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Pharmacological And Non-Pharmacological Management Of Acute Pancreatitis: A Comparative Review

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ABSTRACT:

Acute pancreatitis is a complex inflammatory condition of the pancreas with a wide spectrum of clinical severity, ranging from mild, self-limiting episodes to severe, life-threatening forms associated with organ failure and high mortality rates. The management of acute pancreatitis is challenging, with a growing need for effective treatment strategies due to increasing incidence and hospital admission rates globally. This review explores and compares pharmacological and non-pharmacological approaches to managing acute pancreatitis.

Non-pharmacological management primarily focuses on supportive care, including fluid resuscitation, oxygen therapy, and nutritional strategies aimed at pancreatic rest. Early and adequate fluid resuscitation within the first 24 hours is critical to improving outcomes. Nutritional interventions, such as early enteral feeding and, in select cases, total parenteral nutrition (TPN), are emphasized to maintain metabolic stability and minimize complications.

Pharmacological management involves addressing the disease's symptoms and complications. Pain relief, often with NSAIDs or opioids, is a cornerstone of care. Antibiotics are reserved for confirmed cases of infected necrosis, while secretory inhibitors such as somatostatin and trypsin inhibitors are employed in moderate to severe cases. Novel pharmacological interventions, including the use of Neostigmine and other repurposed drugs, are being explored in clinical trials to target specific pathophysiological mechanisms.

This review underscores the importance of a multidisciplinary, patient-centered approach to treatment. While pharmacological strategies are essential for managing complications, non-pharmacological interventions remain foundational in acute care. Ongoing research is critical to refine existing therapies and develop new modalities to improve outcomes and prevent recurrence, ultimately bridging the gap between supportive care and disease-specific treatment.

PHARMACOLOGICAL VS NON-PHARMACOLOGICAL MANAGEMENT OF ACUTE PANCREATITIS: A COMPARATICE REVIEW

Introduction:

Acute Pancreatitis is inflammation of the exocrine pancreas, mainly due to oxidative stress and the disintegration of pancreatic acinar cells. With around 30,000 emergency department visits every year, acute pancreatitis has become the leading cause of hospital admission from gastrointestinal disease in the United States. [1]

Abdominal pain that radiates to the back is the most common presenting symptom in acute pancreatitis. Subjective and objective observations are used for the diagnosis. This includes imaging that is compatible with the diagnosis, increased serum or urine lipase/amylase, and epigastric upper abdominal pain. Satisfying two of these three requirements contributes to a proper diagnosis. [2] It is an erratic and perhaps fatal illness. The inflammation may go away on its own or worsen to the point where the pancreas or the surrounding fatty tissue becomes necrotic. [3]

According to a Chinese study conducted in April 2024, with a rising incidence, 20-30% of acute pancreatitis cases progress to severe acute pancreatitis, which is in turn associated with a mortality rate of 30-50%. [4] In the United States, alcohol consumption (25–35%) and gallstone disease (40–70%) are the most frequent causes of pancreatitis.[2] The other causes include hypertriglyceridemia and drugs. The underlying cause of acute pancreatitis should be sought in all patients.

Pancreatic fluid collections, including acute ones, pancreatic pseudocysts, acute necrotic collections, and walled-off necrosis are among the complications.[5] While mild episodes of acute pancreatitis typically just necessitate a brief hospital stay and do not result in further complications, around 80% of cases can be fairly difficult to treat. Radiological criteria, scores, and classifications have been devised to correctly predict the course and severity of disease. [6] The development of organ failure and a subsequent infection are the key factors influencing the outcome. Over the last ten years, a multidisciplinary, customized, and minimally invasive strategy has become the standard for treating acute pancreatitis. [7]

The non-pharmacological approach involves oxygen, fluid and nutrition. Fluid resuscitation is the cornerstone of initial care for all patients. Within the first 24 hours of presentation, resuscitation should be started because delaying treatment increases the risk of morbidity and death.[4] The goal is to provide pancreatic rest and an on-demand diet. Total parenteral nutrition (TPN) is of value in patients with moderately severe or chronic pancreatitis. [8]

The pharmacological management involves opiates or NSAIDs for pain. Antibiotics are particularly used in individuals with infected necrotizing pancreatitis [7] According to a randomized control trial, Neostigmine was suggestively more effective than conventional treatment in reducing Intra-Abdominal Pressure (IAP) in patients.[9] Pancreatitis results in inappropriate trypsin activation, hence secretory trypsin inhibitors like Pantoprazole, somatostatin, Ulnistatin, gabazate in moderate to severe cases.

Acute pancreatitis can have catastrophic effects, so long-term treatment is necessary to reduce the risk of recurrence and development to chronic pancreatitis with an increased chance of pancreatic cancer. It is imperative to conduct clinical trials using novel and repurposed medications to address the lack of a conclusive, globally licensed treatment. However, a number of medications can help with acute pancreatitis complications and, in some cases, can prevent recurrence. [10]

OBJECTIVE: Effective management is becoming more and more necessary as acute pancreatitis incidence and admission rates rise. The management of patients with acute pancreatitis is reviewed, with particular emphasis on pharmacological and non-pharmacological approaches in the treatment.

HISTORICAL PERSPECTIVE

Pancreatitis was first described by Dutch anatomist and surgeon, Nicolaes Tulp. The prognostic scoring systems and the management of acute pancreatitis have evolved over the centuries. [11,16]

EVOLUTION OF PROGNOSTIC SCORING METHODS:

TIME LINE	SCORING METHOD
PRIOR TO 1977	There were 43 variables for determining the severity of pancreatitis
1977	Ransons Criteria was developed which involved only 11 variables including age, white blood cell count (WBC), blood glucose, serum aspartate transaminase (AST), serum lactate dehydrogenase (LDH), serum calcium, fall in hematocrit, arterial oxygen (PaO2), blood urea nitrogen (BUN), base deficit, and sequestration of fluids. [12,13]

1989	Acute Physiology and Chronic Health Enquiry (APACHE-II) was developed with a better sensitivity than Ranson's scoring with evaluation at time of presentation and 48 hours later. [14]
1990	Bathazar Scoring (helped predict complications such as pancreatic absesses) [13]
2008	BISAP Scoring (BUN, impaired mental status, systemic inflammatory response syndrome, age greater than 60 years, and pleural effusion)- this also helped predict mortality. [15]
Currently	CT scans and Serum amylase and lipase are the major diagnostic tools used to predict severity. [16]

Table 1 : Evolution of prognostic scoring systems

EVOLUTION IN THE MANAGEMENT OF ACUTE PANCREATITIS OVER TIME:

There has always been a debate regarding the benefit of medical and surgical management of pancreatitis. [8]

