New Day in Medicine
Новый День в Медицине
NDM

TIBBIYOTDA YANGI KUN

Ilmiy referativ, marifiy-ma'naviy jurnal

AVICENNA-MED.UZ

ISSN 2181-712X.
EiSSN 2181-2187

12 (74) 2024

ТИББИЁТДА ЯНГИ КУН
НОВЫЙ ДЕНЬ В МЕДИЦИНЕ
NEW DAY IN MEDICINE

Илмий-рефератив, маънавий-маърифий журнал
Научно-реферативный,
духовно-просветительский журнал

УЧРЕДИТЕЛИ:

БУХАРСКИЙ ГОСУДАРСТВЕННЫЙ МЕДИЦИНСКИЙ ИНСТИТУТ
ООО «ТИББИЁТДА ЯНГИ КУН»

Национальный медицинский исследовательский центр хирургии имени А.В. Вишневского является генеральным научно-практическим консультантом редакции

Журнал был включен в список журнальных изданий, рецензируемых Высшей Аттестационной Комиссией Республики Узбекистан (Протокол № 201/03 от 30.12.2013 г.)

12 (74)

2024

ноябрь

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Received: 20.10.2024, Accepted: 02.11.2024, Published: 10.11.2024

UDC- 616.37-002.1:616.37-089

ACUTE PANCREATITIS: PATHOPHYSIOLOGY, DIAGNOSIS, COMPLICATIONS, AND CURRENT MANAGEMENT STRATEGIES

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✓ ***Resume***

Acute pancreatitis is a sudden inflammatory condition of the pancreas with diverse etiologies, including gallstones, alcohol consumption, hyperlipidemia, and certain medications. Globally, the incidence of acute pancreatitis has risen, with approximately 2.8 million new cases reported in 2019, reflecting significant morbidity and mortality. The condition presents in a spectrum ranging from mild, self-limiting inflammation to severe necrotizing pancreatitis with systemic complications. Premature activation of digestive enzymes within pancreatic acinar cells is central to its pathophysiology, triggering autodigestion, inflammation, and, in severe cases, systemic inflammatory response syndrome.

Diagnosis requires clinical, biochemical, and imaging criteria, with elevated serum amylase or lipase being pivotal markers. Management includes aggressive fluid resuscitation, pain control, early nutritional support, and treatment of underlying causes such as gallstones or alcohol abuse. Severe cases demand multidisciplinary approaches to prevent or treat complications like necrosis, infections, and organ failure. Ongoing research focuses on predictive biomarkers, anti-inflammatory therapies, and minimally invasive techniques, aiming to improve patient outcomes and reduce global disease burden.

Key words: Acute Pancreatitis, Mortality, Age-Standardized Mortality Rate, Acinar Cell Injury, Cytokines, Systemic Inflammatory Response Syndrome, Alcohol Consumption, Hypertriglyceridemia

ОСТРЫЙ ПАНКРЕАТИТ: ПАТОФИЗИОЛОГИЯ, ДИАГНОСТИКА, ОСЛОЖНЕНИЯ И СОВРЕМЕННЫЕ СТРАТЕГИИ ЛЕЧЕНИЯ

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✓ ***Резюме***

Острый панкреатит — это внезапное воспалительное состояние поджелудочной железы, имеющее различные этиологии, включая желчные камни, употребление алкоголя, гиперлипидемию и прием определенных медикаментов. В глобальном масштабе заболеваемость острым панкреатитом увеличивается: в 2019 году было зарегистрировано около 2,8 миллиона новых случаев, что подчеркивает значительную заболеваемость и смертность. Заболевание проявляется в спектре от легкого, самоограничивающегося

воспаления до тяжелого некротического панкреатита с системными осложнениями. Основой патофизиологии является преждевременная активация пищеварительных ферментов в ацинарных клетках поджелудочной железы, что приводит к аутодигестии, воспалению и, в тяжелых случаях, синдрому системной воспалительной реакции.

