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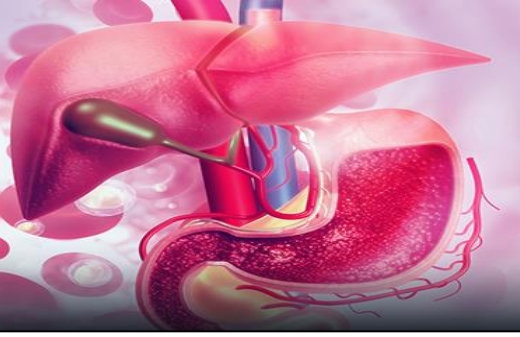

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Dear Doctor,

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:

1. Proton Pump Inhibitor Use, Hypomagnesemia and Risk of Cardiovascular Diseases. The Atherosclerosis Risk in Communities (ARIC) Study
2. Role of Gastrointestinal Hormones as a Predictive Factor for Long-Term Diabetes Remission: Randomized Trial Comparing Metabolic Gastric Bypass, Sleeve Gastrectomy, and Greater Curvature Plication.
3. A Network Meta-Analysis of Randomized Controlled Trials on the Treatment of Eosinophilic Esophagitis in Adults and Children

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

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Idiopathic acute pancreatitis - A myth or reality? Role of endoscopic ultrasonography and magnetic resonance cholangiopancreatography in its diagnosis

Introduction:

In most of the cases, that is around 10% to 30% patients with acute pancreatitis(AP) do not have a cause after the routine investigations, and are considered as having idiopathic acute pancreatitis (IAP). Establishing the etiology in such patients will prevent recurrences and evolution to chronic pancreatitis. Endoscopic ultrasonography (EUS) and magnetic resonance cholangiopancreatography (MRCP) characteristically are used to diagnose IAP when routine methods fail but their exact role is not determined.

Methods

This prospective study was undertaken in a tertiary care hospital, in which patients admitted initially with diagnosis of IAP were evaluated. These patients underwent MRCP and EUS at least 4 weeks after an attack of AP. The results of EUS and MRCP were compared and analyzed with various clinical variables using suitable statistical tests.

Results

A total of 31 patients with IAP were included. EUS and/or MRCP was able to establish at least one etiology in 17 patients (54.8%). The diagnoses revealed were gallbladder (GB) microlithiasis, GB sludge, choledocholithiasis, pancreatobiliary ductal anomalies, pancreatic adenocarcinoma, and intraductal papillary mucinous neoplasm.

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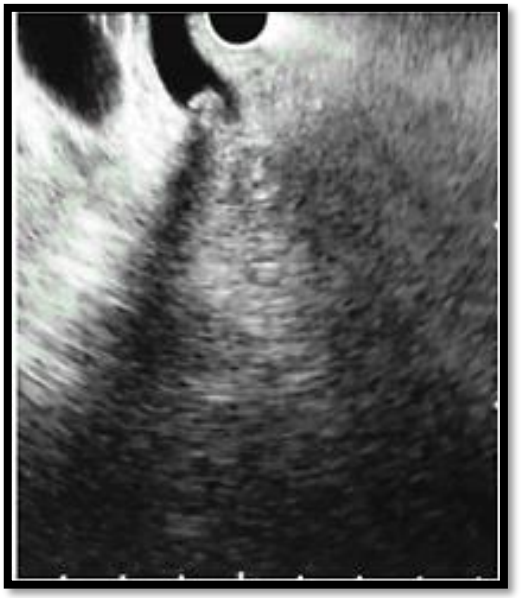

Endoscopic ultrasound image of a patient showing an echogenic focus within the common bile duct giving an acoustic shadow suggestive of choledocholithiasis

Comparison of etiology established by endoscopic ultrasonography and magnetic resonance cholangiopancreatography in patients initially labeled as having idiopathic acute pancreatitis

Etiology	Total cases	Diagnosis by EUS	Diagnosis by MRCP	*p*-value
Gallbladder (GB) microlithiasis/GB sludge/cholelithiasis	9	9	2	*0.04*
Choledocholithiasis	3	3	1	0.61
Pancreatobiliary ductal anomalies	3	0	3	0.24
Pancreatic adenocarcinoma	1	1	1	1
Intraductal papillary mucinous neoplasm (IPMN)	1	1	1	1
Total	17	14	8	0.18