TIME LINE	MANAGEMENT
Prior to 1866	Surgery was considered risky and ineffective [17,18]
1867	August Socin, a surgeon from Switzerland, drained a pancreatic abscess in a 45-year-old woman. However, she died within 24 hours of the procedure. During autopsy, it was discovered that the cyst was a haematoma of the pancreas which probably developed as a complication of acute pancreatitis. Following this, surgical management of pancreatitis was explored and was practiced. [19]
1888-1930's	Laparotomy and surgical drainage was the preferred management. However, mortality rate was more than 50%.[19,20]
1930s-1960s	Serum amylase was used to differentiate between severe and non-severe forms of acute pancreatitis and surgeries were reserved only for severe cases. The number of surgeries performed reduced drastically. [20]
1960s	Enteral feeding through a jejunostomy tube was tested in the 1960 but this posed a significant risk of local complications [17]
1962	ICU care and constant monitoring of vitals and organ function was found to improve outcomes significantly.[21]
1960s-1970s	Given the poor results of medical treatment, surgical management was reconsidered even in initial stages of the disease. [20]
1970s	The high mortality rates continued to persist. Surgical management was now reserved for infected necrotising pancreatitis. Sterile necrosis was managed medically.[22,23]

1979	Surgeons attempted CT and USG guided abdominal abscess and subsequent culture of peripancreatic tissues and fluid collections, which allowed early diagnosis of the infection. Antibiotic usage for acute pancreatitis begun. In New York, laparoscopic necrosectomy was attempted.[23,25]
1984	Prophylactic antibiotics, most commonly cefotaxime was prescribed to all acute pancreatitis patients to prevent sepsis induced multi-organ failure.[24]
1986	Conservative management with rehydration and analgesics were attempted. Nasogastric aspiration, was subsequently used to a limited degree. Various drugs such as inhibitors of pancreatic secretion-such as atropine, glucagon, calcitonin, somatostatin and octreotide, as well as drugs that had an inhibitory effect on pancreatic proteolytic enzymes like aprotinin, gabexate mesylate and phospholipase inhibitors were explored. However, these drugs did not achieve satisfactory results.[26]
1990s	Enteral feeding through a nasojejunal tube and later, nasogastric tube was proposed.[27,28]
2000- 2010	Pre-clinical studies on mice were conducted to test the effect of pancreatic duct ligation and biliary duct ligation on pancreatitis. This proved the effectiveness of biliary stenting as a mode of treatment of acute pancreatitis. [29] Mutations such as SPIN-K1 and its association with pancreatitis was also studies. [30]
2010-2020	Oral feeding 72 hours after diagnosis was studies and showed similar morality rated to early nasogastric feeding. [31]
2022	PROCAP trial showed that procalcitonin can be used to differentiate infection related complications from inflammatory symptoms to reduce the need for antibiotics prophylactically. [32]
Currently	Multi-disciplinary approach (Gastro-enterologists, interventional radiologists, critical care units and surgeons)[17]

Table 2 -EVOLUTION IN THE MANAGEMENT OF ACUTE PANCREATITIS OVER TIME

PATHOPHYSIOLOGY:

Pancreatic duct obstruction, regardless of its cause, leads to a blockage of pancreatic secretions, which subsequently hinders the exocytosis of zymogen granules from acinar cells. This obstruction causes the zymogen granules to merge with intracellular lysosomes, forming autophagic vacuoles that contain both digestive and lysosomal enzymes. The enzyme cathepsin B within these vacuoles can activate trypsinogen to trypsin. Studies indicate that pancreatitis is associated with lysosomal dysfunction and an imbalance between the trypsinogen-activating enzyme cathepsin B and the trypsin-degrading enzyme cathepsin L [33]. The accumulation of active trypsin triggers the activation of digestive enzymes, leading to autodigestive injury, a theory originally proposed by Hans Chiari [34]. When normal apical exocytosis of zymogen granules is disrupted, exocytosis may occur at the basolateral side of the acinar cell, releasing active zymogens into the interstitial space and causing protease-induced damage to cell membranes [35]. The role of premature trypsinogen activation and autodigestion in acute pancreatitis is further supported by the discovery of a mutation in the trypsinogen gene in patients with hereditary pancreatitis, leading to the formation of active trypsin that resists degradation [36]. Additionally, genetically modified mice lacking the trypsinogen 7 gene show protection against acinar injury induced by supramaximal caerulein, supporting this hypothesis [36].

The autodigestive damage to acinar cells triggers an inflammatory response, characterized by the infiltration of neutrophils and macrophages, and the release of cytokines such as tumor necrosis factor-α and interleukins 1, 6, and 8 within the pancreatic parenchyma. However, inflammation in trypsinogen-null mice following caerulein hyperstimulation suggests that this inflammatory response can occur independently of trypsinogen activation [37]. In severe cases, this inflammatory reaction can lead to multiorgan failure and sepsis, with the latter thought to result from increased bacterial translocation from the gut lumen into the circulation [38]. The toxic effects of bile acids on acinar cells have also been considered a potential pathogenic factor in biliary pancreatitis. Bile acids can enter acinar cells through bile acid transporters on the apical and basolateral plasma membranes or via the G-protein-coupled receptor for bile acids (Gpbar1) [39, 40]. Once inside the cell, bile acids increase intra-acinar calcium levels by inhibiting sarco endoplasmic Ca2+-ATPase and activating signaling pathways, including MAPK and PI3K, as well as transcription factors like NF-κB, which induce the synthesis of proinflammatory mediators [41]. However, the clinical significance of these processes remains uncertain due to limited evidence for biliopancreatic reflux in clinical settings.

DIAGNOSIS OF ACUTE PANCREATITIS:

The internationally recognized guidelines for classifying acute pancreatitis, based on the revised Atlanta Standards:

1. Abdominal pain typical of acute pancreatitis, most often centered in the epigastric region.
2. Elevated serum amylase or lipase levels, exceeding three times the normal upper limit.
3. Distinctive imaging features of acute pancreatitis observed on CT, MRI, or ultrasound.

A diagnosis of acute pancreatitis requires the presence of at least two of three criteria. [42]

Grades of Acute Pancreatitis Severity:

1.Mild acute pancreatitis: a.Absence of organ failure b.No local or systemic complications

2.Moderately severe acute pancreatitis: a.Organ failure that resolves within 48 hours (transient organ failure) b.Presence of local or system complications without persistent organ failure

3.Severe acute pancreatitis: a.Persistent organ failure lasting more than 48 hours b.Can involve either single organ failure or multiple organ failure

Cross-sectional imaging, such as CT or MRI, is not necessary for diagnosing acute pancreatitis (AP), but it offers the most accurate diagnosis and can assess the extent of pancreatic and peripancreatic necrosis.[43] Figure-2 demonstrates CT findings in AP.