Диагностика основывается на клинических, биохимических и визуализационных критериях, при этом повышенные уровни амилазы или липазы в сыворотке являются ключевыми маркерами. Лечение включает агрессивную инфузионную терапию, контроль боли, раннюю нутритивную поддержку и устранение первопричин, таких как желчные камни или злоупотребление алкоголем. В тяжелых случаях требуется мультидисциплинарный подход для профилактики или лечения осложнений, таких как некроз, инфекции и органная недостаточность. Современные исследования сосредоточены на поиске прогностических биомаркеров, противовоспалительных терапий и минимально инвазивных методов, с целью улучшения исходов лечения и снижения глобального бремени заболевания

Ключевые слова: острый панкреатит, смертность, возраст-стандартизированный коэффициент смертности, повреждение ацинарных клеток, цитокины, синдром системной воспалительной реакции, употребление алкоголя, гипертриглицеридемия

O‘TKIR PANKREATIT: PATOFIZIOLOGIYA, DIAGNOSTIKA, ASORATLAR VA ZAMONAVIY DAVOLASH STRATEGIYALARI

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✓ ***Rezyume***

O‘tkir pankreatit — bu oshqozon osti bezining turli etiologiyalarga ega bo‘lgan to‘satdan yuzaga keladigan yallig‘lanish holati bo‘lib, bunga o‘t toshlari, spirtli ichimliklarni iste’mol qilish, giperlipidemiya va ayrim dori vositalari sabab bo‘lishi mumkin. Dunyo bo‘yicha o‘tkir pankreatitning uchrash darajasi oshib bormoqda: 2019-yilda taxminan 2,8 million yangi holat qayd etilgan bo‘lib, bu kasallikning yuqori darajada kasallanishi va o‘lim darajasini aks ettiradi. Kasallikning klinik ko‘rinishi yengil, o‘z-o‘zidan o‘tib ketadigan yallig‘lanishdan tortib, og‘ir nekrotik pankreatitgacha bo‘lgan keng spektrni qamrab oladi. Patofiziologiyaning asosida oshqozon osti bezining atsinar hujayralarida ovqat hazm qilish fermentlarining erta faollashuvi yotadi, bu o‘z-o‘zini hazm qilish, yallig‘lanish va og‘ir holatlarda tizimli yallig‘lanish reaksiyasi sindromiga olib keladi.

Diagnostika klinik, biokimyoviy va vizualizatsiya usullari asosida amalga oshiriladi, bunda qonda amilaza yoki lipaza darajasining oshishi asosiy marker hisoblanadi. Davolash suyuqlik balansini tiklash, og‘riqni boshqarish, erta ovqatlanishni ta’minlash va o‘t toshlari yoki spirtli ichimliklarni suiiste’mol qilish kabi sabablarni bartaraf etishni o‘z ichiga oladi. Og‘ir holatlarda nekroz, infeksiya va organ yetishmovchiligi kabi asoratlarning oldini olish yoki ularni davolash uchun ko‘p tarmoqli yondashuv zarur bo‘ladi. Zamonaviy tadqiqotlar prognoz biomarkerlari, yallig‘lanishga qarshi terapiyalar va minimal invaziv usullarni rivojlantirishga qaratilgan bo‘lib, bemorlarning sog‘ayishini yaxshilash va kasallikning global yukini kamaytirishni maqsad qiladi.

Kalit so‘zlar: o‘tkir pankreatit, o‘lim darajasi, yoshga standartlashtirilgan o‘lim darajasi, atsinar hujayralarning shikastlanishi, sitokinlar, tizimli yallig‘lanish reaksiyasi sindromi, spirtli ichimliklarni iste’mol qilish, gipergliseridemiya

Relevance

Acute pancreatitis (AP) is a sudden inflammation of the pancreas and stands as a significant global health concern due to its rising incidence and associated morbidity and mortality. In 2019, approximately 2.8 million new cases of AP were reported worldwide, reflecting a 62.9% increase from 1990. However, the global age-standardized incidence rate (ASIR) exhibited a modest decline, decreasing from 37.9 to 34.8 per 100,000 population between 1990 and 2019, representing an annual reduction of 8.4%[12].