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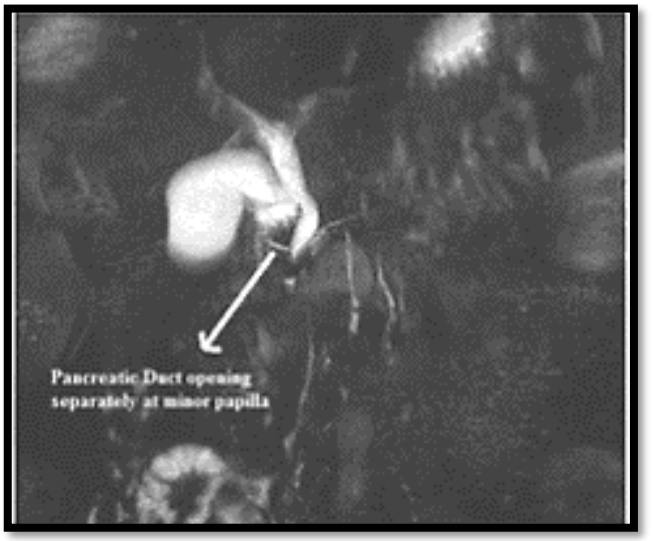

Magnetic resonance cholangiopancreatography image of a patient showing separate openings of ventral and dorsal pancreatic ducts with dorsal duct opening at the minor papilla suggestive of pancreas divisum

Comparing the diagnostic accuracy of both the modalities, EUS (14/31) was able to diagnose more cases than MRCP (8/31). The diagnostic capability of EUS was lower inpatients who had a cholecystectomy (12.5% vs.56.5%; $p = 0.03$).

Conclusions

EUS and MRCP are useful modalities in the etiological diagnosis of IAP and should be used in conjunction. EUS is better for establishing a possible biliary etiology and MRCP for an anatomical alteration in pancreatobiliary ducts.

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Bullet points of the study highlights

What is already known?

- Around 10% to 30% patients with acute pancreatitis do not have an established etiology.
- Magnetic resonance cholangiopancreatography (MRCP) and endoscopic ultrasonography (EUS) obtain high quality images of the biliary tract and pancreas.
- Determining the etiology improves management.

What is new in this study?

- EUS and/or MRCP were able to establish an etiology of pancreatitis in 54.85% of our patients.
- EUS and MRCP at present should be considered supportive rather than competitive investigations for idiopathic acute pancreatitis.

What are the future clinical and research implications of study findings?

- Establishing the etiology in such patients will prevent recurrent attacks of pancreatitis.
- Treating the cause will prevent evolution to chronic pancreatitis.

Source: Mitra, T., Dixit, V.K., Yadav, D.P. et al. Idiopathic acute pancreatitis—A myth or reality? Role of endoscopic ultrasonography and magnetic resonance cholangiopancreatography in its diagnosis. Indian J Gastroenterol (2021).

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An Unusual Cause of Watery Diarrhea

A 54-year-old man presented to the emergency department with nausea, vomiting, left lower quadrant abdominal pain and profuse watery diarrhea for the last 2 hours before presentation. Patient was unable to tolerate oral intake for the last few days before presentation. Patient denied recent travel, sick contacts, and consuming raw milk or meat. Patient denied smoking, drinking alcohol, or using illicit drugs. Patient's vitals were remarkable for tachycardia at 106/min. Patient was afebrile. Laboratory tests revealed the following: haemoglobin 17.6 g/dL, haematocrit 54%, white blood cell count 12.5 cells/L, bicarbonate of 8 mmol/L (reference rage, 24–32 mmol/L), anion gap of 16 mmol/L, chloride 107 mmol/L (reference range, 98–108 mmol/L), blood urea nitrogen 31 mg/dL (reference range, 6–20 mg/dL), serum creatinine 2.23 mg/dL (reference range, 0.5–1.5 mg/dL), calcium 11.2 mg/dL (reference range, 8.6–10.6 mg/dL), sodium 131 mmol/L, potassium 4.8 mmol/L, and albumin of 4.8 g/dL. An arterial blood gas revealed a pH of 7.11, pCO2 25, and bicarbonate of 8. Lactic acid was 1.3 mmol/L. His point-of-care coronavirus disease-2019 test was negative.

A computed tomography scan of the abdomen with and without contrast showed a large infiltrating heterogeneously enhancing pancreatic body mass encasing the splenic artery and splenic vein, and invading the portal venous confluence with peripancreatic and retroperitoneal lymph nodes and innumerable arterially enhancing liver lesions largest measuring 5.5 cm.