Pancreatic Fluid Collection:

The management of pancreatic and peripancreatic collections has significantly advanced over the past decade. According to the 2012 revised Atlanta criteria, four types of peripancreatic fluid collections in acute pancreatitis are distinguished based on their content, level of encapsulation, and timing. [11]

Figure 2: CT findings in acute pancreatitis.

Top left: acute oedematous pancreatitis with peripancreatic fluid which extend below uncinate process up to the level of bifurcation of the duct.Top right: 4.3*3.8 cm pancreatic cyst associated with the pancreatic tail. Bottom left: pancreatic necrosis with peripancreatic fluid collection and pocket of free fluid. Hypo enhancement within the pancreatic body. Focal fluid collection adjacent to the pancreatic tail. Bottom right: Walled-off pancreatic necrosis (WOPN)

PHARMACOLOGICAL MANAGEMENT OF ACUTE PANCREATITIS:

The pharmacological therapy in acute pancreatitis aims for pain management, reducing hospital stay and prevention or treatment of complications. Multimodal approach is used for pain management including opiates and epidural analgesia. Antibiotic use is beginning to become more focused and can treat a large number of people with necrotizing pancreatitis, with carbapenems being the first drug of choice [7]. Another desirable concept is to use immunomodulation by removing systemic cytokines or anti-inflammatory medications. Removing elements of the cytokine storm to modulate this hyper inflammatory response is an appealing strategy that has gained greater attention recently [7].

NSAIDs are advised for pancreatitis following endoscopic retrograde cholangiopancreatography (ERCP). More studies and trials are ongoing to establish the use of medications in acute pancreatitis.

PAIN MANAGEMENT:

Pain management is an important priority in the treatment of acute pancreatitis (AP). Opioids have been the first line to reduce the severe abdominal pain. Continuous intravenous opiate infusions can be used to treat severe pain that doesn't go away.[7] A meta-analysis revealed that opioids were superior to non-opioids in terms of the requirement for rescue analgesia. Opioid based treatments are often associated with many severe adverse effects such as constipation or opioid induced hyperalgesia [45]

Patients on long-term opioid therapy must be kept under close clinical surveillance and it shall be stressed that only about 25% of patients benefit from treatment. Some drugs such as tramadol possesses both a weak opioid agonist activity along with an effect on noradrenaline and serotonin uptake.[45]

NSAIDs reduce the pro-inflammatory response in AP by inhibiting cyclooxygenase (COX) and act as a good choice for management. NSAIDs and opioids had similar effects on reducing the requirement for rescue analgesia.[44] NSAID prophylaxis has become standard treatment to avoid post-ERCP pancreatitis.[7]

Epidural analgesia is one modality of a multimodal pain management approach that may help lessen the unwanted consequences of opiate use. It decreases opioid dependence and addiction.

According to a new retrospective review, thoracic epidural analgesia may offer protection against adult respiratory distress syndrome (ARDS), acute kidney injury (AKI), and even mortality in 352 patients with severe acute pancreatitis who were admitted to the intensive care unit of a Chinese hospital [46].

In some patients unconventional treatment with drugs such as ketamine is beneficial, but only in the hands of pain specialists. Somatostatin-analogue inhibits pancreatic secretion and may theoretically alleviate pain through reduction of pancreatic ductal pressure. [45]

ANTIBIOTICS:

Antibiotic prescriptions are prevalent during acute pancreatitis; during the course of the disease, up to two thirds of patients receive antibiotics, frequently without a culture- or radiologically-verified infection. Carbapenems is the drug of choice. Pro calcitonin (PCT) marker helps to decide the need for antibiotics. The recommendation was to start antibiotics when a PCT test showed >1 ng/ml; at <1 ng/ml, the recommendation was to halt or not start antibiotics. PCT-guided treatment may lower the unnecessary usage of antibiotics without running the risk of serious side effects.[7] However, there was no difference in the prescription of antibiotics between the groups in the subgroup of patients with moderate or severe acute pancreatitis, indicating that PCT-guide care is primarily helpful in reducing antibiotic use during the early hyper-inflammatory phase. Antibiotic prophylaxis in SAP aims to stop the necrotic tissues from becoming super infected. organ dysfunction that deteriorates too late, usually in the second or third week following the start of SAP in order to avoid necrosis. [47]

However, prophylactic antibiotics during hospital admission for acute pancreatitis have not been demonstrated to provide a significant benefit in randomized clinical trials [48]. Patients with AP associated with bacteremia, positive bronchoalveolar lavage, and urinary tract infection should receive antibiotics. [47]

According to abdominal CT, the American Association of Gastroenterology advises antibiotic prophylaxis when there is prolonged necrosis affecting more than 30% of the gland. Prophylaxis shouldn't be given for more than 14 days because the frequency of fungal infections rises with extended antibiotic therapy.[49]

Choice of Antibiotic:

The fluoroquinolones, imipenem-cilastatin, and metronidazole are the most potent antibacterial medicines because they can sufficiently penetrate pancreatic juice and necrotic tissue while also preventing the growth of enteric bacteria.[50] Gram-negative as well as gram-positive bacteria that are both aerobic and anaerobic should be included in the range of empirical antibiotics.[51] Furthermore, as these patients frequently have fungal infections, antifungal therapy or even prophylactic should be taken into consideration, particularly if there are several risk factors for invasive candidiasis. [51]

Table 3: Studies about choice of antibiotics in the management of acute pancreatitis

Sr no.	Study Design	Conclusion
1	Double-blind, randomized, placebo-controlled trials	Antibiotic prophylaxis in SAP is ineffective for reducing the frequency of infected necrosis and to decrease hospital mortality. In necrotizing pancreatitis, evidence-based data do not support late use of antibiotic prophylaxis after onset.[52]
2	Meta-analysis of 8 trials	Antibiotics were beneficial in lowering mortality. The benefit was exclusively to patients receiving broad-spectrum antibiotics that reach therapeutic levels in pancreatic tissue who had severe pancreatitis. Broad-spectrum antibiotics that reach therapeutic levels in pancreatic tissue are advised for all patients with severe pancreatitis.[53]
3	11 RCTs involving 747 participants were included, with an intervention group (prophylactic use of antibiotics, n = 376) and control group (n = 371).	No significant differences were found regarding antibiotic prophylaxis with respect to incidence of infected pancreatic necrosis (OR, 0.74; 95% confidence interval [CI], 0.50-1.09; P = 0.13), surgical intervention (OR, 0.92; 95% CI, 0.62-1.38; P = 0.70), and morality (OR, 0.71; 95% CI, 0.44-1.15; P = 0.16) [54]

