BILIARY CIRRHOSIS AND AUTOIMMUNE HEPATITIS

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Background and Aims: The term 'overlap syndrome' (OS) has been introduced to describe variant forms of autoimmune hepatitis (AIH) which present with characteristics of AIH and primary biliary cirrhosis (PBC). At present, there are no data of predictive factors for the treatment and survival in OS AIH-PBC. Our aim was to determine the predictors of treatment failure and survival.

Methods: Fifty eight patients (52 females, 6 males; mean age 48 yrs) with a diagnosis of OS according to criteria for OS proposed by Chazouillers (Hepatology 1998; 28: 296–301) were included. They have been treated in our clinic with Prednisolone and Ursodeoxycholic acid (URSOSAN®) (15mg/kg/d) for 1–10 years (mean of 4 years). Treatment end points (remission, treatment failure, incomplete response) were the same as for AIH. We analyzed the rate of survival free of liver transplantation. Logistic regression analysis and Kaplan-Meier was utilized to determine independent factors of treatment failure and survival.

Results: Thirty-five patients had remission, 15 pts – incomplete response and 8 pts – treatment failure. Serum bilirubin > 6 ULN (OR, 11.5; 95% CI, 2.06–64.3, $P = 0.035$), ALP > 4 ULN (OR, 9; 95% CI, 1.04–84.2, $P = 0.014$), Mayo risk score > 6 (OR, 9.9; 95% CI, 1.3–74.7, $P = 0.016$) were associated with treatment failure. Patients with treatment failure and serum bilirubin > 6 ULN are significantly more likely to die or need transplantation than those with remission and bilirubin < 6 ULN ($P = 0.021$, Log Rank and $P = 0.008$, Log Rank, respectively). The observed survival was higher than the survival predicted by the Mayo model ($P = 0.018$).

Conclusions: Serum bilirubin > 6 ULN, ALP > 4 ULN, Mayo risk score > 6 identify patients with OS AIH-PBC of risk for the treatment failure. The factors strongly associated with death or liver transplantation were treatment failure and higher bilirubin.

Shirokova E.N., Ivashkin V.T. Predictive factors for treatment failure and survival in overlap syndrome of primary biliary cirrhosis and autoimmune hepatitis. In: *10th International Symposium of Gastroenterology, Prague, Czech Republic, 12–14 June, 2014*. [online].

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HEPATOCELLULAR CARCINOMA: WHAT WE HAVE LEARNED FROM COHORT ANALYSIS 100 + 300?

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NEW IN THE PATHOGENESIS OF NAFLD

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It has been a long time since cardiovascular pathology has lead Russia to leading positions among the industrially developed countries in the world by disease incidence, lethality rate and disability of the working-age population. The lipid storage disorders are the key factor of the risk of development and progression of various cardiovascular diseases, associated with atherosclerosis. Atherogenic dyslipidemia is one of the main links of the “vicious circle” of the metabolic syndrome (MS). Nowadays, the MS incidence is growing inexorably, attracting attention of doctors, specializing in different fields, due to its diversity and severity of clinical manifestations.

With the MS, liver is not only engaged in pathogenesis of atherogenic dyslipidemia, but also is a target organ with the development of the nonalcoholic fatty liver disease (NAFLD). It is known that the NAFLD at the stage of nonalcoholic steatohepatitis (NASH) may progress into liver cirrhosis, lead to hepatic failure and even to development of hepatocellular carcinoma.

Statins have been the long-established “gold standard” in treatment of atherogenic dyslipidemia. However, due to various reasons, in our country the loyalty to therapy with this group of drugs is low. It seems of current concern to develop the optimum regimen of hypolipidemic therapy, characterized by combination of efficacy and safety in the MS patients. Furthermore, quite a number of issues related to pathophysiological and clinical aspects of the MS remain understudied: the data about the lipid spectrum changes in such patients differ, poorly known is the nature of liver injury with the MS, and the effect of the hypolipidemic therapy given for the MS on the liver disease course in such patients. All the foregoing arguments determined

the urgency of studying the lipid metabolism disorder in the MS patients. In certain cases, the use of ursodeoxycholic acid can facilitate management of dyslipidemia.

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ROTAVIRUS INFECTION IN CENTRAL ASIA

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Objective: Rotavirus gastroenteritis is a serious public health problem in both developed and developing countries. New rotavirus vaccines could help reduce health and economic burden of disease. To help decision on introduction of rotavirus vaccination in three Central Asian Republics, we conducted sentinel hospital surveillance for rotavirus and estimated regional burden of disease.

Methodology: Hospital-based active surveillance in children < 5 years of age was established in Kyrgyzstan (KGZ), Uzbekistan (UZB) and Kazakhstan (KAZ) during 2007–2009 based on WHO's Generic protocol for hospital-based surveillance to estimate the burden of rotavirus gastroenteritis in children under 5 years of age. Demographic and clinical information and stool samples were collected from children hospitalized with diarrhea. All samples were tested for rotavirus using an enzyme immunoassay. Selected rotavirus-positive samples were characterized by RT-PCR to determine G and P genotypes.

Results: Of 20,780 children hospitalized with diarrhea and enrolled in the study, 26% (95% confidence interval (CI) 25–27) were positive for rotavirus antigen by ELISA. Annual rotavirus detection rates were significantly different by country: 23.8% in KGZ, 26.1% in UZB, and 35.7% in KAZ. On an annual basis, 4,007 (2.6 per 1,000 child-years) rotavirus hospitalizations occur in KAZ, 5,491 (2.1 per 1,000 child-years) in UZB, and 3,883 (6.8 per 1,000 child-years) in KGZ. Rotavirus is also estimated to cause 68 (0.04 per 1,000 child-years) deaths in children aged < 5 years in KAZ, 662 (0.25 per 1,000 child-years) in UZB, and 156 (0.27 per 1,000 child-years) in KGZ. Children less than 2 years old accounted for 85% of rotavirus cases. The mean age of rotavirus cases differed from 12.5 months in KGZ to 14.2 months in KAZ and 15.7 months in UZB. Rotavirus was present year-round in all countries but autumn peak was observed in KGZ and UZB, whereas winter and fall peaks were detected in KAZ. In 2007, G1 was most predominant genotype (53% in KGZ and 43% in KAZ). In 2008, G2 was the most common genotype (26% in KGZ and 39% in KAZ), followed by G12 (28%) in KGZ and G1 (19%) in KAZ. Each year rotavirus disease is estimated to cause 12,661 hospitalizations and 1,750 deaths in children < 5 years of age in three Central Asian Republics.

Conclusion: This study presents an epidemiological picture of rotavirus disease in Central Asia and illustrates a substantial rotavirus burden. The introduction of rotavirus vaccines could reduce child morbidity and mortality in the region. This data, in combination with information

on the cost-effectiveness of rotavirus vaccination, may be helpful for national decision-makers who are planning preventive and control measures in the involved countries.

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MOTOR DYSFUNCTION CORRECTION IN PATIENTS WITH FUNCTIONAL DYSPESIA

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The prevalence of functional dyspepsia (FD) in countries of Western Europe and in Russia amounts to 30–40% of adult population. Presence of motor-evacuation disorders of upper gastrointestinal tract in patients with FD served the basis for development and wide use of individual group of medications – prokinetic agents. A meta-analysis of 14 studies that included 1,053 patients with FD demonstrates high efficiency (61%) of prokinetic agents in treatment of this disease, which significantly exceeds the efficiency of placebo (41%). The NNT index in treatment with prokinetics appeared to be only 4.

