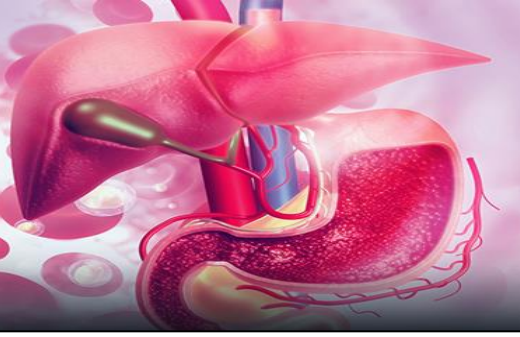
Enteron



Volume 2|Issue 25|2021

Dear Doctor,

Greetings from Micro Labs limited. We are happy to bring you "ENTERON" which contains latest and interesting news in the field of Gastroenterology.

Inside This Issue:

Should you require any specific article or medical information, please feel free to contact us at medicalservices@microlabs.in

Looking forward to your valuable feedback

Best Regards,

Medical Team, Micro Labs Ltd

Enteron

Volume 2|Issue 25|2021

Infliximab-induced seizures in a patient with Crohn's disease: a case report

Introduction

Infliximab is currently used as the first-line treatment for Crohn's disease(CD). During the 20 years since its first approval in 1998, infliximab has revolutionized the treatment of inflammatory bowel disease(IBD). Over half a million patients have been treated with tumor necrosis factor (TNF)-α antagonists, but concerns regarding their safety have been raised worldwide.The most commonly reported adverse reactions to infliximab include acute or delayed hypersensitivity reactions; serious infections including reactivation of tuberculosis and hepatitis B virus; malignancy, especially lymphoma and hematologic reactions. However, new and rare side effects have been increasingly reported in post-marketing reports. Here, we have reported a rare case of a patient with CD who experienced infliximab induced seizures, diagnosed on normal magnetic resonance imaging (MRI) of the brain. Moreover, the rechallenge with infliximab was positive.

Case presentation

A 60-year-old female presented with a 10-day history of small intestinal stenosis due to CD. The patient was diagnosed with CD in 2015 due to chief complaints of abdominal pain and watery diarrhea (3−4 times per day). Patient was treated with mesalazine (3 g/day), which partially alleviated the symptoms of abdominal pain and diarrhea (2−3 times per day). Ten days before admission, patient underwent colonoscopy, but it was difficult to advance the colonoscope due to secondary intestinal stenosis. Biopsy and three-dimensional computed tomography of the small intestine confirmed the diagnosis of CD. Following admission, a series of related examinations were performed. Electrocardiography revealed a normalized rhythm. Further evaluation revealed slight leukopenia. T cell spot test for tuberculosis (T-SPOT. TB) revealed negative findings. No history of alcohol use or drug abuse. Subsequently, treatment with infliximab was initiated at a dosage of 5 mg/kg. Patient did not experience any side effects after the first infliximab infusion. Two weeks later, patient received the second infliximab infusion (5 mg/kg), but after 5 days, patient suddenly developed short episodes of impairment of consciousness at home along with limbs twitches and the extroversion of eyeball. During this episode, patient bit her tongue and head was hurt. The episodes lasted for approximately 3 min, and patient was taken to a local hospital for treatment. However, patient was not treated after observation at the hospital (details unspecified).

According to the schedule, the patient received the third infliximab infusion at a loading dose of 5 mg/kg. Patient experienced repeated episodes after 5 days of the third infusion. Patient was admitted for further evaluation. Laboratory data showed normal findings, except a high L-cholesterol level (3.35 mmol/L; normal range, 1.89−3.1 mmol/L) and low lencocyte count (2.7 × 109/ L; normal range, 3.5−9.5 × 109/ L). All physical examination findings were unremarkable. On the third day of admission, patient experienced another similar seizure episode. Therefore, diazepam (5 mg) and sodium valproate(800 mg) were administered intravenously to control the seizures. No recurrence was observed after treatment during hospitalization. Patient underwent a brain 3.0 T magnetic resonance angiography (MRA), which showed no apparent abnormality. Video electroencephalography revealed background activity in the alpha range with an amplitude reduction but a good waveform. On both sides of the forehead and temporal area, scattered sharp waves were observed; the waves were more obvious on the right side. The Electroencephalogram (EEG) confirmed the diagnosis of seizures is highly suspected that the occurrence of the seizures may be associated with the use of infliximab. The patient started maintenance therapy with valproic acid (500 mg/day) and was discharged after 6 days. Although there was a clear response to infliximab with a reduction of diarrhoea and abdominal pain, the infliximab treatment was ceased and no seizures occurred after discharge.