Despite the slight decrease in ASIR, the absolute number of AP cases has escalated, likely due to population growth and aging demographics. Mortality associated with AP has also risen; deaths increased from approximately 69,818 in 1990 to 115,053 in 2019, marking a 64.8% surge. Nevertheless, the age-standardized mortality rate (ASMR) declined by 17.2% annually during the same period, dropping from 1.7 to 1.4 per 100,000 population [12].

Regional disparities are evident, with Eastern Europe exhibiting the highest incidence and mortality rates. The Russian Federation, in particular, leads in national-level AP burden [1; 2; 13].

These variations underscore the influence of region-specific risk factors, healthcare infrastructure, and preventive strategies.

Materials and methods

The increasing global burden of AP necessitates enhanced preventive measures, early diagnostic protocols, and effective management strategies to mitigate its impact on public health.

Pathophysiology: AP is an inflammatory disorder of the pancreas initiated by the premature activation of digestive enzymes within pancreatic acinar cells. This process triggers a cascade of events that lead to autodigestion of pancreatic tissue, local inflammation, and systemic complications. Below is a detailed exploration of its pathophysiology with references.

1. Acinar Cell Injury and Enzyme Activation

- **Premature Activation of Enzymes**: The initial event in AP is the premature conversion of trypsinogen to trypsin within the acinar cells. Trypsin activates other digestive enzymes, such as elastase and phospholipase A2, which degrade cellular structures and cause tissue damage. This occurs due to stimuli like gallstones, alcohol, or hyperlipidemia. [2; 14; 26]
- **Co-localization Hypothesis**: Under physiological conditions, zymogens and lysosomal hydrolases are segregated. In AP, they co-localize in intracellular vesicles, where lysosomal enzymes activate zymogens. This abnormal co-localization is a hallmark of early acinar injury [4; 5; 25].
- **Calcium Overload**: Increased intracellular calcium levels disrupt cellular homeostasis and promote zymogen activation. Sustained calcium signaling also leads to mitochondrial dysfunction and necrosis [19; 20].

2. Amplification of Inflammation

- **Pro-inflammatory Cytokines**: Injured acinar cells release cytokines such as interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α). These mediators recruit immune cells, amplifying local and systemic inflammation. [15; 23]
- **Oxidative Stress**: Reactive oxygen species (ROS) generated during acinar injury exacerbate cellular damage and inflammatory responses. ROS also activate transcription factors like nuclear factor-kappa B (NF-κB), which upregulate inflammatory cytokines [9; 21; 22].
- **Neutrophil Activation**: Neutrophils release enzymes and form neutrophil extracellular traps (NETs), which can further damage pancreatic tissue [11; 23].

3. Pancreatic Necrosis

- **Apoptosis vs. Necrosis**: Acinar cells may undergo apoptosis (controlled cell death) or necrosis (unregulated cell death). Necrosis is associated with the release of intracellular contents, which amplifies inflammation and increases the risk of infection [3; 7; 27].
- **Microcirculatory Dysfunction**: Inflammatory mediators increase vascular permeability and promote ischemia in the pancreatic tissue, which exacerbates necrosis.

4. Systemic Inflammatory Response Syndrome (SIRS)

- **Cytokine Storm**: The systemic release of cytokines leads to widespread endothelial activation and increased capillary permeability. This results in hypovolemia, tissue hypoxia, and multi-organ dysfunction. [16; 28; 29]
- **Organ-Specific Complications**:
  - **Lungs**: Cytokines and inflammatory mediators damage the alveolar-capillary barrier, causing acute respiratory distress syndrome (ARDS).
  - **Kidneys**: Hypoperfusion and inflammation lead to acute kidney injury (AKI).
  - **Heart**: Inflammatory mediators cause myocardial depression and hypotension.