There are four prokinetic agents registered in Russia with an international non-proprietary name. These are metoclopramide, domperidone, itopride and prucalopride. Prucalopride is an enterokinetic and is not used for the FD treatment. The adverse event issues associated with clinical administration of metoclopramide and domperidone, which occurred in Europe during the last years, make it especially important to examine clinical and pharmacological properties of such prokinetic as itopride.

Itopride hydrochloride is a prokinetic agent with combined mode of action. The medication demonstrates properties of peripheral dopamine type-2 receptor antagonist and acetylcholinesterase inhibitor. In Russia, itopride is represented by two trade names: Ganaton (brand) and Itomed® (generic). When Itomed® was registered in Russia, according to the law, only its brand bioequivalence was established. Therefore, it is still essential to conduct post-registration clinical studies to evaluate clinical efficiency of the generic medication because bioequivalence only implies therapeutic equivalence.

These considerations encouraged us to conduct an independent study of clinical efficiency of Itomed® (itopride hydrochloride) produced by PRO.MED.CS Praha a. s. in treatment of patients with FD. According to its design, the study was open-label, controlled, randomized, parallel group, and multicenter.

The initial screening was conducted using “Roman criteria III” and the standard laboratory-instrumental examination (fiberoptic gastroduodenoscopy with biopsy, urease test, abdominal ultrasonography, RRS or colonoscopy, if medically necessary, ECG, and blood chemistry). The social and psychological section included the following questionnaires: Spielberg-Hannin scale of trait and state anxiety and Beck’s depression inventory. The life quality dynamic was evaluated with the help of SF-36. No patient had the red flag symptoms.

Total of 60 patients with FD syndrome were selected. 30 out of them had epigastric pain syndrome prevalent and 30 out of them had postprandial distress syndrome (PDS). Each group of 30 subjects was randomized into two sub-groups of 15 subjects. In one sub-group (“control”) the patients were given non-absorbable antacid. The preservation of possibility to administer single-dose antacid in this sub-group was warranted by ethical considerations. In the second “main” sub-group, along with this, Itomed® was given in the dose of 150 mg/day during three weeks. Thus, we selected four sub-groups, and 30 patients with FD underwent course treatment with Itomed®. During the follow-up period, no proton pump inhibitors were applied and the eradication therapy was not conducted. The efficiency of treatment with Itomed® was evaluated by dynamic studying of clinical and experimental and psychological characteristics.

Expressed positive dynamics of the clinical status of patients with EPS resulted from treatment with Itomed®. The intensity of pain syndrome reasonably decreased. No patient who received Itomed® was observed to have intensive pain in the epigastric area. In the course of treatment with Itomed®, the intensity of heaviness in the epigastric area was truly decreased. Out of the symptoms which were conditionally designated as “non-dyspeptic”, Itomed® mostly affected the presence and intensity of heartburn. This seems to be quite natural since this medication tones up lower esophageal sphincter, thus, decreasing the likeliness of gastroesophageal reflux.

As compared to the control group, patients with PDS, who received course treatment with Itomed®, demonstrated more expressed reduction of the key symptoms – heaviness in the epigastric area and early satiation. This dynamic allows concluding that in this variant of FD Itomed® improves stomach accommodation and the processes of antral-duodenal transfer of food substrates. Treatment with Itomed® while promoting expressed reduction of pain and dyspeptic symptoms resulted in true improvement of patients’ life quality due to improvement of the psychological component of health.

Conclusions: Presented results of the conducted study allow presuming that Itomed® (itopride) is an efficient and safe prokinetic medication which can be successfully used as the monotherapy in patients with various clinical variants of functional dyspepsia. Fast reduction of clinical symptoms in the course of treatment with Itomed® leads to improvement of the quality of patients’ lives.

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THE ROLE OF ENDOSCOPY IN PORTAL HYPERTENSION

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Portal hypertension in the gastrointestinal tract (GIT) may be presented as gastroesophageal varices, ectopic varices, gastric antral vascular ectasia (GAVE), portal hypertensive biliopathy, gastropathy, enteropathy and colopathy. Endoscopy is an effective method for diagnostics of these complications with standard endoscopes, ultrathin endoscopes or wireless capsule endoscopes.

Estimates are that 30 percent of patients with compensated cirrhosis and 60 percent of patients with decompensated cirrhosis have varices at the time of diagnosis. All patients with cirrhosis should undergo screening for esophageal varices so that prophylactic therapy can be given to those with varices that are at increased risk for bleeding. In patients with compensated cirrhosis who do not have varices, screening is repeated every two to three years. In patients with decompensated cirrhosis it is repeated every year or at the time of first decompensation.

Variceal hemorrhage occurs in 25 to 40 percent of patients with cirrhosis and accounts for about one-third of all deaths related to cirrhosis. Identifying and treating patients with high-risk varices leads to improved clinical outcomes as each episode of variceal hemorrhage is associated with up to 15 to 20 percent risk of mortality. Only 50 percent of patients with variceal hemorrhage stop bleeding spontaneously (spontaneous cessation rate in patients with other forms of upper gastrointestinal hemorrhage is 90 percent). Following cessation of active hemorrhage, there is risk of recurrent hemorrhage, which is greatest within the first 48 to 72 hours, and over 50 percent of all early rebleeding episodes occur within the first 10 days.

There are four major issues related to the prevention and treatment of variceal hemorrhage: (1) prediction of patients at risk, (2) prophylaxis against a first bleed, (3) treatment of an active bleed, (4) prevention of rebleeding. Predictive factors for variceal bleeding are location, size and appearance of varices, clinical features of the patient and variceal pressure. Esophageal varices at the gastroesophageal junction have the thinnest layer of supporting tissue and are most likely to rupture and bleed. In the stomach bleed most frequently varices in the fundus (IGV1, GOV2) and bleeding is more serious with higher transfusion requirement in comparison with esophageal varices.

The risk of variceal bleeding correlates independently with the size of the varix. Esophageal varices can be classified as F1 (small, straight varices), F2 (enlarged, tortuous varices that occupy less than one-third of the lumen) and F3 (large, coil-shaped varices that occupy more than one-third of the lumen). It is important to insufflate the esophagus while estimating variceal size, as failure to do so leads to overestimation. Appearance of varices – morphologic features of varices observed at endoscopy can be correlated with increased risk of hemorrhage. These “red signs” represent red wale marks, cherry red spots and hematocystic spots.

Prevention of the first bleeding episode – patients with small varices with red wale marks or Child C class have an increased risk of bleeding and should be treated with nonselective beta-blockers (NSBB). Patients with small varices without signs of increased risk may be treated with NSBB to prevent progression of varices and bleeding. For patients with medium-large varices either NSBB or endoscopic band ligation (EBL) is recommended for the prevention of the first variceal bleeding of medium or large varices.

During the bleeding episode vasoactive drugs (terlipressin, somatostatin, octreotide) should be started as soon as possible, before endoscopy and continued for up to 5 days. Antibiotic prophylaxis is an integral part of therapy for patients with cirrhosis presenting with upper gastrointestinal bleeding and should be instituted from admission. Upper endoscopy is indicated as soon as possible after admission and endoscopic therapy is recommended in any patient with bleeding esophageal varices. Endoscopic variceal ligation (EVL) is the recommended form of endoscopic therapy for acute esophageal variceal bleeding, although sclerotherapy may be used in the acute setting if ligation is technically difficult. Endoscopic therapy with tissue adhesive (e.g. N-butyl-cyanoacrylate) is recommended for acute bleeding from gastric varices, EVL or tissue adhesive can be used in bleeding from gastroesophageal varices type 1 (GOV1).