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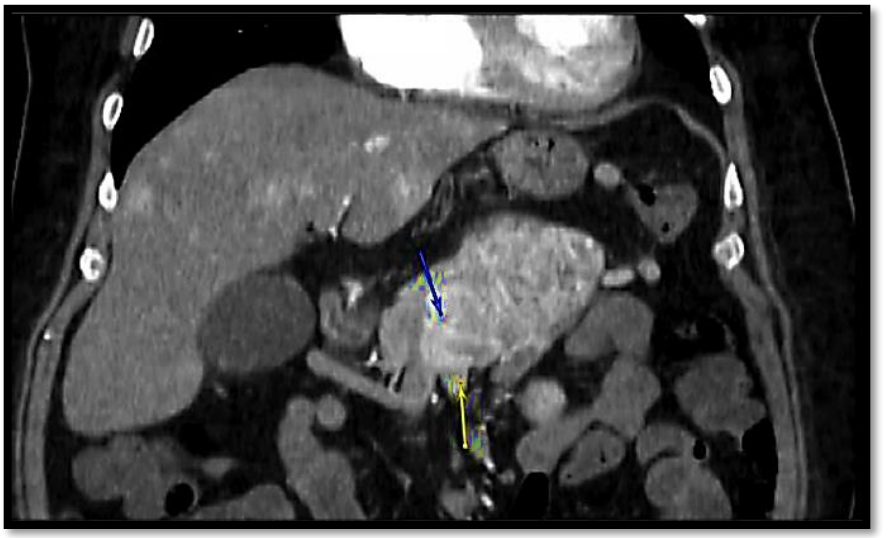
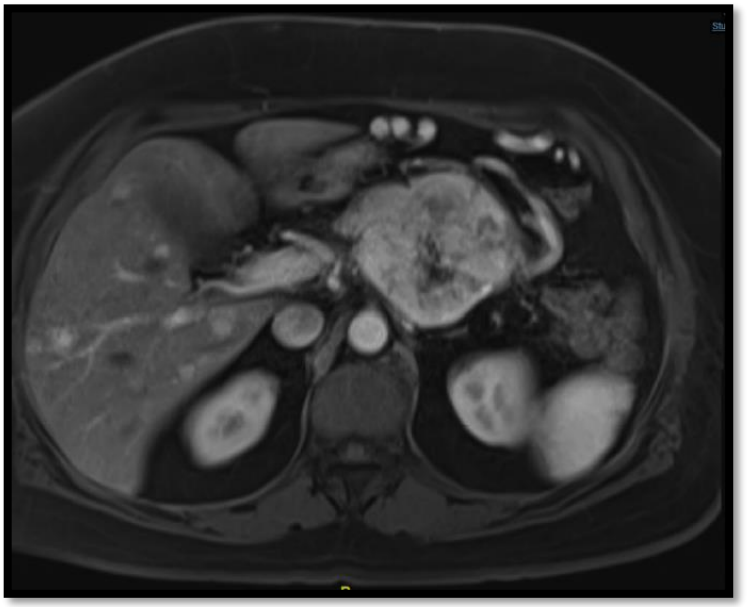


Magnetic resonance cholangiopancreatography revealed a large multilobulated mass of the pancreatic body T1 hypointense and T2 heterogenous signal with heterogenous enhancement, with an area without enhancement possibly representing central necrosis, and severe atrophy of pancreatic tail in addition to numerous hepatic lesions with diffusion restrictions.



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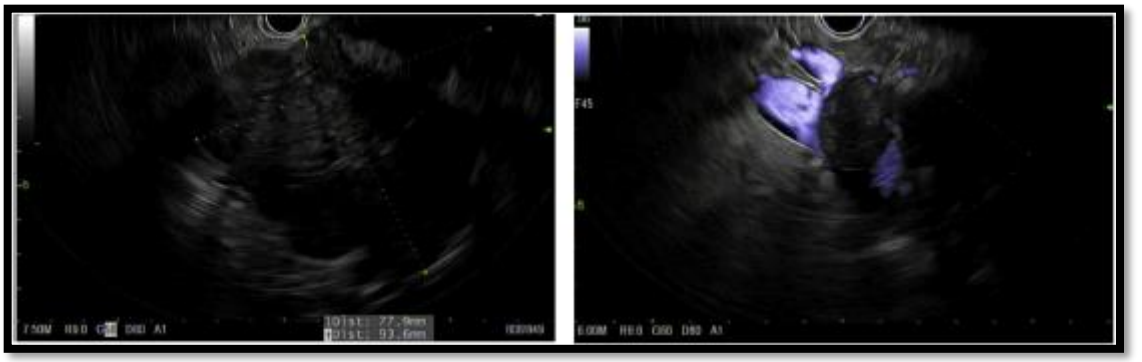
Stool pathogen and Clostridioides difficile polymerase chain reaction were negative. Fecal calprotectin and elastase were normal (<16 and >500, respectively).