4	Seven trials involving 467 patients were included.	Analysis suggested infected pancreatic necrosis rates were not significantly different (antibiotics 17.8%, controls 22.9%), RR 0.81 (95% CI 0.54-1.22). There was nonsignificantly decreased mortality with antibiotics (9.3%) versus controls (15.2%), RR 0.70 (95% CI 0.42-1.17). Subsequent subgroup analysis confirmed antibiotics were not statistically superior to controls in reduction of infected necrosis and mortality. [55]
5	Eight RCTs including 540 patients were assessed.	Prophylactic antibiotic use leads to a significant reduction of infected necrosis (relative risk (RR) 0.69, 95% CI, 0.50-0.95; p=0.02), non-pancreatic infections (RR 0.66 95% CI, 0.48-0.91; p=0.01), and length of hospital stay (p=0.004) but was not associated with a statistically significant reduction in mortality (RR 0.76 95% CI, 0.50-1.18; p=0.22) and surgical intervention (RR 0.90 95% CI, 0.66-1.23; p=0.52). [56]
6	RCT with one control group and other receiving prophylactic antibiotics and	Between the group that received a prophylactic antibiotic and the group that did not (58% vs. 56%), there was no discernible difference. In addition, it was shown that patients on imipenem experienced septic problems more frequently than those not on antibiotics (15%), with a frequency of 29%. Although none of the comparisons reached statistical significance, pancreatic necrosis infection occurred in 12.5% of patients treated with imipenem and only 6% of patients in the group of patients not receiving antibiotic prophylaxis.[57]
7	Seven studies (n = 429) that met the inclusion criteria	Preventive antibiotics for acute necrotizing pancreatitis notably reduced hospital stay duration (P = 0.04) and non pancreatic infection rate (P < 0.01). Regarding mortality (P = 0.22), infected necrosis (P = 0.18), and surgical intervention (P = 0.40), no significant differences were seen. [58]

ENZYMES AND PROBIOTICS:

Probiotics (Bacillus subtilis and Enterococcus faecium) in mild pancreatitis and synbiotics (Bifilac) in moderate and severe pancreatitis, respectively, shortened hospital stays without affecting clinically significant outcomes, according to two recent randomized trials. [59] The endogenous nature of postbiotics and their safety profile make them appealing targets for bacterial products derived from fibers. Butyrate, a short chain fatty acid, has shown promise in preventing severe problems in mice, according to a recent preclinical study [49]. Currently being developed is a proof-of-concept experiment that will use micro-encapsulated tributyrin, a butyrate prodrug, as prophylaxis in patients suffering from acute pancreatitis.[59]

During their inpatient stay for acute pancreatitis, more than 50% of patients have pancreatic exocrine insufficiency detected. When treating moderately to very severe acute pancreatitis with oral or enteral feeding, pancreatic enzyme replacement treatment is likely to be helpful until stool elastase-1 testing is consistently normal (≥ 200 μg/g).[60]

When everything else fails, therapeutic plasma exchange may be the last option for treating patients with refractory multiple organ failure.

Neostigmine treatment used for intra-abdominal hypertension patients. [59]

INSULIN, HEPARIN AND FIBRATES IN TRIGLYCERIDE INDUCED PANCREATITIS:

A meta-analysis pointed to possible benefits of intravenous heparin, glutamine, ω-3 fatty acids, and/or traditional Chinese medicine in treating severe acute pancreatitis [60][61].

Insulin reduces the levels of total TGs by accelerating the breakdown of chylomicron and activating lipoprotein lipase (LPL) activity [62]. In addition to resting pancreatic tissue, insulin has the potential to enhance immunoparalysis by reducing cell death and increasing the expression of human leukocyte antigen on monocytes [63]. Over two to three days, insulin reduces TGs levels by 50–75% [62].

For severe HTG (TGs > 500 mg/dL), fibrates are still the preferred medication; niacin is used as an adjuvant [22].17 It has been demonstrated that fibrates, statins, niacin, and omega-3 fatty acids can lower TG levels by 36.3%, 10% to 18%, 20%, and 25 to 33.8%, in that order [64]

Heparin lowers the levels of TGs by releasing lipoprotein lipase that has been accumulated in endothelial cells. In case reports and case series, the combination of insulin and heparin has been utilized to lower TGs levels; the mean drop in TGs levels within 24 hours was observed [65].

Heparin should ideally be avoided due to concerns about rebound hypertriglyceridemia and the possibility of bleeding into the pancreas during an acute episode when receiving continuous heparin infusion. [63]

INTERVENTIONS IN THE MANAGEMENT OF ACUTE PANCREATITIS:

INDICATION	INTERVENTION
Infected Walled Off Abscess	European Society of Gastro-intestinal Endoscopy recommends **percutaneous or endoscopic drainage**. In case the infection is not cleared, endoscopic **necrosectomy** or invasive surgeries can be performed. [66]
Biliary Stones	Endoscopic Ultra-sound or MRCP for diagnosis followed by therapeutic ERCP (Endoscopic Retrograde Cholangio-pancreastography) : This allows diagnosis and removal of any calculi in the same sitting. [66] However, this is associated with the complication of post- ERCP Pancreatitis due to allergy to contrast media or elector-cautery induced injury. [67] Early ERCP in patients with biliary obstruction is associated with a significant reduction in local complications. [69]
Necrosis with suspected infection	Image guided Fine Needle Aspiration and culture should be performed to identify the organism and to start appropriate antibiotics only if culture is positive. Antibiotics are not indicated for culture negative or sterile necrosis. [68]
Gall Stone Pancreatitis	Elective Cholecystectomy is done 4 weeks post recovery. A systematic review and meta-analysis from the Eastern Association for the Surgery of Trauma which consisted of nine studies compared three different cut-offs (72 h, 12 days, and 30 days). In all cut-offs, late surgery resulted in a survival benefit due to a demarcation of necrosis from vital tissue resulting in lesser bleeding. [69,70]
Hemodynamically unstable patients	Open laparotomy and exploration is performed as an emergency procedure. Proper sterile dressing in the post-operative period is necessary for recovery of the patient. [71]

Table 4: INTERVENTIONS IN THE MANAGEMENT OF ACUTE PANCREATITIS

NON-PHARMACOLOGICAL MANAGEMENT OF ACUTE PANCREATITIS:

Acute pancreatitis is an inflammatory condition of the pancreas that can cause severe abdominal pain and systemic complications. Non-pharmacological interventions are crucial in the treatment of acute pancreatitis, with an emphasis on supportive care, reducing complications, and improving recovery.