Management of treatment failures – balloon tamponade should only be used in massive bleeding as a temporary “bridge” until definitive treatment can be instituted (for a maximum of 24 hours, preferably in an intensive care facility). Self-expanding covered esophageal metal stents may be an option in refractory esophageal variceal bleeding. Persistent bleeding despite combined pharmacological and endoscopic therapy is best managed by TIPS. Re-bleeding during the first 5 days may be managed by a second attempt at endoscopic therapy or by TIPS.

Prevention of re-bleeding (secondary prophylaxis) should start as soon as possible from day 6 of the index variceal episode. In patients with cirrhosis combination of beta-blockers and band ligation is the preferred therapy as it results in lower re-bleeding compared to either therapy alone.

GAVE or watermelon stomach is an unusual but clinically significant source of recurrent upper gastrointestinal hemorrhage and iron-deficiency anemia. The diagnosis of watermelon stomach is most commonly based on the characteristic endoscopic appearance of red antral stripes radiating in linear arrays to the pylorus. Symptomatic patients should be treated with bipolar or argon plasma coagulation.

Portal hypertensive biliopathy (PHB) is defined as biliary abnormalities (stenoses) associated most commonly with extrahepatic portal vein obstruction and presented as biliary obstruction with jaundice. PHB may be complicated with bile duct stones and/or cholangitis. MRCP is the method for diagnostics and ERCP is the method of choice both for diagnostics and treatment.

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SAFETY OF UDCA IN PREGNANCY

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Intrahepatic cholestasis of pregnancy (ICP) is a frequent condition affecting approximately 0.5–1.5% pregnant women in the second half of pregnancy. ICP manifests typically with pruritus and elevation of liver enzyme activities, and characteristically also with increased serum levels of bile acids (BA). Although being relatively benign for pregnant women, ICP represents serious risk for fetus mainly due to arrhythmogenic effects of accumulated BA. Determination of serum bile acids is thus essential for diagnosis as well as prognosis. Ursodeoxycholic acid (UDCA) treatment has been proposed by hepatologists as a therapeutic measure of choice and is being generally considered safe. However, since the use of UDCA in treatment of ICP is not widely accepted by obstetricians, despite clear guidelines by European Association for the Study of the Liver Diseases, we aimed in our study to assess safety of use of UDCA in pregnancy. Our retrospective multicentric study was performed on 261 consecutive pregnant women recruited from 4 large Obstetrics centers in the Czech Republic who developed pregnancy-associated hepatopathy, which, in turn, was treated with UDCA. We have primarily searched for any maternal and/or fetal complications of UDCA treatment, as well as neonatal status. The UDCA treatment was very well tolerated, with only negligible skin reactions (0.8%) and mild diarrhea developed in nine women (3.4%). No complications attributable to UDCA treatment were detected during the fetal life, delivery or the early neonatal period. Thus, we could confirm in our large multicentric study the safety of UDCA treatment in pregnancy for both mothers and fetuses, which is practically free of any serious adverse effects. Determination of serum bile acid concentration should be implemented in the routine laboratory diagnostic program of pregnant women with pruritus and/or deterioration of liver function tests, and UDCA treatment should be initiated in all pregnant women with serum bile acids above the critical threshold.

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ELASTOGRAPHY

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A number of methods for diagnosis of liver disease have been developed over recent years, including Transient Elastography (Fibroscan®), a non-invasive method of determining liver stiffness (measured as kPa) using an ultrasound transducer in a probe containing a vibrator unit. A mechanical impulse is generated by the vibrator and transmitted transcutaneously towards the liver, where it induces a shear wave propagating through the tissue. Liver stiffness can be calculated using the measurements of wave velocity by ultrasound.

By comparison of liver stiffness (LS) values with histologic results from liver biopsies in large series references for different fibrosis stages, usually expressed as F0 to F4 according to the Metavir Scale were developed. Transient elastography (TE) was first evaluated in HCV patients, but is used in any kind of liver disease including chronic HBV infection, alcoholic liver disease and non-alcoholic fatty liver disease (NAFLD) among others. There are, however, specific cut-offs for different etiologies of liver disease. Prediction of cirrhosis-related complications is also possible to some extent, data are available for the detection of portal hypertension, the prediction of esophageal variceal bleeding, development of ascites and encephalopathy (increase

in frequency with elevated LS). Furthermore, the incidence of HCC is increased in cirrhotic patients with elevation of LS.

The combination of TE with other non-invasive tests for liver fibrosis (e.g. serum marker panels) can increase diagnostic accuracy.

Although TE was developed for evaluation of chronic liver disease, acute liver damage reflects in elevated LS with prognostic information to be derived from the course of LS over time.

A novel feature of TE is the estimation of fat deposition inside the hepatocytes (i.e. hepatic steatosis) by using “controlled attenuation parameter”, or CAP. The results correlate well with the percentage of steatotic hepatocyte, thus making CAP a non-invasive tool for the diagnosis of non-alcoholic fatty liver disease (NAFLD).

The main limitations of TE are the relatively low applicability (around 20% of patients cannot be examined – mostly due to obesity) and the lack of differentiation between fibrosis and acute (inflammatory) liver damage, that – if in question – has to be established by complementary methods.

It has to be mentioned that other methods of non-invasive elastography (e.g. shear-wave elastography) are available with comparable diagnostic accuracy in some studies, the data background on TE, however, is the most extensive to date.

Transient Elastography:

Pros:

- + Non-invasive test with good reproducibility
- + High performance for diagnosis of liver cirrhosis in established chronic liver disease
- + Predictive value on complications of liver disease
- + Quantification of steatosis

Cons:

- Relatively low applicability (\pm 80%)
- Lack of differentiation between chronic (fibrosis) and acute (inflammation) liver damage
- Dedicated device required

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DANIS STENT IN THERAPY OF OESOPHAGEAL VARICEAL BLEEDING

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Summary:

Acute variceal bleeding together with ascites and liver encephalopathy are the most severe complications of portal hypertension, which is mainly caused by liver cirrhosis.

In the general population of patients with liver cirrhosis, the annual risk of variceal bleeding is around 4%; however, in patients already diagnosed with major varices (F2–F3) this exceeds 10–15%. Varicose bleeding is therefore the most common lethal complication of portal hypertension, and at the same time the third leading cause of bleeding in the upper gastrointestinal tract. Even with intensive therapy, the first episode of bleeding has high lethality (15–20%); two-thirds of patients who die due to bleeding do so in the first 24 hours. Especially in the first five days, the attack is associated with a high risk of recurrent bleeding (40% relapse).

Treatment always requires an intensive multidisciplinary approach to the patient with the participation of the endoscopic team and intensivists. Basic treatment consists of a combination of vasoactive drugs, which must be given to each patient with suspected variceal bleeding already in pre-hospital care, volumexpansion, appropriate hemosubstitution, broad spectrum antibiotics and endoscopic treatment. In the case of treatment failure, TIPS can be indicated or to bridge the critical period one can use a balloon tamponade or dedicated esophageal stent.

Balloon tamponade can have a life-saving effect, but on the other hand, improper use brings a number of complications. This method is pushed pharmacologically in intractable bleeding situations to secure the patient until endoscopic treatment or TIPS can be performed. Even in this case, the tube must not be insufflated for longer than 12–24 hours, it should only be used by an experienced physician.

Urgent transjugular intrahepatic portosystemic shunt (TIPS) is indicated in cases of first-line methods failure, i.e. pharmacologic therapy and endoscopic treatment of varices.

As a salvage therapy, it is currently difficult to find an alternative. Studies with a larger number of patients achieved immediate control of bleeding in the range 91–100% of cases. Even TIPS has its contraindications and limitations dependent on the progress of the liver disease, and there is still a proportion of patients with advanced disease who die due to variceal haemorrhage episode.