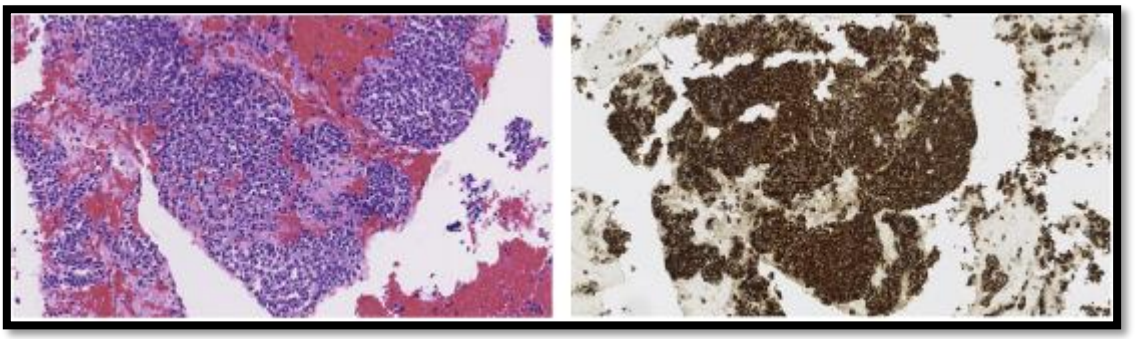
Diagnosis and management

Serum vasoactive intestinal peptide (VIP) levels were elevated at 475 pg/mL.

Endoscopic ultrasound examination showed an irregular, hypoechoic mass in the pancreatic body/tail junction with invasion into the splenic vein with a thrombus, multiple malignant appearing lymph nodes, and multiple left liver lobe metastatic lesions.



Endoscopic ultrasound-guided fine-needle biopsies from the pancreatic lesion and liver lesions were performed.



Pathology confirmed the diagnosis of a metastatic pancreatic neuroendocrine tumor with positive expression on immunohistochemistry, chromogranin, and synaptophysin with a proliferative index Ki-67 of less than 1% in the sample.

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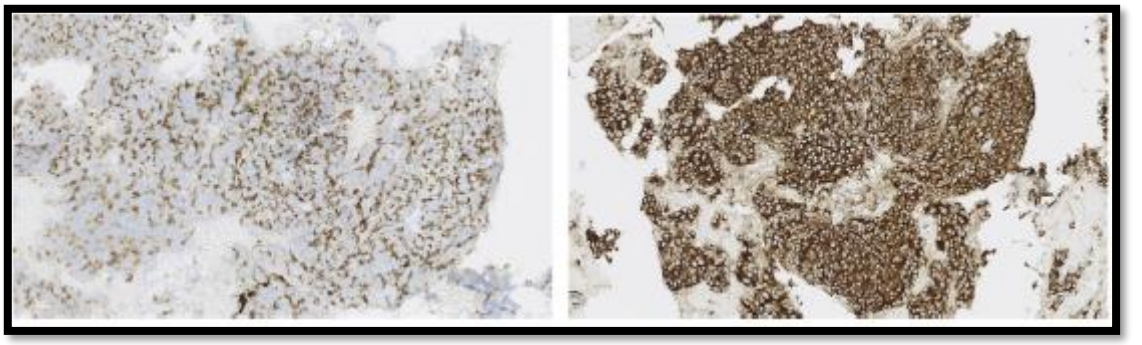

A neuroendocrine tumor secreting excessive amounts of VIP defines the VIPoma syndrome. The diagnosis of VIPoma syndrome is made based on the presence of a large-volume secretory diarrhea that persists with fasting, along with an elevated serum VIP concentration. The diagnosis should not be based on elevated serum VIP levels alone in a patient with diarrhea, because they can be falsely elevated in conditions including prolonged fasting, small bowel resection, radiation enteritis, inflammatory bowel disease, chronic kidney disease, and hyperinsulinemic hypoglycaemia.

Treatment should be directed to fluid and electrolytes repletion initially. Somatostatin analogues (octreotide) have been shown to control the diarrhea in most cases. Surgical resection is attempted for nonmetastatic VIPoma, whereas metastatic VIPoma management is more complex and can involve surgical resection, hepatic artery embolization, radiofrequency and cryoablation, liver transplantation, systemic chemotherapy, and molecular targeted therapies.

Source: Nassani N, Melitas C, Villa E. An Unusual Cause of Watery Diarrhea. Gastroenterology. 2021 Feb;160(3):671-674.