Grading: The GRADE strength of recommendation(1 =strong, 2 =weak) and quality of evidence (A =high, B=moderate, C =low) are provided along with the strength of agreement during plenary voting (strong/weak)the GRADE strength of recommendation(1 =strong, 2 =weak) and quality of evidence (A =high, B=moderate, C =low) are provided along with the strength of

agreement during plenary voting (strong/weak) during IAP/APA Joint Annual Meeting on October 31st, 2012 in Miami, Florida, USA.[72,73]

Grade of Recommendation	Clarity of risk/benefit	Quality of supporting evidence	Implications
1A. Strong recommendation, high quality evidence	Benefits clearly outweigh risk and burdens, or vice versa.	Consistent evidence from well performed randomized, controlled trials or overwhelming evidence of some other form. Further research is unlikely to change our confidence in the estimate of benefit and risk.	Strong recommendations, can apply to most patients in most circumstances without reservation. Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.
1B. Strong recommendation, moderate quality evidence	Benefits clearly outweigh risk and burdens, or vice versa.	Evidence from randomized, controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other research design. Further research (if performed) is likely to have an impact on our confidence in the estimate of benefit and risk and may change the estimate.	Strong recommendation and applies to most patients. Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.
1C. Strong recommendation, low quality evidence	Benefits appear to outweigh risk and burdens, or vice versa.	Evidence from observational studies, unsystematic clinical experience, or from randomized, controlled trials with serious flaws. Any estimate of effect is uncertain.	Strong recommendation, and applies to most patients. Some of the evidence base supporting the recommendation is, however, of low quality.

2A. Weak recommendation, high quality evidence	Benefits closely balanced with risks and burdens.	Consistent evidence from well performed randomized, controlled trials or overwhelming evidence of some other form. Further research is unlikely to change our confidence in the estimate of benefit and risk.	Weak recommendation, best action may differ depending on circumstances or patients or societal values.
2B. Weak recommendation, moderate quality evidence	Benefits closely balanced with risks and burdens, some uncertainly in the estimates of benefits, risks and burdens.	Evidence from randomized, controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other research design. Further research (if performed) is likely to have an impact on our confidence in the estimate of benefit and risk and may change the estimate.	Weak recommendation, alternative approaches likely to be better for some patients under some circumstances.
2C. Weak recommendation, low quality evidence	Uncertainty in the estimates of benefits, risks, and burdens; benefits may be closely balanced with risks and burdens.	Evidence from observational studies, unsystematic clinical experience, or from randomized, controlled trials with serious flaws. Any estimate of effect is uncertain.	Very weak recommendation; other alternatives may be equally reasonable.

Table 6: Grading of Acute Pancreatitis

Main non-pharmacological approaches in the management of acute pancreatitis:

1. Fluid Resuscitation

Early Aggressive Hydration: This is the foundation of acute pancreatitis management. Intravenous (IV) fluids, usually isotonic crystalloids such as Ringer's lactate, are given to maintain hemodynamic stability and prevent organ failure.

Timely and vigorous intravenous fluid replacement is essential to address hypovolemia resulting from third space losses, vomiting, sweating, and increased vascular permeability due to inflammatory mediators. Hypovolemia adversely affects the microcirculation of the pancreas and significantly contributes to the onset of necrotizing pancreatitis. Depletion of intravascular volume leads to hemoconcentration (hematocrit ≥44), tachycardia, hypotension, reduced urine output, and prerenal azotemia[74]. Substantial experimental evidence indicates that prompt and aggressive fluid resuscitation, along with enhanced oxygen delivery, can prevent or reduce pancreatic necrosis and improve survival rates [75,76,77]. While similar studies have not been conducted in clinical settings, there is general consensus on the critical role of aggressive fluid resuscitation in acute pancreatitis. One study highlighted that all patients who presented with hemoconcentration upon admission and whose hematocrit further increased after the first 24 hours due to insufficient fluid resuscitation ultimately developed pancreatic necrosis [78]. Clinically, the effectiveness of fluid resuscitation should be assessed by vital signs, urine output, and hematocrit decrease at 12 and 24 hours following admission. Central venous pressure

monitoring is rarely required[72].

Parameters	Ringer Lactate[79,80,81]	Normal Saline[80]	Hydroxyethyl starch[82]
pH	pH balanced solution since it is lactated.	Can cause non-anion gap metabolic acidosis	No proven acidosis or alkalosis in patients
Systemic inflammatory response syndrome	Lower	Higher	Studies are associated with high risks of renal failure.
Electrolyte balance	Good electrolyte balance	Can cause Hyperchloremia	No proven electrolyte imbalance in patients
Osmolality	Isotonic	Isotonic	Hypertonic
Recommendations	GRADE 1B, strong agreement	NA	NA

Table 7: Comparison of fluids used in the management of acute pancreatitis

Only a limited number of studies have examined the effects of various fluid types on the outcomes of acute pancreatitis[79,80,81]. While Ringer's lactate and Hartmann's solution are quite similar, they are not identical. While there is developing evidence that adding HES to fluid resuscitation in acute pancreatitis may be useful [81], its adverse effects in severe sepsis warrant enough caution to not advocate its use in the current guidelines.

Goal-directed intravenous fluid treatment at 5-10 ml/kg/h should be administered initially until resuscitation goals are met.(Grade 1B, weak agreement)

In most patients, a total infusion of 2500-4000 ml is sufficient to meet resuscitation goals during the first 24 hours. Two RCTs from the same research group provide moderate quality evidence that intensive fluid treatment increases morbidity and mortality. The first RCT found that patients receiving a fluid infusion rate of 5-10 ml/kg/h had lower rates of mechanical ventilation, abdominal compartment syndrome, sepsis, and death compared to those receiving 10-15 ml/kg/h [83]. In a second RCT, patients assigned to gradual hemodilution (aiming for a hematocrit >35% within 48 h) had lower incidence of sepsis and mortality compared to patients assigned to rapid hemodilution (aiming for a hematocrit <35% within 48 h) [84]. Because age and comorbidities such as heart failure necessitate individualization of fluid management, the rate of infusions recommended in these guidelines should be read with caution and adapted to the patient's condition.

Monitoring Fluid Status: Continuous monitoring of vital signs, urine output, and hematocrit levels is required to guide fluid therapy.

The preferred method for evaluating the response to fluid resuscitation should be based on one or more of the following:

S. No.	Target	Parameters	Agreed Range	Recommendations
1.	Non-invasive clinical targets[72]	Heart rate	Less than 120 bpm	Grade 2B, weak agreement
		Mean arterial pressure	65-85 mmHg (8.7-11.3 kPa)	

		Urine Output	>0.5-1ml/kg/h.	
2.	Biochemical targets[72]	Hematocrit	35-44%	
		Urea	16 mg/dl	
3.	Invasive clincal targets (ICU Set up) [72]	Stroke volume variation	10-13%	
		Intrathoracic blood volume	1.25 (Global End Diastolic Volume)	
		Central Venous Pressure	8 – 12 mm Hg	
		Central Venous Oxygen Saturation	>=70%	

Table 8 : Parameters for monitoring response to treatment of acute pancreatitis

Non-invasive targets are useful on a standard ward, whereas intrusive targets are better suited for the intensive care unit. A single parameter is unlikely to be as dependable as a combination of parameters. Recent research has concentrated on blood urea nitrogen as a predictor of outcome, but not on its utility as a response measurement [85]. For biochemical measures (e.g., hematocrit, blood urea nitrogen), not only the absolute amount but also the trend should be recorded. A recent study found that central venous pressure alone may be insufficient as a crude predictor of good resuscitation [86].