Danis stent

Self-expandable metallic stents (SEMS) have, for a long time, been used in the treatment of malignant oesophageal stenosis, leaks and perforations of the oesophagus or tracheo-oesophageal fistula. The idea of using the force of the self-expandable stent to compress the bleeding oesophageal varicosity and stop the bleeding originated at the turn of the millennium. Its father was a Slovak, born in Lučenec – Associate Professor Jan Danis MD – who placed the stent for the first time in this indication, in 2002. After a period of development in cooperation with the manufacturer, and testing the stent in animal models, the first stents dedicated for this therapy were used in clinical trials in 2003 and today carry the name Danis. Currently, based on literature data, Baveno included this method in a 2010 recommendation, as a possible alternative treatment for refractory variceal bleeding from oesophageal varices (evidence 4; C), based on a consensual workshop in Italy (Baveno V). Compared to the balloon tube it ensures a longer period of securing the patient, and bridges the gap of high risk of recurrent bleeding with the possibility of subsequent initiation of adequate secondary prophylaxis. In patients with progressed liver disease at high risk of recurrence, it allows even longer restitution of liver function after the haemorrhage and, in some cases, allows subsequent treatment with TIPS. The big advantage above all seems to be the relatively easy way of introduction.

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ACUTE PORTAL VEIN THROMBOSIS – DIAGNOSIS AND TREATMENT

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Portal vein thrombosis – is more frequent diagnosis nowadays, which is associated with local and systemic risk factors. All laboratory findings are not specific for portal vein thrombosis, and if no adjacent liver disease is present, liver enzymes are completely (or nearly) normal. However, the diagnosis can be established easily and quickly using non-invasive visual diagnostic techniques. Two completely different forms of this disease – acute and chronic portal vein thrombosis – are distinguished, therewith requiring different treatment tactics. The main purpose in the case of chronic portal vein thrombosis is to treat its complications. Methods used are: endoscopic esophageal vein ligation, sclerotherapy and use beta blockers. In the case of acute portal vein thrombosis, it is important to prevent further growth of thrombus, find and treat its causes and complications. The main treatment options are formation of shunts, thrombolysis and thrombectomy. However anticoagulant treatment is advisable for both, acute and chronic portal vein thrombosis. It was earlier thought that anticoagulants are not suitable when treating patients with portal vein thrombosis and liver cirrhosis because of the higher bleeding risk, however recent studies showed that it is a safe and effective treatment and prevention method. Usually the treatment is initiated with low molecular weight heparins and continued with vitamin K antagonists. Still, the dosage and interval of international normalized ratio in the case of liver cirrhosis is still a concern of discussion.

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A NEW NON-INVASIVE PREDICTIVE MODEL OF INFLAMMATORY ACTIVITY IN PATIENTS WITH TYPE I AUTOIMMUNE HEPATITIS

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Autoimmune hepatitis (AIH) is a chronic hepatitis of unknown etiology characterized by hypergammaglobulinemia, the presence of circulating autoantibodies, and inflammatory changes on liver histology with good response to therapy with immunomodulating drugs.

The main aims of the AIH treatment are downregulation of inflammatory activity within the liver tissue and achievement of sustained remission defined as a complete normalization of aminotransferases activity and immunoglobulin level. These goals are reached in the overwhelming majority of patients, but histological remission lags far behind normalization of the serum parameters. Moreover, in some AIH patients normalization of aminotransferases do not exclude the presence of mild to moderate liver inflammation, but even low residual disease activity is a risk for fibrosis and cirrhosis development. Presently, it is likely that liver biopsy is the “gold standard” for the assessment of hepatic inflammatory activity in AIH patients. But this method is not suitable for regular monitoring of the disease due to invasive nature, low acceptance by patients, intra and interobserver discrepancies and unavoidable sampling error. Therefore, precise, safe, acceptable, frequently performed and reproducible tool assessing inflammatory activity would be very helpful in identification of patients requiring more intensive immunosuppressive therapy. Thus, we attempted to construct a non-invasive diagnostic score as an alternative to liver biopsy to help optimize treatment for AIH type I patients and monitor disease activity.

We enrolled eighty two patients with type I AIH into the study. Forty four created training group and were recruited prospectively (22 in the active stage of the disease and 22 in clinical remission under immunosuppressive treatment). The validation group was performed retrospectively and consisted of 25 patients in the active stage of AIH and 13 in clinical remission under treatment. The liver biopsy was performed and two experienced histopathologists evaluated inflammatory activity according to the Histological Activity Index (HAI; score 0–18). High inflammation was defined as HAI > 4. The stepwise linear regression was used to search for the best model describing the severity of inflammation. The value of constructed score in prediction of high inflammatory activity was evaluated by ROC analysis.

Constructed score was based on 4 serum parameters that is: albumin, bilirubin, aspartate aminotransferase and C-reactive protein. The value of the area under the ROC curve for the score was 0.93 with sensitivity and specificity equal to 100% and 85% and PPV and NPV values of 81% and 100% respectively. The corresponding values in the validation group were sensitivity 100%, specificity 56%, PPV 88% and NPV 100% respectively.

In summary, we propose a new non-invasive grading model which is able to discriminate between AIH patients with low and high inflammatory activity within the liver tissue. This non-invasive diagnostic tool may be very helpful in monitoring of the AIH inflammatory activity during immunosuppressive therapy and guiding therapeutic decisions without the need of repeat liver biopsy.

Gutkowski K. A new non-invasive predictive model of inflammatory activity in patients with type I autoimmune hepatitis. In: *10th International Symposium of Gastroenterology, Prague, Czech Republic, 12–14 June, 2014*. [online].

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URSODEOXYCHOLIC ACID IN STANDARD INTERFERON THERAPY OF PATIENTS WITH CHRONIC HEPATITIS C AND B

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The purpose of study: estimate the efficiency of ursodeoxycholic acid (UDCA) in standard antiviral therapy (SAT) of chronic hepatitis C or/and B.

Methods: Research included 580 patients with the chronic virus hepatitis received standard antiviral therapy. During 48 weeks patients with hepatitis B and B + D received peg-interferon, and patients with C and B + C hepatitis received combined peg-interferon and ribavirin. 1st group of 300 patients (B – 130, C – 96, B + C – 73, B + D – 10; 190 men, 110 women, middle age of 32.9 ± 10.1 years) additionally took UDCA not less than 6 months. The preparation was prescribed in 2–4 weeks before SAT in a dose of 12.5 mg/kg not less than for 3 months, with the subsequent decrease to 6–7 mg/kg. 75% of patients took UDCA during the whole course of interferon therapy, and 15% continued UDCA after interferon therapy. The 2nd group of 280 patients (B – 133, C – 98, D + C – 26, B + D – 14; 172 men, 108 women, middle age of 35.9 ± 7.5 years) took only SAT. ALT, AST, bilirubin, γ -glutamyltranspeptidase, alkaline phosphatase levels, and blood analysis were evaluated.

Results: Due to UDCA introduction period before SAT 1st group showed decrease of epigastric pains, nausea, right hypochondrium pains, itching, weakness, dream violations in comparison with patients of 2nd group. Normalization of the raised ALT and AST levels was observed by 6th week of SAT in 50 patients (from 80 patients with initially raised ALT and AST) of 1st group. ALT and AST levels reached norm in 1st group by 12th week whereas in 60 (21.4%) patients of 2nd group ALT, AST remained raised.

Cholestasis remained at 30% of patients in the 1st group by the beginning of SAT and in 35.7% of patients in the 2nd. By 12th week cholestasis was observed only at 3.3% of patients of 1st group (32.1% – in the 2nd group). By 24th week the raised level of bilirubin remained in 7.1% of patients in the 2nd group whereas in 1st group cholestasis was only at 1 patient.