5. Gut-Pancreas Axis

- **Gut Barrier Dysfunction**: Breakdown of the intestinal barrier during AP allows translocation of bacteria and endotoxins into the systemic circulation and pancreatic tissue, increasing the risk of infections in necrotizing pancreatitis [19; 20].
- **Dysbiosis**: Altered gut microbiota has been implicated in the severity of AP. Modulating the gut microbiome may represent a therapeutic strategy [24].

6. Resolution and Chronicity

- **Immune Resolution**: Anti-inflammatory mediators, such as interleukin-10 (IL-10), play a role in resolving inflammation. However, in some cases, the inflammation may persist, leading to recurrent or chronic pancreatitis [8].
- **Fibrosis**: Repeated injury to the pancreas can lead to fibrotic changes, resulting in loss of exocrine and endocrine function [6].

Results and discussions

Etiology

AP is an inflammatory condition of the pancreas with multiple etiologies. Understanding these causes is crucial for effective management and prevention [16; 30].

1. **Gallstones**

Gallstones are the leading cause of AP, accounting for approximately 40-70% of cases. They obstruct the common bile duct, leading to pancreatic enzyme activation and inflammation. The incidence of gallstone-induced AP varies geographically, with higher rates observed in Latin America.

2. **Alcohol Consumption**

Chronic alcohol intake is responsible for about 25-35% of AP cases. Alcohol-induced AP is more prevalent in regions with high alcohol consumption, such as Eastern Europe. The risk increases with prolonged and excessive alcohol use.

3. **Hypertriglyceridemia**

Elevated serum triglyceride levels, particularly above 1000 mg/dL, can precipitate AP. Hypertriglyceridemia-induced AP accounts for 1-4% of cases and is often associated with genetic lipid metabolism disorders.

4. **Medications**

Certain drugs have been implicated in AP, including azathioprine, valproic acid, and tetracyclines. Drug-induced AP is relatively rare, contributing to less than 2% of cases.

5. **Hypercalcemia**

Elevated calcium levels, often due to hyperparathyroidism, can lead to AP by promoting premature activation of pancreatic enzymes. Hypercalcemia-induced AP is uncommon, accounting for a small percentage of cases.

6. **Genetic Factors**

Mutations in genes such as PRSS1, SPINK1, and CFTR are linked to hereditary pancreatitis, increasing the risk of AP. Genetic predispositions are more common in individuals with a family history of pancreatitis.

7. **Autoimmune Pancreatitis**

This rare form of AP results from immune-mediated inflammation of the pancreas and is often associated with other autoimmune disorders.

8. **Infections**

Viral infections, such as mumps and hepatitis, can cause AP, particularly in pediatric populations. Infection-induced AP is relatively rare in adults.

9. **Trauma**

Abdominal trauma, whether blunt or penetrating, can lead to pancreatic injury and subsequent AP. Traumatic AP is more common in younger individuals and accounts for a small percentage of cases.

10. **Endoscopic Procedures**

Procedures like endoscopic retrograde cholangiopancreatography (ERCP) can induce AP, with an incidence ranging from 3-10% post-procedure.

11. **Idiopathic Causes**

In approximately 10-20% of cases, no identifiable cause is found, classifying them as idiopathic AP.

The etiology of AP varies globally, influenced by regional risk factors and lifestyle habits. For instance, gallstone-related AP is more prevalent in Latin America, while alcohol-induced AP is common in Eastern Europe.

Understanding these etiological factors is essential for developing targeted prevention and treatment strategies.