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Fibrates for Itch (FITCH) in Fibrosing Cholangiopathies: A Double-Blind, Randomized, Placebo-Controlled Trial

Background:

Primary sclerosing cholangitis (PSC) and primary biliary cholangitis (PBC) are rare progressive fibrosing cholangiopathies leading to cirrhosis and liver failure without treatment. More common in men with a median age at diagnosis of 35 to 40 years. Major clinical symptoms in PSC and PBC are pruritus and fatigue. Pruritus in cholestasis is characterized by a diurnal rhythm, with the highest itch intensity early at night and often by predilection sites at the limbs. Including the palms of the hands and soles of the feet, although patients may also experience generalized pruritus. Pruritus may seriously impair quality of life in patients with cholestatic diseases such as primary or secondary sclerosing cholangitis (PSC, SSC) and primary biliary cholangitis (PBC). Current guideline-recommended medical treatment options for pruritus of cholestasis include the anion exchange resin cholestyramine, the pregnane X receptor (PXR) agonist rifampicin, the opioid antagonist naltrexone, and the selective serotonin reuptake inhibitor sertraline. There has been increasing interest recently in the potential benefits of the peroxisome proliferator activated receptor agonist bezafibrate for the management of cholestatic pruritus in general, and PBC in particular.

Aim: To assess effects of bezafibrate on pruritus in patients with PSC, PBC, and SSC.

Methods: Prospective, randomized, double blind, placebo controlled Trial.

Inclusion criteria:

- Patients aged 18 years or older.
- Patients with severe or moderate pruritus in cholestasis caused by PBC, PSC, or SSC.
- Patients were eligible if they reported an itch intensity of at least 5 of 10 (with 0 indicating no itch and 10 indicating the worst itch possible) on a visual analog scale (VAS), twice within the week before inclusion.

Exclusion criteria:

- Prior treatment with bezafibrate.
- Patients with pruritus due to primary dermatologic abnormalities and patients with cholestasis due to obstruction that required invasive treatment
- Patients with a creatinine clearance <60 mL/min.

Clinical Outcomes:

- Primary end point: Clinically relevant > 50% reduction of itch intensity as measured on a VAS after 21 days of treatment with bezafibrate or placebo in patients with severe or moderate itch before start of treatment.
- Secondary end points: Daily morning and evening pruritus VAS scores, changes in quality of life. Changes in the 5D itch scale, a validated questionnaire reflecting itch in 5 dimensions: degree, duration, direction (improvement or worsening), disability (effect on daily activities) and distribution). Effect of bezafibrate on serum levels of bilirubin, alkaline phosphatase (ALP), g-glutamyltransferase (gGT), ALT, AST, albumin, and lipid profile (cholesterol, low- and high-density lipoprotein–cholesterol, triglycerides).

Results:

Of 74 randomized patients, 70 completed the trial (95%; 44 PSC, 24 PBC, 2 SSC). For the primary end point, bezafibrate led in 45% (41% PSC, 55% PBC) and placebo in 11% to >50% reduction of severe or moderate pruritus (P ¼ .003).