2. Nutritional Support

- Early Enteral Nutrition: Starting enteral feeding (ideally with a nasojejunal tube) within 24-72 hours of admission can assist maintain gut integrity and avoid bacterial translocation, lowering the risk of infections and sequelae. In mild pancreatitis, oral feeding can be resumed if abdominal pain subsides and inflammation signs improve. (Grade 2B, strong agreement). It is not necessary to wait until pain or test abnormalities have entirely resolved before resuming oral feeding[72]. One RCT found that prompt oral refeeding with a normal diet is safe in patients with mild pancreatitis and results in a shorter hospital stay (4 vs 6 days) [86]. A second RCT showed that feeding can begin with a full solid meal without first introducing a liquid or soft diet [88]. A third RCT found no need to wait for lipase levels to normalize before beginning oral feeding [89]. Patients with severe acute pancreatitis who require nutritional support should get enteral tube feeding as their primary therapy. (Grade 1B, strong agreement). Two meta-analyses found that enteral nutrition, when compared to parenteral nutrition, reduces systemic infections, multi-organ failure, surgical intervention, and death [90,91]. The vast majority of trials were conducted on patients with severe acute pancreatitis. Patients who can eat do not need supplemental enteral nourishment through a feeding tube. A recent RCT in 60 patients with 'severe acute pancreatitis' indicated that starting enteral nutrition within 48 hours was more effective than starting it after 7 days of fasting [92].

Acute pancreatitis can be treated with both elemental and polymeric enteral nutrition formulas. (Grade 2B, strong agreement).

A recent meta-analysis of 20 RCTs found that no single form of enteral nutrition or immunonutrition improved outcomes in acute pancreatitis [93]. Polymeric feeding formulations were found to be equally beneficial to more expensive semi-elementary formulations in terms of lowering infection complications and death.

In acute pancreatitis, enteral nourishment can be delivered by the nasojejunal or nasogastric routes.(Grade 2A, strong agreement). Two short RCTs indicate that naso-gastric tube feeding is practical and safe [94,95]. Although nasogastric tube feeding is likely easier than nasojejunal tube feeding, some patients will be unable to tolerate it due to delayed gastric emptying.

- Parenteral Nutrition: Only recommended if enteral feeding is not viable. It is connected with an increased risk of infection and should be used with caution. In acute pancreatitis, parenteral nutrition can be used as a second-line treatment if nasojejunal tube feeding is not tolerated and nutritional assistance is required.(GRADE 2C;

strong agreement). Parenteral nutrition should only be used if oral or enteral feeding fails to meet nutritional needs [90,96].A delay of up to 5 days in initiating parenteral nutrition may be reasonable to allow for the resume of oral or enteral feeding

.

3. Fasting (NPO - Nil Per Oral)

- Traditionally, patients with acute pancreatitis were placed on NPO to relax the pancreas. However, early restoration of oral intake is now recommended, beginning with clear liquids and progressing as tolerated, particularly in mild instances.

4. Pain Management

· Non-pharmacological approaches, such as positioning (e.g., leaning forward or sitting up), can provide pain relief. Warm compresses and breathing exercises may also provide help.

· Multimodal treatments, including psychological assistance, may be useful, particularly in chronic situations.

5. Lifestyle Modifications

- Alcohol Abstinence: To avoid recurrence, persons with alcohol-induced pancreatitis must abstain from alcohol completely.
- Dietary Adjustments: Low-fat, high-protein meals are indicated for reducing pancreatic stimulation. Small, regular meals are often recommended.

6. Monitoring and Supportive Care

Monitoring for Complications: Regular monitoring for local and systemic complications like necrosis, abscesses, or organ failure is critical. This may include imaging studies like CT scans. In acute pancreatitis, initial CT evaluation may be necessary due to diagnostic ambiguity, confirmation of severity based on clinical predictions, or failure to respond to conservative treatment or clinical deterioration. The optimal time for an initial CT scan is at least 72-96 hours after the onset of symptoms[72].(GRADE 1C; strong agreement). The majority of individuals do not require CT scans to diagnose acute pancreatitis. Early CT is not recommended for acute pancreatitis due to a lack of evidence that it improves clinical outcomes or early detection of necrosis. Additionally, CT scoring systems do not outperform clinical scoring systems in predicting disease severity [97]. There is evidence that an early (inappropriate) CT may lengthen hospital stays [98], have low yield with no obvious management implications [99], do not improve clinical outcomes [100], and offer hazards of contrast allergy and nephrotoxicity. Because the full amount of pancreatic and peri-pancreatic necrosis may not become apparent 72 hours after the onset of acute pancreatitis, a CT scan to determine the severity of pancreatitis using the CT severity index (CTSI) criteria [101] should be performed only after that. Early CT can help rule out intestinal ischemia or intra-abdominal perforations in patients who have both acute pancreatitis and acute abdomen. Follow-up CT or MR in acute pancreatitis is recommended when there is no clinical improvement, clinical deterioration, or when invasive intervention is contemplated.(GRADE 1C; strong agreement). Although numerous guidelines recommend routine follow-up CT (e.g., weekly) in acute pancreatitis, there is less evidence to support this approach. The current guidelines do not propose routine CT for first evaluation because the great majority of problems can be suspected from clinical and biochemical testing. One significant risk, arterial pseudoaneurysm development, may not be clinically apparent until bleeding occurs, but this complication of acute pancreatitis is so uncommon that it may not warrant a 'regular' follow-up CT. At least 4 weeks following the initial episode of acute pancreatitis, magnetic resonance imaging may be necessary to differentiate between pseudocysts and walled-off necrosis, as defined by the updated Atlanta classification system. CT is frequently unable to detect necrosis in a fluid-rich collection[72].

Respiratory Support: In severe situations, oxygen treatment or mechanical ventilation may be required.

7. Infection Control

Sterile Technique: To prevent infections, use sterile techniques throughout surgeries and manage catheters and lines correctly.

8. Interventional Procedures

Endoscopic Retrograde Cholangiopancreatography (ERCP): For individuals with gallstone pancreatitis or biliary obstruction, ERCP can be a non-pharmacological way to remove stones or ease obstructions.