Discussion and conclusions

Infliximab is a monoclonal antibody against the soluble and membrane tumour necrosis factor (TNF)-α. It is effective in inducing and maintaining remission in patients with moderate-to-severe CD refractory to conventional therapy. However, administration of infliximab is associated with a well-recognized risk of infusion-related adverse events, such as infusion reactions, autoimmune disorders, malignancies, opportunistic infections, and serious infections. The neurological effects of infliximab have also been reported. Headache is the most commonly reported, occurring in 12–18 % of patients studied in the clinical trial setting. The other commonly reported events include peripheral neuropathy and central nervous system and/or spinal cord demyelination. Most patients have good tolerance to infliximab; however, with its wide use in various auto-inflammatory and immune diseases, it is expected that more adverse drug reactions will be reported in the future. A literature review revealed that infliximab-related seizures has been rarely reported.

Enteron

Volume 2|Issue 25|2021

Summary of patient characteristics, seizures, and outcome

Patients	Age at presentation, gender	Inflammatory disorder	TNF-alpha inhibitor onset to seizures	Features of seizures	EEG	CSF	Other	Treatment for the seizures	Seizures outcome	Inflammatory disorder outcome	Study author and year of publication
1	14, male	Crohn's disease	5 days after the first infliximab administration	Repeated episodes each lasting about 1 min and followed by several periods of generalized tonic clonic seizures lasting more than 6 min	Mild excess slow wave activity	Normal	MRI revealed abnormal T2 and fluid-attenuated inversion recovery signal hyper-intensities in a broadly symmetrical distribution affecting the cerebellar hemispheres, occipital poles, medial parietal lobes, and peripheral frontal lobes	TNF-alpha inhibitor stopped, phenytoin	No more seizures occurred	Remission for 6 months and finally relapse, culminating in colectomy and ileos-tomy.	Zamvar,2009[9]
2	74, male	Crohn's disease	2 days after the second infliximab administra-tion	Impairment of conscious-ness, amnesia and arrest of volitional movements, confusion and diso-rientation, aggressive-ness	Focal paroxys-mal activity	Not recorded	MRI showed encepha-lopathy involving mainly corti-cal regions	TNF-alpha inhibitor stopped	No more seizures occurred	Not recorded	Brigo,2011[10]
3	24, female	Crohn's disease	3 days fol-lowing the second infliximab infusion	Experienced 2 episodes of generalized tonic clonic seizures	Diffuse nonspecific cerebral dysfunction	Not recorded	MRI showed scattered T2/FLAIR signal abnormalities in the sub-cortical white matter pre-dominantly in the frontal and posterior parietal lobes	TNF-alpha inhibitor stopped	No more seizures occurred	Not recorded	Chow,2016[12]

The mechanism of infliximab-induced seizures is unclear. However, it may be due to the systemic proinflammatory effects of α-TNF agents that cause an inflammatory response in the nerves. Therefore, infliximab should be cautiously administered to patients to minimize possible morbidity for patients. Medication withdrawal is the first step in managing patients with suspected drug-induced neuropathy. Neurological assessment and tight clinical monitoring before and during therapy with infliximab should be performed in patients with pre-existing seizure disorders. If absolutely necessary, prior assessment and appropriate measures should be still taken before initiating therapy.

Source: Lv Z, Zhang X, Wu L. Infliximab-induced seizures in a patient with Crohn's disease: a case report. BMC Gastroenterol. 2021 Apr 27;21(1):193.

Enteron

Volume 2|Issue 25|2021

Aggressive fluid hydration plus non-steroidal anti-inflammatory drugs versus non-steroidal anti-inflammatory drugs alone for post-endoscopic retrograde cholangiopancreatography pancreatitis (FLUYT): a multicentre, open-label, randomised, controlled trial

Introduction:

Pancreatitis is the most common complication of endoscopic retrograde cholangiopancreatography (ERCP). Prophylactic rectal administration of non-steroidal anti-inflammatory drugs (NSAIDs) is considered as standard of care to reduce the risk of post-ERCP pancreatitis. Aggressive hydration might further reduce this risk. Guidelines recommend aggressive hydration in patients who are unable to receive rectal NSAIDs.

Aim: To evaluate the added value of aggressive hydration in patients receiving prophylactic rectal NSAIDs.