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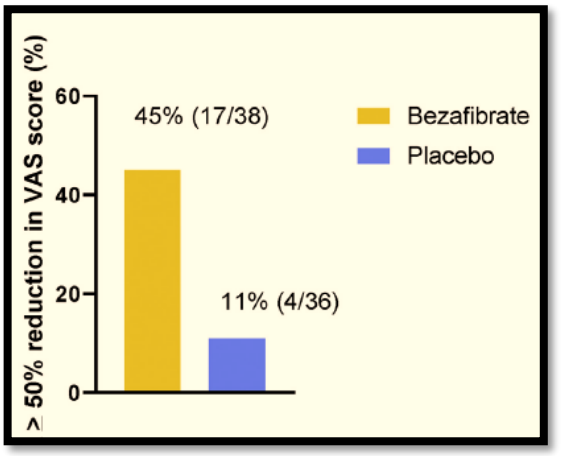
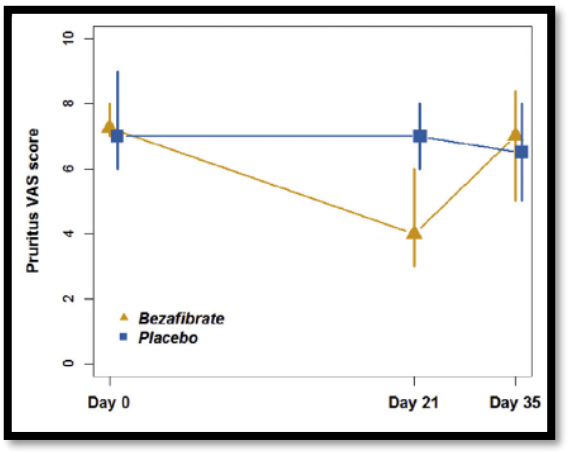
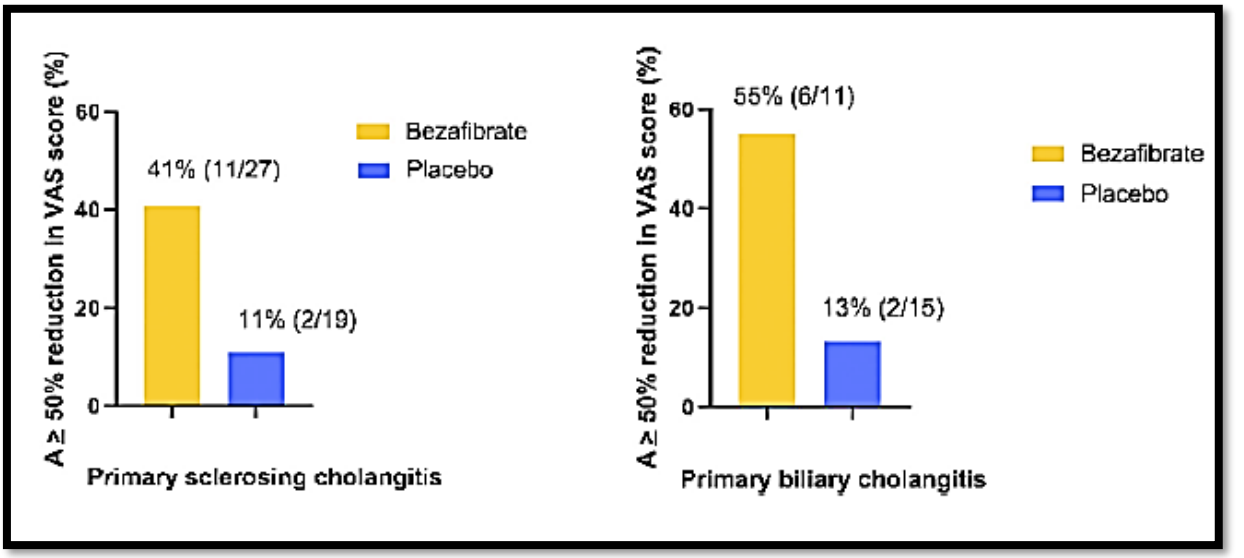




Bezafibrate reduced morning (P ¼ .01 vs placebo) and evening (P ¼ .007) intensity of pruritus (VAS) and improved the validated 5D-Itch questionnaire (P ¼ .002 vs placebo).



Daily pruritus VAS scores according to pruritus diaries during the study period of 21 days improved in the bezafibrate group (the yellow line represents the median of 38 individual scores) vs the placebo group (the blue line represents the median of 36 individual scores) in morning (P ¼ .01) and evening (P ¼ .007).

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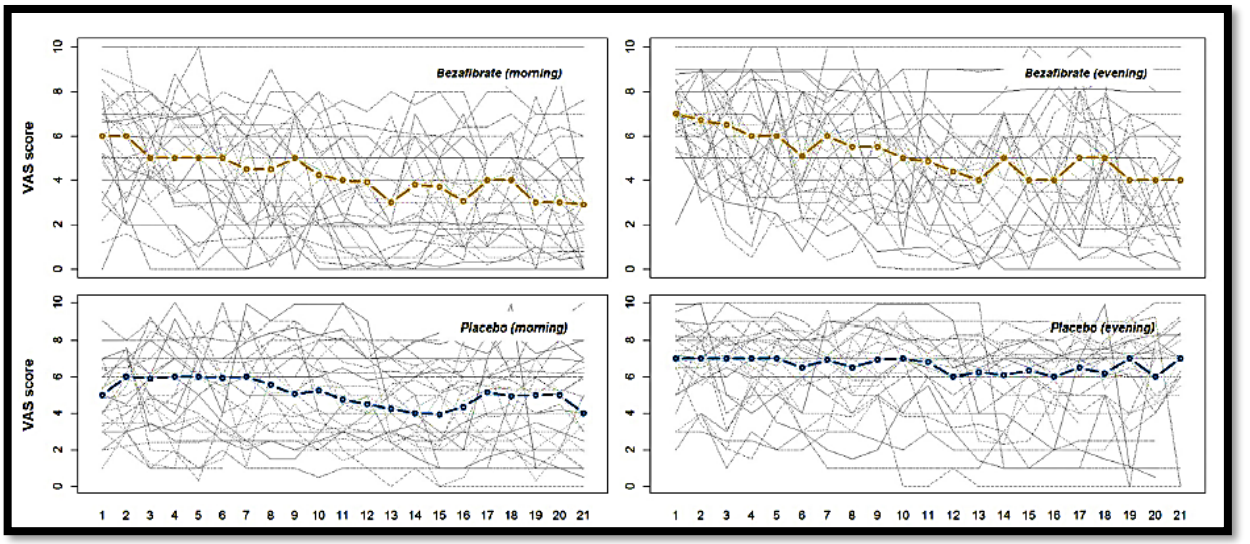