ERCP is not recommended in patients with mild biliary pancreatitis without cholangitis (GRADE 1A, high agreement). ERCP is unlikely to be needed in anticipated severe biliary pancreatitis without cholangitis (GRADE 1B, good agreement). ERCP is most likely indicated for biliary pancreatitis with common bile duct occlusion.(GRADE 1C; strong agreement). ERCP is recommended for individuals with biliary pancreatitis and cholangitis(GRADE 1B, strong agreement)[72].

A recent meta-analysis of 7 RCTs with 757 patients found no indication that early routine ERCP reduces mortality or local/systemic complications, regardless of the predicted severity of biliary pancreatitis [101]. The meta-analysis recommended ERCP for individuals with cholangitis or co-existing biliary blockage. Predicting the existence of CBD stones in early stages of biliary pancreatitis using laboratory findings, transabdominal ultrasonography, or CT is inconsistent [102]. The individual studies, as well as the pooled data in the meta-analyses, did not include enough patients with 'predicted severe biliary pancreatitis without cholangitis' to analyze hard clinical objectives like mortality (potential type-2 statistical error). Acute cholangitis patients require urgent ERCP (within 24 hours). There is currently no data to support the appropriate time of ERCP in patients with biliary pancreatitis without

cholangitis.(GRADE 2C; strong agreement).A recent meta-analysis demonstrated no significant effect of ERCP timing (<24 vs. <72 h) on mortality [101]. However, no trials were explicitly planned to investigate the timing of ERCP in biliary pancreatitis. Because it is unclear when an early ERCP should be performed (24-72 hours), it is advisable to wait 24-48 hours for spontaneous resolution of biliary blockage. It is critical that ERCP is conducted as soon as possible in patients with cholangitis[77].

MRCP and EUS may avert certain ERCPs that would otherwise be performed for suspected common bile duct stones in patients with biliary pancreatitis who do not have cholangitis, without altering the clinical course. EUS can detect tiny (<5mm) gallstones more effectively than MRCP. MRCP is less intrusive, operator-independent, and perhaps more widely available than EUS. As a result, in clinical practice, neither MRCP nor EUS have a clear advantage.(GRADE 2C; strong agreement).

MRCP, EUS, and ERCP are generally not recommended for patients with mild biliary pancreatitis who do not have clinical signs of persisting common bile duct obstruction, as this can be addressed with (early) cholecystectomy with/without intraoperative cholangiography. One RCT discovered that EUS could safely substitute diagnostic ERCP in individuals with biliary pancreatitis[103]. It is important to highlight that most hospitals would likely have limited access to urgent MRCP and EUS. A negative MRCP does not rule out the presence of tiny (<5 mm) common bile duct stones [104]. This is especially important since tiny stones might cause biliary pancreatitis [105].

Drainage of Fluid Collections: Pseudocysts and abscesses may require percutaneous or endoscopic drainage.

To treat suspected or confirmed (walled-off) infected necrotizing pancreatitis, patients should initially undergo percutaneous catheter or endoscopic transmural drainage.(Grade 1A, strong agreement).Remarks: Percutaneous catheter drainage alone can avoid 23-50% of necrosectomies in patients with infected necrotizing pancreatitis [106,107,108,109,110]. Percutaneous catheter drainage is technically viable in over 95% of individuals with infected necrosis[107]. A prospective, observational multi-center analysis of 40 patients indicated that a decrease in the size of the collection of at least 75% after the first 10-14 days after percutaneous draining (n= 9, 23%) accurately predicts effective percutaneous therapy [106], although more data is needed to confirm this conclusion. Following catheter drainage, the patient must be monitored by an expert physician, who, in the absence of clinical improvement, can direct the next appropriate therapeutic step (e.g., surgical or endoscopic necrosectomy). Although wider bore drains are occasionally suggested to produce superior performance, evidence is weak. Overall, there is less experience with endoscopic transluminal drainage compared with percutaneous drainage.

9. Physical Therapy

Physical treatment may be essential in severe cases or during long-term hospitalization to avoid muscle loss and maintain mobility.

10. Patient Education

Long-term care and prevention of chronic pancreatitis require educating patients on the need of lifestyle modifications, recognizing early signs of recurrence, and understanding their illness.

Figure 3: Flow chart depicting non-pharmacological management of acute pancreatitis

COMPARATIVE ANALYSIS BETWEEN PHARMACOLOGICAL AND NON-PHARMACOLOGICAL MANAGEMENT OF ACUTE PANCREATITIS:

EFFICACY:

Studies have been conducted to compare the use of surgical management as compared to conservative management for necrotising infected pancreatitis. A cross-sectional study conducted in Pakistan showed that there was no statistically significant difference in hospital stay, complication rate, and hospital mortality between surgical and conservative management. [114]

ERCP is preferred in pancreatitis associated with cholangitis. A meta-analysis conducted by Dan Tang including 1639 patients with Acute biliary pancreatitis were included,out of which 823 were in the observation (ERCP or ERCP + endoscopic sphincterotomy) group and 816 were in the conservative treatment group. The observation group showed a significantly higher response rate, lower incidence of complications, and superior postoperative abdominal pain relief time, serum amylase recovery time and hospital stay than the conservative treatment group.[113]

However, in patients with gallstone pancreatitis without cholangitis, urgent ERCP with sphincterotomy did not reduce the incidence of major complications or mortality, compared when compared to conservative treatment.[115]

In case of infective necrotising pancreatitis, a multicenter study showed that endoscopic necrosectomy was associated with a clinical success in 80% of the patients, with a 26% complication and a 7.5% mortality rate at 30 days. After a mean follow-up period of 43 months, 84% of the initially successfully treated patients had sustained clinical improvement. 10% of patients received further endoscopic treatment and 4% received surgical treatment due to complications during the follow up period, and 16% suffered recurrent pancreatitis. [116]

A retrospective comparative study by Pramod Kumar Garg showed that patients with infective necrotising pancreatitis who received primary conservative treatment had significantly higher survival rates than those who received surgery. [117]

SAFETY :

Conservative management is associated with lower morbidity rates and a shorter hospital stay as compared to surgical management. A retrospective study conducted by L P Lefter including 151 participants showed that The conservatively treated group had a statistically significant better outcome and lower morbidity when compared to the surgically treated group, suggesting that conservative management should be preferred as the first option in acute severe pancreatitis. [119]

ERCP is associated with post- ERCP Pancreatitis due to allergy to contrast media or elector-cautery induced injury. This can be prevented by the administration of rectal indomethacin.

According to a multi-center study conducted in Turkey, prophylactic NSAIDs were not given to 44 % of the patients with post-ERCP pancreatitis (n = 86). [120]

A randomized clinical trial by Olaf J.Bakker showed a reduced incidence of multiple organ failure and pancreatic fistulas in endoscopic necrosectomy as compared to open surgical necrosectomy. [121]

These studies hence show the need to identify specific indications for surgical management and prioritize non-invasive and minimally invasive treatment options .