Diagnosis

The diagnosis of AP relies on a combination of clinical presentation, laboratory findings, and imaging studies. Timely and accurate diagnosis is crucial for initiating appropriate management and preventing complications. According to the Revised Atlanta Classification (2012), the diagnosis of AP requires the presence of at least **two of the following three criteria**:

12. **Characteristic abdominal pain** (acute onset, severe, epigastric, often radiating to the back).
13. **Elevated serum amylase or lipase levels** (≥3 times the upper limit of normal).
14. **Characteristic imaging findings** on computed tomography (CT), magnetic resonance imaging (MRI), or ultrasound.

1. Clinical Presentation

- **Abdominal Pain**:
- The hallmark symptom of AP is severe, constant epigastric pain, often radiating to the back.
- Pain is typically worsened by food intake and relieved by leaning forward.
- **Nausea and Vomiting**:
- Accompanying symptoms include persistent nausea and vomiting, often refractory to antiemetics.
- **Systemic Symptoms**:
- Fever, tachycardia, hypotension, and signs of SIRS may occur in severe cases.

2. Laboratory Findings

Laboratory tests are critical for confirming the diagnosis and assessing severity:

- **Pancreatic Enzymes**:
- **Serum Amylase**: Elevated in 75–92% of patients. However, it lacks specificity as levels may also rise in other conditions (e.g., perforated ulcer, intestinal obstruction).
- **Serum Lipase**: More sensitive and specific than amylase for diagnosing AP. Elevated levels are present in 82–100% of cases and remain elevated longer than amylase.
- **Inflammatory Markers**:
- **C-reactive Protein (CRP)**: Levels >150 mg/L at 48 hours predict severe disease.
- **Procalcitonin**: Associated with the risk of infection in necrotizing pancreatitis.
- **Hematological Changes**:
- Elevated hematocrit and leukocytosis may indicate hemoconcentration and inflammation.
- Hypocalcemia may result from fat necrosis and calcium sequestration.
- **Other Laboratory Abnormalities**:
- Elevated liver enzymes (e.g., ALT, AST) and bilirubin suggest biliary obstruction or gallstone etiology.
- Hypertriglyceridemia (>1000 mg/dL) in cases of triglyceride-induced AP.

3. Imaging Studies

Imaging is indispensable for confirming the diagnosis, identifying the etiology, and assessing complications.

- **Abdominal Ultrasound**:
- First-line imaging modality to detect gallstones, biliary sludge, and ductal dilatation.

- Useful for identifying free fluid or peripancreatic edema but limited in visualizing the pancreas in obese patients or those with excessive bowel gas.
- **Contrast-Enhanced Computed Tomography (CECT)**:
- The gold standard for evaluating pancreatic inflammation and complications (e.g., necrosis, abscesses, pseudocysts).
- Performed 48–72 hours after onset to allow full development of necrosis if clinically indicated.
- **Magnetic Resonance Imaging (MRI)**:
- Superior to CT in visualizing ductal anomalies and fluid collections.
- Magnetic resonance cholangiopancreatography (MRCP) is particularly useful for identifying bile duct obstructions or choledocholithiasis.
- **Endoscopic Ultrasound (EUS)**:
- Highly sensitive for detecting microlithiasis, biliary stones, and small pancreatic masses.
- Useful in idiopathic pancreatitis or recurrent cases without obvious causes.
- **Endoscopic Retrograde Cholangiopancreatography (ERCP)**:
- Reserved for therapeutic purposes, such as removing bile duct obstructions.
- Indicated in cases of cholangitis or persistent biliary obstruction.

4. Scoring Systems for Severity Assessment

Several scoring systems help assess the severity of AP and guide management decisions:

- **Clinical Scoring Systems**:
- **Ranson Criteria**: Based on 11 parameters assessed at admission and 48 hours.
- **Glasgow-Imrie Score**: Uses 8 parameters to predict severity.
- **APACHE II Score**: A general intensive care scoring system used for predicting outcomes.
- **Imaging-Based Systems**:
- **Balthazar CT Severity Index (CTSI)**: Combines pancreatic inflammation and necrosis on CT to assess severity.
- **Biochemical Markers**:
- Elevated CRP, hematocrit, and BUN levels predict severe disease and complications.