Bezafibrate also reduced serum alkaline phosphatase (_35%, P ¼ .03 vs placebo) correlating with improved pruritus (VAS, P ¼ .01) suggesting reduced biliary damage. Serum bile acids and autotaxin activity remained unchanged. Serum creatinine levels tended to mildly increase (3% bezafibrate, 5% placebo, P ¼ .14).

Discussion

In this prospective, randomized, double-blind, placebo controlled, investigator-initiated, multicenter trial, bezafibrate is found to be superior to placebo in treatment of moderate to severe cholestasis-associated pruritus in patients with PSC, PBC, and SSC as determined by validated VAS scores, a 21-day diary, the validated 5D itch questionnaire, and the pruritus domain of the Liver Disease Symptom Index questionnaire. There is improvement of cholestasis-associated pruritus under bezafibrate treatment was associated with improvement of serum ALP activity but not serum ATX activity as well. Bezafibrate may play a prominent role in future treatment of cholestasis-associated pruritus in patients with PSC and PBC beyond the guideline-recommended approaches with anion exchange resins, rifampicin, opioid antagonists, such as naltrexone, or the serotonin reuptake inhibitor sertraline. In a post hoc subgroup analysis, which may carry the risk of overinterpretation and bias, patients with PSC as well as PBC treated with bezafibrate reported marked improvement of pruritus compared with placebo. The additional anticholestatic effects of bezafibrate justify prospective evaluation of a long-term benefit of PPAR agonist treatment in PSC in the near future, not only on established surrogate markers of prognosis but also on long-term quality of life.

Conclusions:

Patients with PSC and PBC, bezafibrate can be considered as a new treatment option for cholestasis associated pruritus given its antipruritic and anticholestatic properties and a favorable safety profile. Further prospective studies are needed to confirm long-term efficacy and safety of bezafibrate in patients with PSC, PBC, and SSC.

Source: de Vries E, et al. Netherlands Association for the Study of the Liver-Cholestasis Working Group. Fibrates for Itch (FITCH) in Fibrosing Cholangiopathies: A Double-Blind, Randomized, Placebo-Controlled Trial. Gastroenterology. 2021 Feb;160(3):734-743.

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AGA Clinical Practice Update on Medical Management of Colonic Diverticulitis: Expert Review

Colonic diverticulitis is a painful gastrointestinal disease that recurs unpredictably and can lead to chronic gastrointestinal symptoms. Although diverticulitis is most common in older adults, the relative increase in diverticulitis in recent decades has been greatest in younger adults. Diverticulitis can be uncomplicated or complicated. Uncomplicated diverticulitis involves thickening of the colon wall and peri-colonic inflammatory changes. Complicated diverticulitis additionally includes the presence of abscess, peritonitis, obstruction, stricture, and/or fistula. The most common complication is phlegmon or abscess followed by peritonitis, obstruction, stricture, and fistula. Although the majority of individuals recover from an episode of acute uncomplicated diverticulitis, approximately 5% of patients will experience smoldering diverticulitis, characterized by abdominal pain and continued evidence of inflammation on computed tomography (CT) scan. Gastroenterologists commonly care for patients with this disease.

Objective: To provide practical and evidence-based advice for management of diverticulitis. **Methods:** Review of systematic reviews, meta-analyses, randomized controlled trials, and observational studies to develop 14 best practices.

Best Practice Advice:

1. Computed tomography should be considered to confirm the diagnosis of diverticulitis in patients without a prior imaging confirmed diagnosis and to evaluate for potential complications in patients with severe presentations. Imaging should also be considered in those who fail to improve with therapy, are immunocompromised, or who have multiple recurrences and are contemplating prophylactic surgery in order to confirm the diagnosis and location(s) of disease.