Decrease of hemoglobin level by 12th week of treatment within 110–100 g/l was observed at 10% of patients in 1 group, at 17.9% – in the 2nd. By 24th week anemia was observed only in 2nd group (1st group – 0%; 2nd group – 14.3%).

Decrease in platelets level in the first 2 months of treatment was in both groups, but normalization of their quantity went earlier in 1st group. By 12th week of treatment level of platelets in all patients receiving UDCA was higher than 120 000/ml (3.6% – in the 2nd group).

Conclusions: UDCA within SAT of hepatitis B and C allowed to reach the biochemical answer (ALT and AST level normalization) in earlier terms, and to better control of cholestasis. In UDCA group were less frequency of hematologic side effects of peginterferon and peginterferon + ribaviriny.

Kurmanova G.M., Kurmanova K.B., *et al.* Ursodeoxycholic acid in standard interferon therapy of patients with chronic hepatitis C and B. In: *10th International Symposium of Gastroenterology, Prague, Czech Republic, 12–14 June, 2014.* [online].

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RESULTS OF SCREENING AIMED AT DETECTION OF NAFLD AND DETERMINATION OF RISK FACTORS INCIDENCE IN MEDICAL PATIENTS OF MUNICIPAL POLYCLINICS OF THE CENTRAL ASIA REGION, BISHKEK C.

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SUMMARY

Non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steato-hepatitis (NASH) are characterized by an increased fat deposition in the liver (NAFLD) which might be accompanied by elevated transaminases (NASH). Today terminology is still inconsistent. Before the diagnosis is made, other causes, especially alcoholic liver disease must be ruled out. Increased fat deposition in the liver without elevated transaminases is found in obese patients.

NASH with elevated transaminases may develop in these patients without known causes. Fibrosis is observed in 15–50% of this patients and cirrhosis in 7–16%.

Unfortunately in Kyrgyzstan nationwide, as well as in other countries of the Central Asian Republic, there is no epidemiological data on the prevalence NAFLD even according to ultrasound studies. At the same time researches in other countries, for the example the first pilot study on the prevalence of NAFLD in Almaty (a nearby town), showed that 29% of patients who regularly visit physicians clinics suffer NAFLD. The results of this pilot study highlighted the need for research in Kyrgyzstan.

The results of survey aimed at the detection of Non-Alcoholic Fatty Liver Disease (NAFLD) in medical patients of municipal clinics of the Bishkek.

In total 359 patients over 18 years old and less than 80 years old were examined from June 2010 till end of October 2010.

At the initial stage of the screening the persons with the established risk factors of NAFLD were singled out on the basis of clinical and medical history data and physical examination. The further targeted examination if this group using biochemical, serological and instrumental methods (liver US) allowed confirming NAFLD in 2 patients: in 131 men (36.5%) and in 228 women (63.5%) aged 52 ± 14 . Among patients attending Bishkek physicians municipal polyclinics about various diseases, NAFLD was detected in 38% of cases.

In patients with confirmed NAFLD steatosis was found in 75.5% of cases, steatohepatitis in 19.5% and hepatic cirrhosis in 4% of cases. A sharp increase in the incidence of these diseases starts in the age group of 30–39 and the incidence continues to rise steadily up to the age of 60.

The most frequently detected known risk factors were overweight and obesity.

Umarova S.I. Results of screening aimed at detection of NAFLD and determination of risk factors incidence in medical patients of municipal polyclinics of the Central Asia region, Bishkek c. In: *10th International Symposium of Gastroenterology, Prague, Czech Republic, 12–14 June, 2014*. [online]. Available from URL: http://www.promedcs.eu/sites/default/files/abstractbook_2014_web_a4_19-06-2014.pdf

PREVALENCE OF LIVER DISEASES IN RUSSIAN MEGAPOLIS

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BACKGROUND AND AIM: Difficulties in accessing data from individual countries, especially Russia, hinder global evaluation of liver disease in Europe. The goal of this study was to estimate the prevalence of liver diseases in the Russian megalopolis.

METHODS: 5,000 random Moscow residents from 18 to 75 yo, were screened for liver diseases from October 2012 till November 2012. Socio-demographic, health and lifestyle information was obtained via the questionnaire, alcohol screening was done by CAGE and AUDIT tools; BMI, liver tests (ALT, AST, GGTP, bilirubin, ALP, ALT/AST) anti-HCV, HBsAg, γ -globulins were investigated.

RESULTS: Socio-demographic data: male 1,671 (33,42%), female 3,329 (66,58%), average age 44.58 yo, average BMI 25.68 kg/m². 1,461 subjects (30,6%) of 4,768 participants had any abnormalities in liver functional tests, 232 participants were excluded from the further analysis due to missing data. According to occupation BMI > 25 kg/m² was observed in retired, disabled, businessmen, military. Health care workers and students (24.75 kg/m² and 21.8 kg/m² respectively) belonged to the “slimmest” group. According to CAGE and AUDIT more than average alcohol quantity consumed 84% (4,027) of all participants. An alcohol dependent was observed in 9.8% of all participants, heavy drinkers were 4.36%, more commonly workers, employee, culture workers, businessmen and military. The most common liver disease in Russian megalopolis were NAFLD 13.6%, ALD 6.9%, followed HCV-infected 6.67%, HBV-infected 1.9%, DILI 0.82%, AIH 0.78% and cholestasis 0.69%.

CONCLUSION: According to our trial about 30% of Moscow residents have abnormal functional liver tests. NAFLD, ALD and HCV-infection were the main reasons for it. Health care workers and students had the lowest BMI in comparison with other groups according to occupation.

Maevskaya M.V., Ivashkin V.T., *et al.* Prevalence of liver diseases in Russian megalopolis. In: *10th International Symposium of Gastroenterology, Prague, Czech Republic, 12–14 June, 2014.* [online].

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DRUG-INDUCED LIVER INJURY

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The programmatic polychemotherapy (PCT) is the primary method of leukemia acute (LA) treatment. The success of the PCT of LA depends on the using of the adequate doses and intervals of administration of cytotoxic medications. Liver injuries on the background of PCT

are the limiting factor for the PCT in its entirety. The application of anthracycline antibiotics is associated with the risk of development of the drug-induced liver injury (DILI).

The purpose is to improve the effectiveness of treatment options of DILI, induced anthracyclines.

We examined 54 LA pts (38 – LA myeloid, 16 – LA lymphoblastic), in which the dynamics of the PCT with doxorubicin during induction and consolidation of remission developed of DILI. All pts received ursodeoxycholic acid (UDCA) 20 mg/kg 60 days in combination with ademethionine 1200 mg/day jet i.v. 10 days of the transition to 1200 mg/day orally 50 days.

On the background of PCT increased activity of alkaline phosphatase (ALP) in 2.7 times (209 ± 22.9 IU/l vs 77.4 ± 10.8 IU/l; $p < 0.05$), gamma-glutamyl transpeptidase (GGT) – in 4.3 times (94.5 ± 10.39 IU/l vs 21.9 ± 2.42 IU/l; $p < 0.05$), bilirubin – in 4.8 times (58.1 ± 8.71 IU/l vs 12.1 ± 1.33 IU/l; $p < 0.05$), ALT – in 2.1 time (54.8 ± 4.9 IU/l vs 26.1 ± 3.65 IU/l; $p < 0.05$), AST – in 2.9 times (57.1 ± 6.86 IU/l vs 19.7 ± 2.36 IU/l; $p < 0.05$) was found relative to healthy. Under this condition in 2.5 times decreased of arginase blood activity and in 1.9 times increased the concentration of molecules of average weight (MAW).