5. Differentiating from Other Conditions

The symptoms of AP can mimic other abdominal or systemic conditions, requiring careful differentiation:

- **Perforated peptic ulcer**: Ruled out by imaging studies showing free air under the diaphragm.
- **Biliary colic**: Distinguishable by episodic pain and normal enzyme levels.
- **Intestinal obstruction**: Presents with colicky pain and altered bowel sounds.
- **Acute myocardial infarction**: Excluded with ECG and cardiac enzyme studies.

6. Diagnostic Challenges

- **Early Presentation**: Enzyme levels may be normal in the first 6–12 hours of onset.
- **Chronic Pancreatitis**: Differentiating acute-on-chronic pancreatitis may be challenging without imaging.
- **Idiopathic Cases**: In 10–20% of cases, no clear etiology is identified despite extensive evaluation.

Complications

Complications of Acute Pancreatitis

AP can lead to a spectrum of complications, ranging from local pancreatic issues to severe systemic conditions. These complications significantly affect prognosis, with severe forms of AP associated with high morbidity and mortality. Complications are classified into **local** and **systemic** categories, with some patients experiencing both concurrently.

1. Local Complications

Local complications occur primarily in or around the pancreas and are more common in severe AP.

- **Acute Peripancreatic Fluid Collections**:
- Develop within the first 4 weeks of the disease.
- These collections lack a defined wall and are typically sterile.
- May resolve spontaneously or progress to pseudocysts or infected collections.
- **Pancreatic Pseudocysts**:
- Encapsulated fluid collections that develop >4 weeks after the onset of AP.
- They are surrounded by a well-defined fibrous wall and contain pancreatic enzymes.

- Complications of pseudocysts include rupture, hemorrhage, and infection.
- Symptomatic pseudocysts may require drainage via endoscopic, percutaneous, or surgical approaches.
- **Pancreatic Necrosis**:
- A hallmark of severe AP, necrosis can involve pancreatic parenchyma, peripancreatic tissue, or both.
- Sterile necrosis is usually managed conservatively, but infected necrosis requires intervention, such as antibiotics and minimally invasive necrosectomy.
- Infected necrosis increases the risk of sepsis and multi-organ failure.
- **Walled-Off Necrosis (WON)**:
- Develops >4 weeks after AP as necrotic tissue becomes encapsulated.
- Symptomatic WON may require drainage or necrosectomy.
- **Biliary Obstruction**:
- Inflammation or pseudocysts can compress the bile duct, leading to obstructive jaundice.
- ERCP or stenting may be required.
- **Splenic, Portal, or Superior Mesenteric Vein Thrombosis**:
- Thrombosis can result from inflammation or compression by pseudocysts.
- Complications include variceal bleeding and ischemia.
- **Hemorrhage**:
- Pancreatic necrosis may erode adjacent blood vessels, leading to gastrointestinal or retroperitoneal bleeding.
- Vascular complications like pseudoaneurysm rupture often necessitate angiographic embolization or surgery.
- **Gastrointestinal Obstruction**:
- Inflammation or pseudocysts can compress adjacent organs, causing gastric outlet or intestinal obstruction.

2. Systemic Complications

Systemic complications arise from the systemic inflammatory response triggered by AP and are common in severe disease.

