

COVERING THE COVER

Combined treatment of gastric cancer: Immunological approach

This is a prospective controlled study aims to investigate new therapeutic approaches for the treatment of gastric cancer. A total of 62 patients with locally advanced gastric cancer and 25 healthy volunteers were included in this study. The patients divided into 2 groups. Group 1 received neoadjuvant multi-agent chemotherapy, which consists of Docetaxel 75 mg/m² on day one + 5-Phthoruracil 500 mg/m² on days two-five + Calcium Folate 50 mg/m² on days two-five. Group 2 used Thymalin 20 mg daily for 6-10 days after the multi-agent chemotherapy course. The cell-mediated and humoral immunity was studied via blood cell differentiation into cells in the immune system. The authors found that the comparison of indices in gastric cancer patients before treatment and healthy persons found a significantly lower synthesis of IgM and G antibodies in gastric cancer patients before treatment. Additionally, the immunity indices in the gastric cancer group that underwent neoadjuvant chemimmunotherapy were safer. See page 151.

HPV16 integration status in esophageal carcinoma

Esophageal cancer is one of the most aggressive malignant tumors worldwide. It has been suggested that high-risk human papillomavirus (HPV) plays a causative role in the development of esophageal squamous cell cancer (ESCC). Nevertheless, this hypothesis remains controversial. In this study from China, Li et al. investigated the association between HPV infection and ESCC. They collected 189 fresh surgically resected tissue samples. Genomic DNA were extracted and HPV were detected using polymerase chain reaction (PCR) with HPV L1 gene primers of My09/11, and HPV16 was detected using HPV16 E6 type-specific primer sets. The copies of HPV16 E2, E6, and human housekeeping gene β -actin were tested by Quantitative PCR for analysis the relationship between HPV16 integration and ESCC. A total of 168 specimens were detected HPV DNA positive from 189 samples and 76 specimens were HPV16 positive. Among HPV16 positive samples, 2 case (with E2/E6 ratio >1) was 2.6% (2/76) purely episomal, 65 cases (with 1 > E2/E6 ratio >0) were 85.6% (65/76) mixture of integrated and episomal, 9 cases (with E2/E6 ratio=0) were 11.8% (9/76) purely integrated. These results indicates that Integration of HPV16 more common than episome genome in the host

genome. Moreover, the prevalence rate of HPV16 integration is increasing with the pathological stage progression of esophageal carcinoma. A high prevalence of HPV16 suggested that HPV16 may play an etiological effect in the progress of ESCC. Integration of HPV16 more common than episome genome in the host cells indicates that continuous HPV infection is key for esophageal epithelial cell malignant conversion. See page 157.

Bacteremia in cirrhotic patients with upper gastrointestinal bleeding

In this retrospective cohort study, Shih et al. evaluated the association of the development of bacteremia with in-hospital mortality and risk factors of bacteremia in cirrhotic patients with upper gastrointestinal bleeding (UGIB). They collected data for a total of 202 cirrhotic patients with UGIB who were admitted to their hospital. Multivariate analysis revealed that the development of bacteremia was associated with a higher mortality rate (adjusted odds ratio [OR] 9.7; 95% CI: 1.9-50.6, p=0.007), while shock and bandemia were associated with the development of bacteremia (adjusted OR 5.3; 95% CI: 2.3-12.7, p<0.0001 and adjusted OR 4.0; 95% CI: 1.6-9.9, p=0.0003, respectively). Present study demonstrates that bacteremia in cirrhotic patients with UGIB is one of the major risk factors leading to in-hospital mortality. Moreover, patients with initial shock and bandemia had a higher incidence of developing bacteremia and prophylactic antibiotics would be more beneficial to these patients. See page 165.