After 30 days of starting treatment decreased the activity of ALT, AST in 1.9 and 2.1 times respectively, ALP, GGT, total bilirubin in 1.4, 2.3, 2.8 times respectively. At the 56th–60th days of treatment were normalized indices of cytolytic and cholestatic syndromes in 44 (81.5%) pts. Established correlation between the reduction of clinical symptoms of cholestasis and ALP ($r = +0.76$), GGT ($r = +0.85$) activity. Increased in 1.7 times of the arginase activity on the background of decreased in 1.5 times the MAW level, reflecting the increase of the detoxication processes. This allows to prescribing the PCT in full compliance with the mode of administration of cytostatics.

Thus, the combination of UDCA and ademethionine in the high doses is an optimal approach to treatment and prevention options of DILI, induced by anthracyclines.

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Skrypnyk I., Kharchenko N. Drug-induced liver injury. In: *10th International Symposium of Gastroenterology, Prague, Czech Republic, 12–14 June, 2014*. [online].
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FEATURES OF DIAGNOSIS AND TREATMENT OF CHRONIC PANCREATITIS WITH STEATOSIS OF THE PANCREATIC GLAND

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A number of studies has proved an opportunity of development of chronic pancreatic insufficiency at disorders of lipid metabolism and at the same time there are no reliable evidences about associated pathology of chronic pancreatitis and steatosis of the pancreatic gland.

The purpose of our research was to study characteristic features of the progress of chronic pancreatitis in association with steatosis of the pancreatic gland as well as questions of improvement of diagnosis of steatosis of the pancreatic gland.

Material and Methods: We studied 52 patients with chronic pancreatitis from them in 25 patients the steatosis of pancreatic gland was diagnosed. Group 1 included 11 patients with chronic pancreatitis associated with steatosis of pancreatic gland who received proton pump inhibitors (PPI) + enzymatic preparation (EP), group 2 comprised 14 patients with chronic pancreatitis and steatosis of pancreatic gland who received Ursosan® 2 capsule a day additionally to the standard therapy.

All patient underwent the complex examination including: physical examination, interview, data collection about the state of internal organs, measurement of arterial pressure, body mass index, laboratory methods of investigation (amylase content in the blood and urine, cholesterol, triglycerides, lipoproteins, ALT, AST, bilirubin, total protein, glucose level in the blood), coprogram included the general analysis of feces and determination of fecal elastase). For verification of the diagnosis all patient were performed transabdominal investigation. The computed tomography was used for determination of the steatosis of pancreatic gland.

Results: The results of the investigations performed showed that the patients with chronic pancreatitis and steatosis of the pancreatic gland are characterized by the higher level of glycemia, triglyceridemia as well as by higher parameters in the blood serum of gamma-glutamyl-transpeptidase in comparison with persons suffering from CP without steatosis ($p < 0.05$). The performance of computed tomography of the abdominal cavity allows improvement and reliability diagnosis of steatosis of pancreatic gland. On the basis of changes revealed at computer tomography in 14 patients steatosis of pancreatic gland was noted. After the interview performed among the participants it was clear, that in Uzbekistan, in view of regional and mental peculiarities, the chronic pancreatitis is accompanied more often by steatosis of pancreatic gland. At presence of steatosis of pancreatic gland the disorders of carbohydrate metabolism, liver steatosis were diagnosed more often. The comparative studies performed showed that the efficiency of therapy appeared much higher in group 2 of the patients who received Ursosan® additionally to the standard therapy in order to regulate lipid and carbohydrate metabolism with parallel considering of the effect on the liver function due to hepatoprotective, antioxidant and antiapoptosis effect as, at the majority of the patients with steatosis of the pancreatic gland there was found liver steatosis. After therapy with Ursosan® there were observed significant changes in biochemical parameters of blood analysis to the end of the fourth week. It is important that the detailed estimation of the criteria of quality of life of the patients allows to conclude, that the inclusion of preparation Ursosan® into the complex of treatment promotes significant improvement of quality of life of the patients.

Conclusion: Ursosan® seems to be an effective preparation not only for treatment of the pathology of liver, but also during treatment of chronic pancreatitis with steatosis of the pancreatic gland.

Khamrabaeva F.I. Features of diagnosis and treatment of chronic pancreatitis with steatosis of the pancreatic gland. In: *10th International Symposium of Gastroenterology, Prague, Czech Republic, 12–14 June, 2014*. [online]. Available from URL: http://www.promedcs.eu/sites/default/files/abstractbook_2014_web_a4_19-06-2014.pdf

ASSESSMENT OF THE LIVER STATE IN PATIENTS WITH CHRONIC PANCREATITIS ASSOCIATED WITH METABOLIC SYNDROME

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The major ingredients of the metabolic syndrome (MS) closely connect with functional state of the organs of the digestive system. The disturbance of feeding behavior, disbalance of the hormones of digestive tract, liver function state, pancreatic gland function are the key pathogenic factors of the metabolic syndrome development.

Purpose of investigation was to study some features of metabolic disturbances of the liver in the patients with chronic pancreatitis associated with MS.

Material and methods: The study was carried out on 52 patients, of them 9 males and 43 females. The mean age was 52.2 ± 2.6 years. Control group included 14 individuals without signs of chronic pancreatitis (CP) and MS. Metabolic syndrome was diagnosed according to the criteria offered by medical experts of the USA national educational program on cholesterol.

In the blood there were measured glucose concentration and insulin level, as well as level of leptin and contents of the free fatty acids.

As the enzymatic markers of cytoplasmatic localization there was determined: activity of fructose-1-phosphotaldolase, fructose-1,6 diphosphatase, general activity of lactatdehydrogenase and gammaglutamyltranspeptidase, as anzymatic markers for mitochondria there was studied malatdehydrogenase.

Results: There were found reliable changes in the studied blood parameters in the patients with CP associated with MS. The state of dyslipidemia expressed in the majority of patients with associated form of pathology showed formation of the resistance to insulin. The changes revealed in the blood lipid spectrum was accompanied by increase in levels of non-etherificated fatty acids, on the average, tree times and indicated about damage of their transfer by blood and absorption by cells. Increase in blood of the levels of free fatty acids was accompanied by the hyperinsulinemia and provided disorder of the function of the receptors to insulin and absorption glucose by cells.

The damage of receptor-mediated transport of the fatty acid on the basis of hyperinsulinemia results in structure changes of the cell membranes that induce metabolic changes in the body cells. First of all the complex of systemic metabolic changes involves carbohydrate metabolism in the liver hepatocytes and the in the other organs. Under these conditions mitochondria and cellular membranes become insensitive to hormone effect and the pathological syndrome of resistance has been developed to the effect of insulin. The results of blood investigations showed also 2.5-fold higher levels of mitochondrial enzyme malatdehydrogenase ($p < 0.05$).

Conclusion: Thus, in the patients with CP associated with MS there was observed disorders in the glucose-insulin homeostasis related to hormonal disorders and also to change of metabolism in the cells induced by free fatty acids.

CHARACTERISTICS OF LIPID AND CARBOHYDRATE SPECTRUM IN THE PATIENTS WITH CHRONIC PANCREATITIS ASSOCIATED WITH METABOLIC SYNDROME

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The significant advances have been achieved in the study of isolated pathogenesis as chronic pancreatitis (CP) so as metabolic syndrome (MS) as well as insulinoreistance, however in this associated pathology remain many white places among which the role and etiopathogenic value of carbohydrate and lipid metabolism has been seen.

Purpose of this investigation was to study the role of insulin and adipokines (adiponectin, resistin, leptin) in the formation of CP in the patients with MS.

Material and methods: The main clinical group included 52 patients with CP associated with MC at the age from 18 to 68 years. Males were 9 and females 43. Control group was composed of 14 subjects, mainly of women of fertile age without manifestations of CP and MS.