- **Systemic Inflammatory Response Syndrome (SIRS)**:
- SIRS is an early complication of severe AP caused by the release of inflammatory mediators.
- It is characterized by fever, tachycardia, tachypnea, and leukocytosis.
- **Multi-Organ Dysfunction Syndrome (MODS)**:
- Severe AP can lead to dysfunction in multiple organ systems:
- **Respiratory System**: Acute respiratory distress syndrome (ARDS) due to increased vascular permeability in the lungs.
- **Renal System**: Acute kidney injury (AKI) from hypovolemia, systemic inflammation, and sepsis.
- **Cardiovascular System**: Hypotension and shock due to fluid loss, vasodilation, and myocardial depression.
- **Hepatic System**: Jaundice and hepatic dysfunction may result from systemic inflammation and biliary obstruction.
- **Sepsis and Infections**:
- Infected pancreatic necrosis or systemic bacterial translocation can lead to sepsis.
- Sepsis is a major cause of mortality in severe AP.
- **Disseminated Intravascular Coagulation (DIC)**:
- AP can activate the coagulation cascade, leading to widespread clot formation and bleeding tendencies.
- **Hyperglycemia and Diabetes Mellitus**:
- Pancreatic endocrine dysfunction can cause transient or permanent diabetes.
- Recurrent or severe AP increases the risk of chronic pancreatitis and diabetes.
- **Hypocalcemia**:
- Fat saponification during necrosis consumes calcium, leading to hypocalcemia, which may cause tetany and cardiac arrhythmias.
- **Metabolic Complications**:

- Hypertriglyceridemia, hyperglycemia, and acid-base imbalances, such as metabolic acidosis, are common.

3. Late Complications

Late complications of AP typically develop weeks to months after the acute episode.

- **Chronic Pancreatitis**:
- Repeated episodes of AP may lead to chronic inflammation, fibrosis, and loss of pancreatic function.
- **Persistent Abdominal Pain**:
- Chronic pain may result from fibrosis, nerve involvement, or complications like pseudocysts or WON.
- **Pancreatic Exocrine Insufficiency**:
- Loss of pancreatic acinar cells reduces enzyme secretion, leading to malabsorption and steatorrhea.
- **Pancreatic Cancer**:
- Chronic inflammation following recurrent AP episodes is a risk factor for pancreatic ductal adenocarcinoma.

Current Management Strategies for Acute Pancreatitis

The management of AP has evolved significantly, focusing on supportive care, addressing the underlying cause, and preventing or treating complications. Management is stratified based on disease severity, as outlined in the Revised Atlanta Classification: mild, moderate, and severe AP. Below is a detailed review of current strategies.

1. Initial Assessment and Triage

- **Severity Assessment**:
- The first step is identifying the severity of AP to guide treatment decisions. Clinical scoring systems such as the **APACHE II**, **Ranson's criteria**, or biochemical markers (e.g., CRP, procalcitonin) are used.
- Imaging, such as CECT, is reserved for patients with severe disease or suspected complications.
- **Hospitalization**:
- Mild AP: May require brief hospitalization or outpatient care.
- Moderate to Severe AP: Requires hospitalization, often in an intensive care unit (ICU) for severe cases.

2. Supportive Care

Supportive care is the cornerstone of AP management and aims to stabilize the patient and minimize complications.

a. Fluid Resuscitation

- Early aggressive IV hydration with isotonic crystalloids (e.g., lactated Ringer's solution) is essential to maintain perfusion and prevent organ failure.
- Optimal hydration reduces the risk of necrosis and systemic complications.
- Guidelines recommend bolus fluids at **250–500 mL/hour**, with reassessment of fluid responsiveness using clinical and laboratory parameters (e.g., heart rate, urine output, hematocrit).

b. Pain Management

- Pain is a predominant symptom in AP and is managed with **parenteral opioids** (e.g., morphine or fentanyl).
- Non-opioid options, such as ketorolac, may be considered in mild cases.
- Regional nerve blocks (e.g., celiac plexus block) may be used for refractory pain.

c. Nutritional Support

- Early initiation of **enteral nutrition** within 48–72 hours is preferred, using nasojejunal feeding if necessary.
- Enteral feeding helps maintain gut integrity, reduces bacterial translocation, and prevents infections.
- Total parenteral nutrition (TPN) is reserved for patients who cannot tolerate enteral feeding.

