Indian Journal of Gastroenterology September–October 2020

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Published online: 23 November 2020
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Clinical efficacy of infliximab level and anti-infliximab antibody measurement in patients with inflammatory bowel disease: An audit

Anti-TNF therapies have transformed the care of patients with inflammatory bowel disease (IBD). Being immunogenic, these are associated with loss of response; up to 30% of patients have a primary non-response and up to 50% develop loss of response [1]. Treatment failure can be caused by low or undetectable drug concentrations due to immune (anti-drug antibodies) and non-immune clearance [1]. Therapeutic drug monitoring (TDM) has been adopted for anti-TNF dose optimization. Dave et al. Mumbai, India present an experience infliximab (IFX) TDM monitoring in 50 IBD patients and its effect on management decisions [2]. IFX levels were sub-therapeutic in 40 and high antibody titers were present in 8 of 30 patients. IFX dose was altered in 35 patients (increased in 7, decrease in dosing interval in 17, increase in interval in 2 and stopped in 2 patients). Two patients had surgery and 5 had a change in biologic. TDM proved a powerful tool for effective treatment decisions.

Long-term outcomes in perianal fistulizing Crohn's disease in a resource-limited setting: A cohort analysis

The management of fistulising perianal Crohn's disease (pCD) is challenging. The established treatment pathway is

multidisciplinary involving management of proctitis and drainage of sepsis, prior to optimization of medical treatment, usually with a combination of thiopurine and antitumor necrosis factor (TNF) therapies [3]. Initial drainage of sepsis and placement of loose setons are the mainstay of surgical treatment, although surgery aimed at fistula closure may be offered in selected patients, and de-functioning stoma or proctectomy is sometimes required [3]. Data from resource limited settings are limited. Vuyyuru and colleagues report long-term outcomes of patients with pCD from All India Institute of Medical Sciences (AIIMS), New Delhi, India [4]. Among 65 patients (median follow-up 45 months), response rates to immunomodulators, biologicals, fistula surgery and defunctioning were 25%, 39.5%, 42.8% and 45.4%, respectively. Surgery was first-line therapy in 46.1% patients. Fistula surgery was associated with the highest risk of relapse. The authors report a potential role for immunomodulators in resource limited settings, acknowledging gold standard care when possible.

Self-expanding metal stent in esophageal perforations and anastomotic leaks

Esophageal perforations and leaks can be life-threatening and are associated with high in-hospital mortality (25% and 30%, respectively) and surgical treatment is also associated with major complications [5]. Self-expanding metal stents (SEMS) are emerging as a minimally invasive treatment alternative [5]. John and colleagues present a retrospective experience of SEMS in 26 patients for esophageal perforation (17 patients) and anastomotic leaks (9 patients) from Christian Medical College, Vellore, India over a 7-year period [6]. In this small series, stent placement (fully covered SEMS in 25) was successful in all the patients and of 22 patients available for follow-up, 20 had healed mucosal defects. Stent related complications were noted in 5 patients (migration in 3, stricture and reactive hyperplasia in 1 each).

The authors suggest a role for SEMS for bridging and healing of benign esophageal perforation and leaks. Larger

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prospective studies with controlled data and follow-up will enable comparison with surgical outcomes; such studies are needed in this challenging area.

Effect of successive endoscopic procedures in polyp and adenoma detection rate: Too early is not always too good

Effective colorectal cancer (CRC) surveillance hinges on detection and resection of adenomatous lesions, which itself is a function of adequate bowel preparation and endoscopist's key performance indices facilitating high-quality colonoscopy. Among these, endoscopist fatigue from all day colonoscopy, diminishing adenoma detection later in the afternoon has been implicated [7]. Olivera and colleagues from Centro de Educación Médica e Investigación Clínica, Argentina report their retrospective experience of the impact of cumulative fatigue on adenoma detection rates (ADR) among 3388 patients over a 2 year period [8]. Four procedures were performed in 2 time slots (morning and afternoon) and 1 in round 3 later in the evening. Both ADR and number of adenomas per colonoscopy were not affected by the time of the day with the authors suggesting improving psycho-cognitive abilities with successive colonoscopies. These findings notwithstanding, endoscopists must maintain self-awareness and proactively monitor whether and how fatigue may affect their colonoscopic performance, their willingness to carefully inspect the mucosa, and ultimately their ADR.