Effects of δ -tocotrienol supplementation in NAFLD

Oxidative stress and inflammation are well-known factors in the pathogenesis of non-alcoholic fatty liver disease (NAFLD). Vitamin E has potent anti-inflammatory and antioxidant properties and may reduce liver injury in NAFLD. Delta-tocotrienol (δ -tocotrienol) is the most potent isoform of vitamin E. In this issue of TJJ, Khan et al. evaluated the efficacy and safety of δ -tocotrienol for the treatment NAFLD. A total of 71 patients over 20 years, belonging to both sexes, having ultrasound-proven fatty liver, fatty liver index (FLI) of ≥ 60 and persistent elevation of alanine transaminase were enrolled in this randomized, double-blind, placebo-controlled pilot study. The patients were assigned to receive either oral δ -tocotrienol (n=35) 300 mg twice daily or placebo (n=36) for 12 weeks. The authors found that δ -tocotrienol

showed greater efficacy than placebo in decreasing serum aminotransferases, C-reactive protein (hs-CRP), malondialdehyde (MDA) and FLI score ($p < 0.001$), but did not improve hepatic steatosis on ultrasound. They concluded that δ -tocotrienol is safe, effectively improved aminotransferase levels and inflammatory and oxidative stress markers in NAFLD patients. See page 170.

Changes in acute viral hepatitis epidemiology

Both hepatitis A (HAV) and hepatitis B virus (HBV) infections have decreased in incidence and prevalence with use of effective vaccines in several countries. The national routine infant hepatitis B vaccination program started in Turkey in 1998. Karacaer et al. evaluated the changes in the epidemiology of acute viral hepatitis in recent years in an adult Turkish population. They retrospectively analyzed the medical records of 852 patients with acute viral hepatitis from 17 centers. The median age was 31 years old (range 17–89). They found that the most common causes of acute hepatitis were HBV (55.2%) and HAV (37.6%). A total of 84.2% of the patients were hospitalized and the median hospital stay was 9 days (range 1–373). The most frequently reported symptom was fatigue (73.7%), and the most common complications were cholecystitis (0.4%) and fulminant hepatitis (0.4%). From these results, the authors concluded that larger vaccination programs covering older age groups should be implemented in Turkey. See page 177.

Simultaneous endoscopic submucosal dissection for colonic lesions

Endoscopic submucosal dissection (ESD) has been developed for 'en-bloc' resection of large lesions in the gastrointestinal tract. It is still performed in a small number of tertiary centers in Western countries because of technical difficulty, longer procedure times, and increased risk of perforation. In this issue of TJG, Kwak et al. evaluated the feasibility and safety of ESD of two colorectal lesions in one session. The lesions of 16 patients who underwent two ESD procedures were matched with those of 64 patients who underwent single ESD procedures. Compared with single ESD, two simultaneous colorectal ESDs in a single patient did not increase procedure-related complications and achieved similar en bloc and curative resection rates, while the net ESD time was significantly longer in the double ESD group than in the single ESD group (104.0 ± 36.2 minutes vs. 59.1 ± 39.2 minutes, $p < 0.001$). This is an inspiring study that has opened new perspectives on ESD. See page 183.

Pancreatic stump closure using only stapler is associated with high postoperative fistula rate after minimal invasive surgery

Postoperative pancreatic fistula (POPF) is one of the major complications after distal pancreatectomy (DP). It is associated with significant morbidity and mortality and is responsible for prolonged hospital stay and cost. In this issue of TJG, Yüksel et al. evaluated the risk factors which can lead to POPF. They retrospectively analyzed the medical records of 96 patients who underwent DP. The overall morbidity rate was 51% and the most common postoperative complication was POPF (33.3%). POPF rate was %58.6 (17/29) in patients whose pancreatic stump closure was performed with only stapler, whereas the rate was %3.6 (1/28) in the group where the stump was closed with stapler plus over-sewing sutures. Multivariate analysis revealed that minimally invasive surgery (OR: 0.286, 95%CI: 0.106-0.776, $P=0.014$) and intra-operative blood transfusion (OR: 4.210, 95%CI: 1.155-15.354, $P=0.029$) were independent risk factors for POPF. From these results, authors concluded that the risk of POPF is determined by intra-operative variables rather than the demographic or clinico-pathologic characteristics of the patients. Laparoscopic distal pancreatectomy is associated with a higher risk of POPF when stump closure is performed with only staplers. Intraoperative blood transfusion is another risk factor for POPF. On the other hand, over-sewing sutures to the stapler line reduces the risk of POPF. See page 191.