Glucose blood concentration (mmol/l) was measured by glucoseoxidase method; insulinoreistance index was calculated by formulae HOMA-IR. The value more than 2.27 was considered as presence of insulinoreistance. The insulin level in the blood was measured by immune-enzymatic method. At level of insulin on empty stomach higher than 12.5 mcUN/ml the hyperinsulinemia was diagnosed.

Results: The data obtained indicated about reliable change in the lipid spectrum in the patients with CP associated with MS. Thus, total cholesterol level was increased in 53% of patients, triglyceride – in 72.4%, LDLP CS – in 58% of patients with associated form of disease in a part of patients, concentration of total cholesterol increased 1.5–2 times the high limit of references; triglyceride increased 2–4.5 times the norm < and level of LDLP CS – 1.7–2.2 times. Concentration of LDLP CS which is known by its antiatherogenic effect and participating in the processes of cholesterol elimination, was decreased in more than a half of patients with CP associated with MS.

The observed increase level of leptin in the blood serum in studied patients, which concentration increase 1.5 times in studied pathology < may be considered as one of factors of pathogenesis of arterial hypertension in patients with CP associated with MS.

Resistin plays the key role in the appearance of excessive weigh. This hormone is synthesized by fatty cells (adipocytes) and induced resistance to insulin in the body tissue. The decrease in this hormone level results in increase in adipocyte cell sensitivity to insulin and capture of glucose by these cells that promotes increase in body mass and obesity.

Conclusion: Thus in the patients with CP associated with MS there are noted reliable high values of lipid and carbohydrate blood spectrum, the state of hyperleptinemia and lower content of resistin and adiponectin that should be considered during treatment of these patients.

Yuldasheva G.R., Khamrabaeva F.I., *et al.* Characteristics of lipid and carbohydrate spectrum in the patients with chronic pancreatitis associated with metabolic syndrome. In: *10th International Symposium of Gastroenterology, Prague, Czech Republic, 12–14 June, 2014.* [online].

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NON-ALCOHOLIC STEATOHEPATITIS IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION AND METABOLIC SYNDROME: STATINS OR URSODEOXYCHOLIC ACID?

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Non-alcoholic steatohepatitis (NASH) is often diagnosed in pts with acute myocardial infarction (AMI) associated with the metabolic syndrome (MS). Traditional dyslipidaemia treatment of AMI pts is the statins assignment, which prolonged use may cause the increased serum transaminases activity. In order to decrease the cytotoxicity syndrome frequency on the statin therapy background more rational approach to the NASH treatment in AMI pts is to reduce the daily dose statin therapy with concomitant ursodeoxycholic acid (UDCA) use.

The aim was to study the rosuvastatin effectiveness in combination with UDCA in NASH pts with AMI associated with MS.

We examined 121 NASH pts with AMI (with and without Q), of which 38 women. The average age was 53.5 ± 3.4 years, body mass index – 36.4 ± 3.9 kg/m²; waist circumference – 105.4 ± 10.5 cm. The NASH-test was used for the diagnosis of NASH. The dyslipidaemia was confirmed by the cholesterol, triglycerides, high density (CLHD) and low density (CLLD) cholesterol lipoproteins concentration study. The HOMA index was 6.2 ± 2.4 . According to the NASH-test results NASH and dyslipidaemia were found in 47 (38.8%) patients.

38 pts (22 women and 16 men) with NASH were randomized into two groups according to the treatment complex: group I (n = 18) – rosuvastatin 20 mg/day, group II (n = 20) – rosuvastatin 10 mg/day + UDCA 15 mg/kg/day on the AMI basic therapy background. The treatment course was 6 months.

After 4 weeks the increased ALT activity was found in 4 (22.2%) pts of group I, the average in 1.9 times higher compared with baseline ($p < 0.05$). The ALT activity normalization was noted in 18 (90%) pts of group II, which before treatment was 2.1 times higher than normal.

After 6 months the ALT and GGTP activity was 1.3 and 1.5 times higher than normal in 5 (24.4%) pts of group I, while all the biochemical parameters normalization was noted in 100% cases in pts of group II. The blood cholesterol level reduction was noticed in group I from 7.9 ± 1.2 mmol/l to 6.8 ± 0.9 mmol/l, $p < 0.05$; withal CLLD decreased from 5.5 ± 1.4 mmol/l to 4.8 ± 1.6 mmol/l, $p < 0.05$.

Combined therapy with UDCA + rosuvastatin in pts of group II showed much more effective blood cholesterol concentration decrease from 8.1 ± 1.5 mmol/l to 6.4 ± 1.1 mmol/l, $p < 0.05$; withal CLLD decreased from 5.7 ± 1.5 mmol/l to 4.4 ± 1.3 mmol/l, $p < 0.05$.

The blood triglycerides concentration decreased in pts of group I in 1.3 times during therapy, group II – 1.5 times.

Conclusion: Early use of the lipid-lowering half the daily dose therapy combined with UDCA in NASH pts with AMI and MS provides the liver function tests normalization and concomitant atherogenic dyslipidaemia effective decrease compared with the rosuvastatin assignment. These results are the convincing proof of the hepatocyte dysfunction leading role in the dyslipidaemia pathogenesis.

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**ASSESSMENT OF THERAPEUTIC APPROACHES
IN NAFLD IN CONTEMPORARY CIRCUMSTANCES
IN UKRAINE AND IT CORRELATION
WITH RISK FACTORS (ATTRACTION):
RESULTS OF OPEN MULTICENTRAL PROSPECTIVE STUDY
DIREG_L_04443**

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Non-alcoholic fatty liver disease (NAFLD) is one of the most widespread chronic diffuse liver diseases, 5-years expenses on which were increased on 26%. The cause for the carrying out of this research in Ukraine was the necessity of the study of intercommunication of NASH with the risk factors and low level of compliance to treatment of patients with NASH in Ukraine.

The aim is to study the therapeutic approaches to treatment of NAFLD in Ukraine and to define its intercommunication with the risk factors.

2,188 persons (52.2% women and 47.8% men) from 156 centers were in 37 cities of Ukraine examined, average age 51 ± 11.2 years. Among inspected 1,935 (91.6%) persons lived in town, 177 (8.4%) – in rural locality. Diagnostics of NAFLD was based on the criteria of Dionysus study (2007), taking into account anamnesis of disease, objective physical inspection, anthropometry, biochemistry of blood (ALT, AST, GGT, AP, lipid spectrum), negative markers of viral hepatitis, abdominal ultrasonic scanning.

During this registry it was discovered correlation of NAFLD with next risks factors:

- most of pts were in age group 41–60 years old (57.1%);
- NAFLD is associated with high body weight – 35.8% of pts had BMI 25–30, 51.8% of pts – BMI > 30;
- cardio-vascular diseases (with the exception of arterial hypertension) were seen in 28.9% of pts, known hypertension – in 52.9% of pts;
- earlier diagnosed lipid disorders mentioned 63.5% of pts. Lipid disorders were caused mostly by increasing of triglycerides in 31.3% pts, total cholesterol – in 63.3% pts, high-density lipoproteins – in 12.7% and low-density lipoproteins – in 21.4% pts. But during this investigation there were not found any abnormalities in laboratory test results;
- known diabetes mellitus (DM) was registered in medical history in 728 out of 2,075 (35.1%) pts, recently started DM (1–5 years) and DM type 2 being the largest categories (54.4% and 61.7% out of all DM cases respectively);

Next factors determined therapeutic approach to the NAFLD:

- 91.6% of pts suffered from different gastro-intestinal symptoms. 47.2% of pts mentioned syndrome of intestinal dysbiosis, mostly I–II stage (42.5%); total weakness (61.5%), light discomfort in the abdominal (75.4%), liver increase size (72.5%), mostly up to 1 cm (85.8%);
- liver enlargement, that was identified in 76.7% pts; changes in liver structure in 45.9%; wall contraction of gallbladder – in 72.4%.
- 1,379 (63.9%) of pts had already received NAFLD therapy. The prevalent hepatoprotector was essential phospholipids – 7,644 (56.1%) of pts received it, sylimarin – used 290 (21.3%) pts, Galstena – 95 (7.0%) and others – 213 (15.6%) pts.