Short-term mortality in patients with cirrhosis of the liver and acute kidney injury: A prospective observational study

Renal failure is a recognized serious complication of liver cirrhosis and portends an ominous prognosis [9]. In a single-centre prospective observational study, Kumar and colleagues from Patna, Bihar, India assessed development of complications and in-hospital and 30-day mortality in decompensated cirrhotics (52% of alcoholic etiology) with acute kidney injury (AKI) [10]. AKI (rise of serum creatinine ≥ 0.3 mg/dL within 48 h of admission or increase of serum creatinine $\geq 50\%$ from stable baseline over the previous 3 months) developed in 28.45% (142/499) patients. Jaundice, hepatorenal syndrome, AKI stage at peak of creatinine and higher levels of bilirubin, alanine transaminase (ALT), international normalized ratio, Child-Turcotte-Pugh and model for end-stage liver disease (MELD) scores were predictive of mortality. Even as further mechanistic research provides more pathophysiological insights, prevention, early recognition and correction of AKI

mitigate against adverse outcomes and clinicians should remain vigilant to this when managing decompensated cirrhosis.

Difficult-to-treat ascitic fluid infection is a predictor of transplant-free survival in childhood decompensated chronic liver disease

Ascitic fluid infection (AFI) is a serious complication of cirrhosis and needs prompt diagnosis and treatment to reduce morbidity and mortality [11]. Data in the pediatric population are scarce. Mahajan and colleagues from Institute of Liver and Biliary Sciences, New Delhi, India report on outcomes on 252 children undergoing diagnostic paracentesis for suspected ascitic fluid infection from a cohort of 814 children with chronic liver disease [12]. AFI was diagnosed in 79 children of whom 73.4% had culture-negative neutrocytic ascites. Younger age, male gender, higher total leukocyte count, fever, and increase in ascites or new-onset ascites were independent factors to predict AFI. Of 23 children with a positive ascitic fluid culture, 11 were multi-drug resistant. Hepatic encephalopathy, Model for End-stage Liver Disease/Pediatric End-stage Liver Disease (MELD/PELD) and difficult-to-treat AFI were independently associated with death and or liver transplant. The authors advise prompt diagnostic paracentesis in children with ascites with fever, new-onset or increasing ascites and/or raised total leukocyte count given the high-risk of liver transplant or death with AFI.

In vitro analysis of gallstone formation in the presence of bacteria

The role of bacteria in the etiopathogenesis of gallstone formation attracted interest [13]. Sharma and colleagues from Ranchi, Bihar, India report an in-vitro study assessing bacterial isolates for urease activity, slime and β -glucuronidase production and their role in the formation of gallstones at a supersaturated concentration of cholesterol [14].

Using Brilliant Green Bile Broth (BGBB) media (with composition similar to human bile), 4 different experimental sets were prepared and inoculated with *Salmonella*, *Enterococcus*, *Helicobacter* and *Neisseria*, respectively and isolated from gallstones themselves. Of these bacteria, only *Helicobacter* did not possess slime activity. A control set was also established, which was devoid of bacteria. Solidification of gallstone was observed only in bacteria with slime activity leading the investigators to conclude that the slime activity of bacteria leads to solidification of gallstones whereas the other

activities accelerate the nucleation of gallstone formation enhancing the severity of the disease. Further research implicating bacteria in etiopathogenesis of gallstone is needed.

Prevalence of cirrhotic cardiomyopathy and its relationship with serum pro-brain natriuretic peptide, hepatorenal syndrome, spontaneous bacterial peritonitis, and mortality