Effects of hemodialysis combined with hemoperfusion on severe acute pancreatitis

Severe acute pancreatitis (SAP) is characterized by persistent organ failure. Better treatment strategies are needed to improve the clinical outcome of patients. Li et al. evaluated the effect of hemodialysis combined with hemoperfusion on SAP. A total of 37 patients accepted hemoperfusion combined with hemodialysis were in observational group, and 31 patients treated with conventional therapy and hemoperfusion were taken as control. They found that the leukocyte count, neutrophil percentage, amylase (AMY), blood urine nitrogen (BUN), creatinine (Cr), total bilirubin (TBIL) levels and the complication rate after treatment were significantly lower in observational group than in control group. The time of symptoms disappearing was also shorter in observational group compared with the control group. The combination of hemodialysis and hemoperfusion could play a better effect for SAP on removing toxic metabolites and inflam-

mation mediators. It not only shortens the time of symptoms disappearing, but also decreases the incidence of complications and the mortality. See page 198.

The effect of Ursodeoxycholic acid and vitamin E in prevention of liver injury from methotrexate in childhood leukemia

Methotrexate (Mtx) is an antimetabolite agent used as a treatment for some neoplastic and inflammatory diseases. One of the most common side effects of Mtx is hepatotoxicity. Mtx-induced liver toxicity may limit its clinical use. In this randomized controlled study, the authors investigated the efficacy of ursodeoxycholic acid (UDCA) and vitamin E in preventing liver injury in pediatric B-cell acute lymphoblastic leukemia (ALL) who were treated with methotrexate in their maintenance phase of treatment. A total of 80 children with B cell ALL were randomly divided into 4 groups: Group 1 received oral vitamin E 400 mg daily, Group 2 used oral UDCA 15 mg/kg/day, Group 3 took the combination of two drugs and Group 4 served as the control group. Considering liver function tests, the only parameter that changed significantly was the total bilirubin level in Group 1 ($p=0.036$). None of the patients showed evidence of significant fibrosis on liver fibroscan. Eight patients had some evidence of mild to moderate fibrosis (F1, F2), but the results were not different between the groups as well as pre- and post-study in each group. The authors concluded that low-dose methotrexate does not cause significant liver fibrosis in pediatric leukemia. Antioxidant agents such as UDCA or vitamin E has no protective effect on Mtx-induced liver toxicity in children. See page 203.

Is celiac disease misdiagnosed in children with functional constipation?

Celiac disease (CD) is an immune mediated intestinal inflammation that is triggered by gliadin. Prevalence of CD is approximately 1/150-200 in most countries and 0.45-1.15% in healthy Turkish school children. In addition to

typical symptoms, pediatric patients with CD can exhibit atypical symptoms such as chronic constipation. However, there is no general recommendation to test CD in pediatric patients with chronic constipation routinely. In this issue of TJG, Akman et al. evaluated the prevalence of celiac disease in pediatric patients suffering from chronic constipation. A total of 1.046 children (between 2 and 18 years of age) with chronic constipation according to Rome III criteria and who were resistant to conventional treatment were included. Tissue transglutaminase (anti-tTG) and anti-endomysial antibodies (EMA) were positive in 36 patients (3.25%). The CD diagnosis was confirmed by duodenal mucosal biopsies. In this study, ratio of 1:28 of CD was diagnosed in chronic constipated children. From these results, the authors concluded that the use of screening tests for CD should be considered in children with constipation resistant to conventional treatment. This strategy assists in early diagnosis and prevents unnecessary time and money consumption as well as prolonged laxative treatments. See page 210.

Osteoporosis and vitamin K in celiac disease

One of the possible complications of celiac disease (CD) is the inability to develop optimal bone mass in children. In this issue of TJG, Volkan et al. aimed to investigate bone mineral density (BMD) in children with CD and to assess the relationship between low BMD and vitamin K levels. A total of 72 children with CD and 30 age- and sex-matched healthy control subjects were prospectively included in this study. They found that the mean BMD Z-score of CD group was significantly lower than that of the control group (-1.23 ± 1.07 vs -0.35 ± 1.04 , $p=0.001$), while vitamin D and K_2 values did not differ between the two groups. BMD was positively correlated with vitamin D ($r=0.198$, $p=0.001$) and negatively with PTH ($r=-0.397$, $p=0.002$). They concluded that BMD of children with CD was lower than that of the control subjects. Further studies investigating the effect of vitamin K on bone in CD are required. See page 215.