Methods

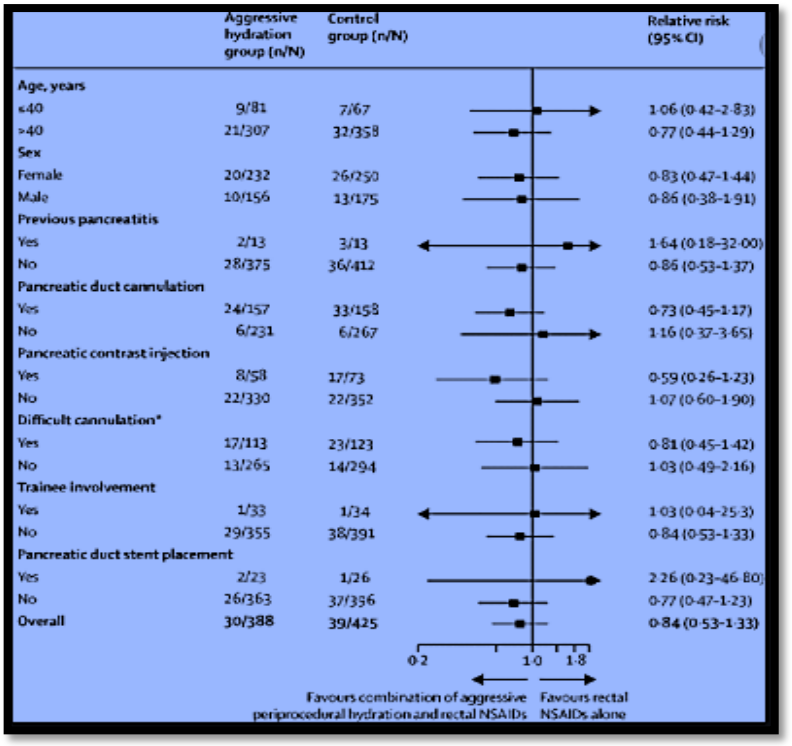
A multicentre, open-label, randomised, controlled trial. Patients with age between 18 and 85 years with moderate to high risk of post-ERCP pancreatitis were included. Patients were randomly assigned to a combination of aggressive hydration and rectal NSAIDs (100 mg diclofenac or indomethacin; aggressive hydration group) or rectal NSAIDs (100 mg diclofenac or indomethacin) alone (control group). Aggressive hydration comprised 20 mL/kg intravenous Ringer's lactate solution within 60 min from the start of ERCP, followed by 3 mL/kg per h for 8 h. The control group received normal intravenous saline with a maximum of 1·5 mL/kg per h and 3 L per 24 h. The primary endpoint was post-ERCP pancreatitis and was analysed on a modified intention-to-treat basis (including all patients who underwent randomisation and an ERCP and for whom data regarding the primary outcome were available).

Results:

Among 826 patients, 388 in the aggressive hydration group and 425 in the control group were included in the modified intention-to-treat analysis. Post-ERCP pancreatitis occurred in 30 (8%) patients in the aggressive hydration group and in 39 (9%) patients in the control group (relative risk 0·84, 95% CI 0·53–1·33, p=0·53).

Enteron

Volume 2|Issue 25|2021



There were no difference in serious adverse events, including hydration - related complications (relative risk 0·99, 95% CI 0·59–1·64; p =1·00), ERCP-related complications (0·90, 0·62–1·31; p=0·62), intensive care unit admission (0·37, 0·07–1·80; p = 0·22), and 30-day mortality (0·95, 0·50–1·83; p = 1·00).

Conclusion

Aggressive periprocedural hydration did not reduce the incidence of post-ERCP pancreatitis in patients with moderate to high risk of developing this complication who routinely received prophylactic rectal NSAIDs. Therefore, the burden of laborious and time-consuming aggressive periprocedural hydration to further reduce the risk of post-ERCP pancreatitis is not justified.

Source: Geenen, et al. Aggressive fluid hydration plus non-steroidal anti-inflammatory drugs versus non-steroidal anti-inflammatory drugs alone for post-endoscopic retrograde cholangiopancreatography pancreatitis (FLUYT): a multicentre, open-label, randomised, controlled trial. The Lancet Gastroenterology & Hepatology. May 01, 2021;6 (5):350-358

Enteron

Volume 2|Issue 25|2021

Lower serum chloride concentrations are associated with increased risk of mortality in critically ill cirrhotic patients: an analysis of the MIMIC-III database

Introduction

Cirrhosis is often complicated with abnormalities in serum electrolyte level. Serum sodium has been considered as an important electrolyte prognostic marker. As suggested, addition of serum sodium to the Model for End-stage Liver Disease (MELD) score would increase its accuracy in predicting mortality. The prognostic value of serum chloride and its interplay with serum sodium in patients with cirrhosis is understood despite its broad availability in routinely used blood chemistry panels. Serum chloride performs a large number of functions in the body including the maintenance of osmotic pressure, acid–base balance, muscular activity, and the regulation of body fluid distribution. Emerging studies have identified hypochloremia as an independent prognostic marker in patients with chronic heart failure and chronic kidney diseases. However, serum chloride has scarcely been investigated as a potential biomarker of cirrhosis.