Decompensated liver cirrhosis with its pathophysiological sequelae such as peripheral vasodilatation and hyperdynamic circulation is associated with cirrhotic cardiomyopathy [15]. Kapoor and colleagues from Maulana Azad Medical College and Lok Nayak Hospital, New Delhi, India report a small prospective study to report on the prevalence of cirrhotic cardiomyopathy [16]. The authors performed 2D-color Doppler, and tissue Doppler echocardiography on 5 cirrhotic patients and compared them with 30 age- and sex-matched healthy controls. Additionally, serum pro-brain natriuretic peptide (pro-BNP) and troponin-T levels were measured. Patients were followed up for 6 months to look for complications and mortality. Diastolic cardiomyopathy was noted in 56.6% of cirrhotic patients and it correlated with the severity of cirrhosis. Serum pro-BNP levels were also higher in patients with diastolic dysfunction with cirrhosis. These patients had shorter survival and an increased risk of hepatic encephalopathy, spontaneous bacterial peritonitis and hepatorenal syndrome as a complication of their cirrhosis. Further mechanistic research on this issue including its biomarker and effect of pharmacological interventions is warranted.

Endoscopic mucosal resection for early esophageal carcinoma is effective and safe but necessitates continued surveillance

Endoscopic mucosal resection (EMR) has been advocated by international guidelines for the treatment of early esophageal cancer (EEC, T1a and T1b lesions) [17, 18]. Hasan and colleagues report their experience of EMR in 79 patients with EEC from University of Iowa Hospitals and Clinics, Iowa, USA between 2006 and 2015 [19]. EMR was curative in 51 patients with a T1a lesion, achieving complete remission in 50 (98%) of them. Cancer recurred locally in 6 (12%) of 50 patients at a median follow-up of 48 months. EMR achieved complete remission in 47 of 50 patients with complete remission with 1 and 5-year cancer-free survival of 94.2% and 88.4%, respectively. Patients with complete eradication of Barrett's had lower risk of recurrence of adenocarcinoma (AC). EMR alone was not curative in 16 patients with T1b AC and 3 with T1a squamous cell carcinoma invading the muscularis mucosae. The AGA recommends that EMR for

high-grade dysplasia (HGD) or early EC is performed by experts who perform minimum of 10 new cases annually [18].

Utility of bowel ultrasound in assessing disease activity in Crohn's disease

Modern treatment paradigms recognize the need to achieve clinical, biochemical and endoscopic and transmural healing in the management of patients with Crohn's disease (CD) [20]. Assessment of transmural healing typically involves a combination of modalities such as small bowel enterography (CT or MR) and ileo-colonoscopy [21] often periodically to assess the target of remission. Resurgent interest in ultrasound in assessing small bowel disease has now extended to bowel ultrasound. Ramasamy and colleagues from Aster CMI Hospital, Bangalore, India describe a prospective series of 35 patients with CD assessed by colonoscopy, MR enterography and gastrointestinal ultrasound within 2 weeks [22]. Bowel wall thickness (BWT) ≥ 3 mm and Doppler activity ≥ 2 had the highest sensitivity (100% and 95.6%, respectively) for detecting active disease on colonoscopy. The role of bowel wall vascularity and thickness and its correlation with inflammatory endoscopic clinical and biochemical activity needs further exploration even if not ready for prime time presently.

Correlation of menstrual distress to severity of gastrointestinal symptoms in inflammatory bowel disease patients

Among the triggers implicated the flare of inflammatory bowel disease (IBD) symptoms are variations in ovarian hormones with the menstrual cycle [23]. Thomas and colleagues from Houston Methodist Hospital, Houston, USA conducted a survey of consecutive women with IBD and administered the short IBD questionnaire (SIBDQ) and evaluated correlation of menstrual symptoms using the Moos Menstrual Distress Questionnaire (MDQ) and endoscopic disease activity as recorded using the Mayo endoscopic score for ulcerative colitis and Simple Endoscopic Score (SES-CD) for Crohn's disease [24]. They noted a statistically negative correlation between MDQ and SIBDQ scores ($p < 0.001$), no correlation between SIBDQ, MDQ and endoscopic scores ($p = 0.094$, 0.626 , respectively). The lack of correlation with objective markers of inflammation suggests other pathophysiological explanations such as from prostaglandin induced smooth muscle contractions. Clinicians should carefully distinguish "inflammatory" from functional symptoms, through an objective assessment and use supportive treatment appropriately in the absence of objective gut inflammation. Further mechanistic research is

urgently needed given the negative impact of these functional symptoms of quality of life.

Compliance with ethical standards

Conflict of interest JKL declares that he has no conflict of interest.

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