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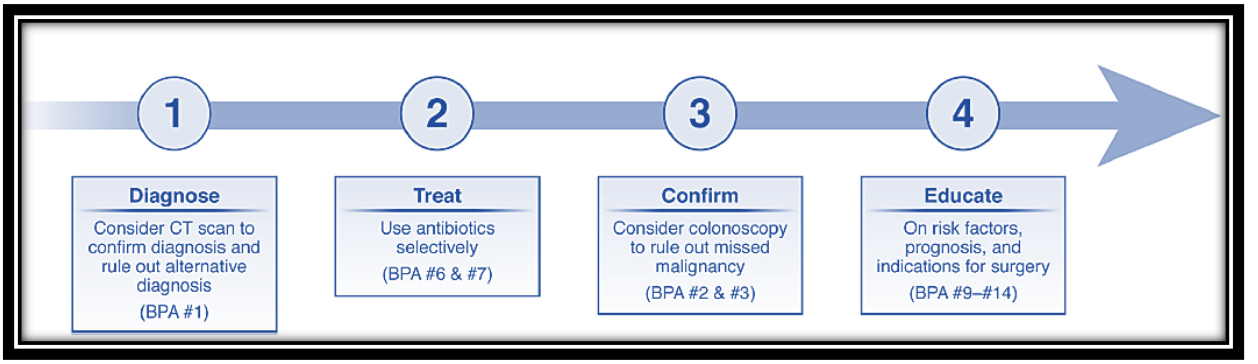

A step-wise approach to the diagnosis and management of acute uncomplicated diverticulitis. BPA, best practice advice.

2. Whether patients should have a colonoscopy after an episode of diverticulitis depends on the patient's history, most recent colonoscopy, and disease severity and course. Colonoscopy is advised after an episode of complicated diverticulitis and after a first episode of uncomplicated diverticulitis, but can be deferred if a recent (within 1 year) high quality colonoscopy was performed.
3. After an acute episode of diverticulitis, colonoscopy should be delayed by 6–8 weeks or until complete resolution of the acute symptoms, whichever is longer. Colonoscopy should be considered sooner if alarm symptoms are present.
4. In patients with a history of diverticulitis and chronic symptoms, ongoing inflammation should be excluded with both imaging and lower endoscopy. If there is no evidence of diverticulitis, visceral hypersensitivity should be considered and managed accordingly.
5. A clear liquid diet is advised during the acute phase of uncomplicated diverticulitis. Diet should advance as symptoms improve.
6. Antibiotic treatment can be used selectively, rather than routinely, in immunocompetent patients with mild uncomplicated diverticulitis.
7. Antibiotic treatment is advised in patients with uncomplicated diverticulitis who have comorbidities or are frail, who present with refractory symptoms or vomiting, or who have a C-reactive protein >140 mg/L or baseline white blood cell count > 15 3 109 cells/L. Antibiotic treatment is advised in patients with complicated diverticulitis or uncomplicated diverticulitis with a fluid collection or longer segment of inflammation on CT scan.

8. Immunocompromised patients are more likely to present with severe or complicated disease. For these patients there should be a low threshold for cross-sectional imaging, antibiotic treatment, and consultation with a colorectal surgeon.
9. To reduce the risk of recurrence, patients with a history of diverticulitis should consume a high-quality diet, achieve or maintain a normal body mass index, be routinely physically active, and not smoke. Additionally, patients with a history of diverticulitis should avoid regular use (2 or more times per week) of nonsteroidal anti-inflammatory drugs except aspirin prescribed for secondary prevention of cardiovascular disease.
10. Patients should understand that approximately 50% of the risk for diverticulitis is attributable to genetic factors.
11. Patients with a history of diverticulitis should not be treated with mesalamine, probiotics, or rifaximin to prevent recurrent diverticulitis.
12. Patients should be educated that complicated diverticulitis is most often the first presentation of diverticulitis. The risk of complicated diverticulitis decreases with recurrences.
13. An elective segmental resection should not be advised based on the number of diverticulitis episodes.
14. A discussion of elective segmental resection for patients with a history of diverticulitis should be personalized to consider severity of disease, patient preferences and values, as well as risks and benefits, including quality of life. Patients should understand that surgery reduces, but does not eliminate, diverticulitis risk, and that chronic gastrointestinal symptoms do not always improve with surgery.

Conclusions

Colonic diverticulitis is a painful disease that occurs unpredictably. Although most patients never experience a perforation or abscess, uncomplicated recurrences are a burden to patients. Gastroenterologists can alleviate many of these concerns by making an accurate diagnosis, addressing chronic sequelae, and educating patients on risk factors, prognosis, and indications for surgery. Although the advice in this document is based on low- to moderate-quality evidence, research is ongoing and has the potential to eventually identify better options for diverticulitis treatment and prevention.

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Source: Perry A F, Shaukat. A, Strate L L. AGA Clinical Practice Update on Medical Management of Colonic Diverticulitis: Expert Review. Clinical practice updates. Gastroenterology 2021; Vol 160 (3); P 906-911.