3. Etiology-Specific Management

Addressing the underlying cause of AP is critical to prevent recurrence and manage complications.

a. Gallstone-Related AP

- **Cholecystectomy**:
- Recommended during the same hospitalization for mild cases once the inflammation subsides.
- For moderate to severe cases, cholecystectomy is delayed until recovery.
- **Endoscopic Retrograde Cholangiopancreatography (ERCP)**:
- Urgent ERCP is indicated within 24–48 hours in patients with cholangitis or persistent biliary obstruction.
- Routine ERCP is not recommended in gallstone pancreatitis without biliary obstruction.

b. Alcohol-Induced AP

- Abstinence from alcohol is crucial to prevent recurrence.
- Referral for counseling and treatment programs for alcohol use disorder is often necessary.

c. Hypertriglyceridemia-Induced AP

- Treated with insulin and/or heparin to reduce triglyceride levels acutely.
- In severe cases, **plasmapheresis** may be required.
- Long-term management includes lipid-lowering therapy (e.g., fibrates) and dietary modifications.

d. Drug-Induced AP

- Discontinuation of the offending medication and supportive care are the primary strategies.

4. Management of Complications

Complications, especially in severe AP, require targeted interventions.

a. Sterile Pancreatic Necrosis

- Managed conservatively with supportive care, including fluids and nutrition.
- Intervention is unnecessary unless symptoms worsen or necrosis becomes infected.

b. Infected Necrosis

- Suspected in patients with fever, leukocytosis, and signs of sepsis.
- Confirmed by imaging-guided fine-needle aspiration.
- Managed with broad-spectrum antibiotics (e.g., carbapenems) targeting gut flora.
- Minimally invasive techniques, such as **endoscopic necrosectomy** or **percutaneous drainage**, are preferred over open surgery.

c. Pseudocysts

- Asymptomatic pseudocysts are monitored without intervention.
- Symptomatic or complicated pseudocysts (e.g., infection, rupture) require drainage, typically via endoscopic or percutaneous methods.

d. Vascular Complications

- Bleeding from pseudoaneurysms or thrombosis is managed with angiographic embolization or surgery.
- Anticoagulation may be indicated for splenic vein thrombosis.

e. Systemic Complications

- **Acute Respiratory Distress Syndrome**:
- Managed with mechanical ventilation and lung-protective strategies.
- **Acute Kidney Injury**:
- Managed with hydration, diuretics, or renal replacement therapy if indicated.
- **Disseminated Intravascular Coagulation**:
- Treated with supportive measures and addressing the underlying cause.

5. Advanced and Emerging Therapies

- **Anti-Inflammatory Therapies**:
- Agents targeting cytokine pathways (e.g., IL-6 inhibitors) are being explored.
- **Probiotic Therapy**:
- Investigated for reducing gut bacterial translocation and infections, though evidence remains inconclusive.
- **Autophagy Modulators**:
- Targeting autophagy pathways in acinar cells is under research.

6. Post-Acute Care

- **Preventing Recurrence**:
- Lifestyle modifications, including alcohol cessation, smoking cessation, and dietary changes.
- Long-term management of hypertriglyceridemia or gallstones.

- **Monitoring and Follow-Up**:
- Regular imaging to monitor for late complications, such as pseudocysts or chronic pancreatitis.
- Assessment of pancreatic function, as chronic pancreatitis and diabetes mellitus are long-term risks.

Conclusion

Acute pancreatitis is a complex and potentially life-threatening condition requiring prompt diagnosis and tailored management. Advances in supportive care, minimally invasive interventions, and etiology-specific treatments have significantly improved outcomes. Continued research into early diagnostic markers and innovative therapeutic approaches holds promise for further reducing the burden of this disease.

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Entered 20.10.2024