Aim: To investigate whether serum chloride levels were associated with mortality of critically ill cirrhotic patients.

Methods:

Critically ill cirrhotic patients were identifed from the Multi-parameter Intelligent Monitoring in Intensive Care III Database.

Primary outcome: ICU mortality.

Logistic regression was used to explore the association between serum chloride levels and ICU mortality. The area under the receiver operating characteristic curves (AUC) was used to assess the performance of serum chloride levels for predicting ICU mortality.

Results:

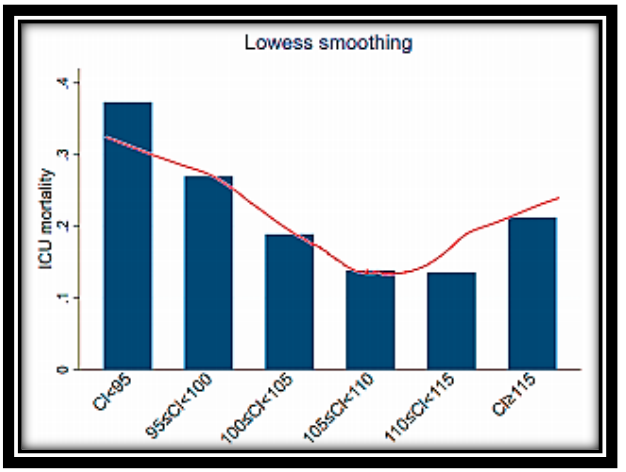
Enteron

Volume 2|Issue 25|2021

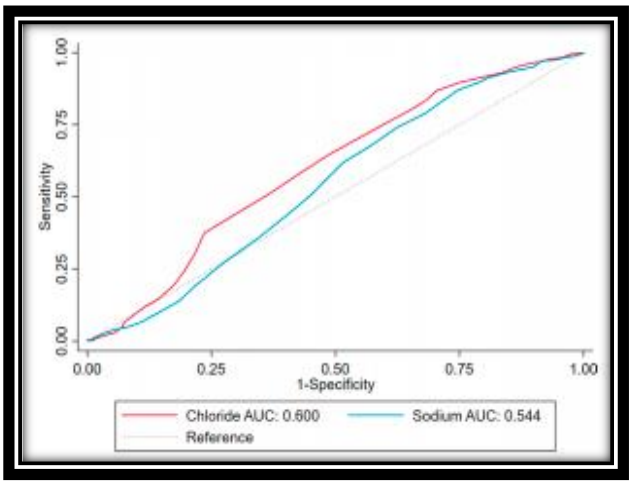
Around 1216 critically ill cirrhotic patients were enrolled in this study. The overall ICU mortality rate was 18.8%. Patients with hypochloremia had a higher ICU mortality than those with non-hypochloremia (34.2% vs. 15.8%; $p < 0.001$).

After multivariable risk adjustment serum chloride levels remained independently associated with ICU mortality (OR 0.94; 95% CI 0.91–0.98; p=0.002) in contrast to serum sodium levels, which were no longer significant (OR 1.03; 95% CI 0.99–1.08; p=0.119).

Association between chloride and ICU mortality determined using the Lowess smoothing technique



Comparison of the receiver operating characteristic curves of sodium and chloride to predict ICU mortality



The AUC of serum chloride levels (AUC, 0.600; 95% CI 0.556–0.643) for ICU mortality was statistically higher than that of serum sodium levels (AUC, 0.544; 95% CI 0.499–0.590) ($p<0.001$).

Conclusions:

Study shows that serum chloride levels are independently and inversely associated with ICU mortality in critically ill cirrhotic patients. This finding highlights the clinical significance of chloride, a routinely measured electrolyte, in prognostication for critically ill cirrhotic patients.

Enteron

Volume 2|Issue 25|2021

Source: Ji Y, Li L. Lower serum chloride concentrations are associated with increased risk of mortality in critically ill cirrhotic patients: an analysis of the MIMIC-III database. BMC Gastroenterol. 2021 May 1;21(1):200.