At visit 1 hepatoprotectors were prescribed to 2,184 (99.8%) pts. Pts were prescribed mostly by essential phospholipids (1.8 g/day) – 2,088 (95.6%) pts during 9.8 ± 2.7 weeks. There no significant differences in laboratory biochemical indices in NAFLD pts at visit 2 after target treatment.

Hepatoprotectors treatment of NAFLD is a long-term targeted program.

Expediently to comply the treatment duration (up to 6–12 months); to increase daily EPL dose (2.4–3.6 g per day), as the use of traditional (1.8 g per day) during 3 months inefficiently; to treat pts with current recommendations of IASL and EASL, based on research evidence.

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GAS-JET LIVER DISSECTION: BENEFITS AND LIMITATIONS

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Background: There exists a great variety of liver parenchyma dissection techniques. The original method of gas-jet dissection was developed in our Institute. The objective of this research lies in comparing gas-jet dissection technique with the existing ones.

Methods: The original method of gas-jet transection of biological tissues and the apparatus for its realization "Pneumojet" (Patent № 41570 U, UA; Patent № 44610 U, UA; Patent № 44608 U, UA; Patent № 54798 U, UA; Patent № 56676 U, UA; Patent № 56677 U, UA; Patent № 54796 U, UA) was developed in the our institute. The way of separation of tissues of parenchymatous organs includes introduction on a surface of operated organ of handling medium under the pressure exceeding its durability, that allows to allocate vessels from a parenchyma till the crossing moment, and then sensitively to clip or legate them and just after that to cross, if necessary applying various ways of achievement of definitive hemostasis. As a handling medium gas that provides minimum injury is chosen and excludes an overhydration of cells in a resection zone (feature of a water jet transection) and optimizes technological process whereas gas leaves from a surgery field independently.

Efficiency comparison of gas-jet (original apparatus "Pneumojet", Ukraine), ultrasonic ("SONOCA 300", Soring, Germany), water-jet ("Hydrojet", Erbe, Germany) methods of dissection and clamp crushing technique was carried out on 24 mini-pigs. Depending on the liver parenchyma dissection technique, the animals have been divided into 4 groups. We never didn't use Pringle maneuver.

We performed biopsy of the resection surface for examining damage and regeneration on days 7 and 21 after surgery.

Results: The sizes of the resected section of liver and, accordingly, wound surfaces that were formed as a result of operation, did not differ in the investigated groups. The mean blood loss at the resection stage was the smallest in the group of animals that had a gas-jet dissection (3.5 ± 0.15 ml/cm²) and the highest in the clamp crushing technique group – 5.5 ± 0.46 ml/cm² ($p < 0.05$). The dissection speed was the highest in the clamp crushing technique group – 2.9 ± 0.25 cm²/min and was credibly higher than in the gas-jet (2.4 ± 0.16 cm²/min), ultrasonic (2.4 ± 0.13 cm²/min) and water-jet (2.5 ± 0.14 cm²/min) dissection groups (Table 1).

All inflammation components appear in the wound evolution at any type of dissection – vascular and cellular reactions, proliferation of vessels and connective tissue cells, formation of collagen and elastic fibers, their covering of the organ wound surface. However in gas-jet dissection are identified visually empty vacuoles extending injury zone in the area of resection surface without being identified in other dissection types. But, morphological and morphometric parameters of adjacent hepatocytes to the vacuoles were within the normal range. In spite of these features, healing dynamics and cicatrix size at later stages were the most favorable in gas-jet dissection.

Conclusions: Gas-jet dissection is not accompanied by thermal damage of hepatocytes, ensures minimal trauma and fast restoration of hepatocytes. However, the penetration of the gas

bubbles inside resection surface restricts the use of this technique in liver cancer with narrow margins of dissection. Gas-jet technique has no credibly advantages of speed and bloodloss.

Table 1. Intraoperative dissection-related features

	Clamp crushing	Gas-jet dissection	Ultrasonic dissection	Water-jet dissection
Mean dissection speed (cm²/min)	2,9 ± 0,25 *	2,4 ± 0,16	2,4 ± 0,13	2,5 ± 0,14
Mean blood loss (ml/cm²)	5,5 ± 0,46 *	3,5 ± 0,15	3,6 ± 0,13	3,6 ± 0,14

* p < 0.05

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PER ORAL ENDOSCOPIC MYOTOMY: THE EXPERIENCE IN THE CZECH REPUBLIC

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Background and aims: Peroral endoscopic myotomy (POEM) is an endoscopic alternative to laparoscopic myotomy. This promising procedure is still considered experimental. Herein, we report short-term results of the prospective study of POEM in the Czech Republic.

Methods: A single center study. All patients had a diagnosis of achalasia based on endoscopic, manometric (high resolution manometry) and radiologic examinations. For mucosotomy, dissection and myotomy, a triangle knife was used. We analyzed results of 37 consecutive patients (16 female, 21 male, mean age 47 years, range 22–77). A 3-month follow-up was completed in 32 patients and 6-month follow up in 25 patients and 12 month follow up was completed in 8 patients. The primary outcome was symptom relief defined as an Eckhard score ≤ 3. At three months, high resolution manometry and 24-hours pH metry monitoring was performed.

Results: **A. PROCEDURE:** POEM was successfully completed in all patients. The median length of procedure (LOP) was 83 minutes (10th–90th percentiles 64–112). The median myotomy length was 12 cm (9–15). In three patients, an inadvertent mucosotomy occurred on the mucosal site and was treated by an endoscopic clip. In 16 patients (43%), capnoperitoneum was decompressed by using a standard venous cannula and 16 patients experienced subcuta-

neous emphysema which resolved spontaneously. Fever was present on postoperative day 1 in 5 patients (13%). No serious intraoperative or postoperative complications occurred and all patients were dismissed the 2nd–4rd postoperative day.

B. TREATMENT RESULTS: Three and six months after POEM, treatment success (Eckhard score ≤ 3) was achieved in 91% and 93%; median score pre- vs. post-treatment 7 vs. 1; $p < 0,001$). The median percentage of overall improvement was 90%. Quality of life significantly improved (median score 107 before POEM vs. 126 three months and 135 six months after POEM, $p < 0,001$). Manometric parameters (IRP and LES pressure) improved in all but one patient. Three patients did not have a sufficient improvement. One patient underwent successful re-POEM and two other patients are awaiting balloon dilatation.

Heartburn was present in 5 patients (13%) three months after POEM and in 1 patient (4%) six months after POEM. Four patients (16%) have been treated with proton pump inhibitors or antacids on demand. Three months after POEM, reflux esophagitis (LA A) was diagnosed in 9 patients (28%) and a pathological gastro-esophageal reflux (DeMeester score >14) was detected in 13 (40%) patients. All 8 patients with 12 months follow-up are symptom free.

Conclusion: POEM is a safe and effective treatment modality in patients with achalasia with excellent short and medium term results. There is a significant (though almost) asymptomatic reflux postoperatively in 40% of patients in 3-months pH metry studies.

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INCOMPLETE COLONOSCOPY: SEQUELS, ALTERNATIVES, FUTURE

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