There were no significant differences in the recurrence rates between patients who had undergone conservative and surgical management. Also, there were no differences in the recurrence rates between patients with mild, moderate and severe pancreatitis. [122,126]

COMPARISION BETWEEN CONSERVATIVE AND SURGICAL MANAGEMENT OF PANCREATITIS:

Parameter	**Conservative Management**	**Minimally invasive surgery/Endoscopic procedures**	**Surgical Management**
Efficacy : Recovery rates	Associated with better recovery rates as compared with surgical management. [113,119]	Biliary pancreatitis: –1.837, (95% CI: –2.347, –1.328) $p < 0.001$ [113] Endoscopic necrosectomy: Initial clinical success in 80% cases, out of which 84% had sustained clinical improvement during follow up. [116]	Since it is used in patients who have complications, it is associated with a higher incidence of morbidity (34-95%) [121,122]
Indications	First line of management of acute pancreatitis, unless associated with biliary pathology. [115,119]	Acute biliary pancreatitis. [113]	Necrotising infected pancreatitis and acute severe pancreatitis only after the failure of conservative management. [114,119]
Survival and Mortality Rates [121]	Improved survival rate as compared to surgical management (76.9% vs 46.4%; $P = .005$)	Early ERCP in biliary pancreatitis is associated with better survival rates. [118] In necrotizing pancreatitis, it is associated with a 7.5% mortality rate within 30 days. [116]	Usually associated with higher mortality rates (10-40%) [121]

Side-effect profile	Aggressive fluid resuscitation is associated with pulmonary edema and new onset acute kidney injury. [123]	Post ERCP pancreatitis which can be prevented by the administration of rectal indomethacin and pancreatic duct stent placement [118]	A higher incidence of multiple organ failure,and pancreatic fistulas as compared to Endoscopic necrosectomy, which did not cause new-onset multiple organ failure (0% vs 50%, RD, 0.50; 95% CI, 0.12-0.76; P = .03) and reduced the no. of pancreatic fistulas (10% vs 70%; RD, 0.60; 95% CI, 0.17-0.81; P = .02). [120]
Cost Effectiveness [114]	It was found to be **more cost effective**: 402,154 pakistani rupees as compared to surgical management - 654,730 rupees (p=0.035)	Laparoscopic CBD exploration is more effective than ERCP. Hence, selective ERCP is recommended- cholangitis associated pancreatitis. [127]	654,730 pakistani rupees as compared to conservative management - 402,154 rupees (p=0.035)
Recurrence [125]	There is no significant difference between recurrence rates in conservative and surgical management.	Early ERCP in acute pancreatitis associated with cholangitis is associated with a lesser recurrence rate as compared to conservative management. [118]	Patients with gallbladder pancreatitis who have undergone cholecystectomy have a lower recurrence rate.

Table 9: COMPARISION BETWEEN CONSERVATIVE AND SURGICAL MANAGEMENT OF PANCREATITIS

COMPARISON OF SAFETY AND SIDE EFFECT PROFILE OF DIFFERENT MODALITIES OF MANAGEMENT OF ACUTE PANCREATITIS:

Management Modality	Efficacy Parameters	Efficacy (% Improvement)	Benefits	Limitations/Concerns	Clinical Use/Recommendations	References
Fluid Resuscitation	Mortality reduction, Reduction in SIRS, Organ failure prevention	-Mortality reduction by 30-35%; -SIRS reduction by 25-30%	Prevents hypovolemia and organ failure, Reduces inflammation	Risk of fluid overload (e.g., ARDS) with aggressive hydration	Ringer's Lactate preferred; Goal-directed therapy recommended	128, 129, 130, 131
Nutritional Support	Mortality, Infectious complications, Hospital stay	-Mortality reduction by 15-20%; -Infections	Maintains gut integrity, Reduces bacterial	-Delayed initiation may worsen outcomes; -TPN less effective	Enteral feeding within 24-48 hours recommended	132, 133, 134

		decreased by 25-30%	translocation			
Pain Management	Pain score reduction, Opioid need	-Pain score reduction by 40-50%; -20-30% reduction in opioid use	Provides symptom relief, improves patient comfort	-Risk of opioid dependence; -Nerve blocks not widely available	Opioids for severe pain; Consider celiac plexus block in refractory cases	135, 136, 137
Antibiotic Therapy	Infection rates, Mortality	-No significant reduction in mortality in sterile pancreatitis; -Infections decreased by 10-15% in confirmed cases	May be beneficial in confirmed infected pancreatic necrosis	Risk of antibiotic resistance, adverse reactions	Not routinely recommended; use in confirmed infection	132, 133, 138
Endoscopic Retrograde Cholangio-pancreatography (ERCP)	Mortality, Need for surgery, Length of hospital stay	-Mortality reduction by 20-25% in cases with cholangitis; -Surgical need reduced by 30-40%	Provides definitive treatment for obstructive causes	Risk of complications: pancreatitis, bleeding, infection	Indicated in gallstone pancreatitis with cholangitis	139, 109, 140
Minimally Invasive Necrosectomy	Mortality, Morbidity (organ failure), Length of stay	-Mortality reduction by 15-20%; -Morbidity reduction by 25-30%	Minimally invasive; Shorter recovery	Requires expertise; availability may be limited	Recommended for infected necrosis not responding to antibiotics	138, 109, 141
Probiotics	Infection rates, Mortality	-Infection rates reduced by 5-10%; -No significant mortality impact	May help maintain gut flora balance	Risk of bacteremia in severely ill patients	Not routinely recommended; more research needed	130, 142, 143
Plasmapheresis	Triglyceride levels, Inflammatory markers	Reduces triglycerides by 50-60% within 24-48 hours	Rapidly decreases triglycerides and inflammation	Limited indications; Invasive; Requires specialized equipment	Consider in severe hypertriglyceridemia-induced pancreatitis	133, 144, 145

TABLE 10 : COMPARISON OF SAFETY AND SIDE EFFECT PROFILE OF DIFFERENT MODALITIES OF MANAGEMENT OF ACUTE PANCREATITIS

CONCLUSION:

In conclusion, the management of acute pancreatitis requires a multifaceted approach that integrates both pharmacological and non-pharmacological strategies to address the diverse clinical presentations and complications associated with the disease. Pharmacological interventions primarily focus on pain management, infection control, and stabilization of inflammatory processes. Opioids and NSAIDs remain standard for alleviating the severe abdominal pain characteristic of acute pancreatitis, though recent studies suggest potential benefits of adjunctive therapies like epidural analgesia to reduce opioid dependency. Antibiotic therapy, while a cornerstone in managing confirmed infections in necrotizing pancreatitis, is increasingly guided by biomarkers such as procalcitonin to prevent overuse and reduce antibiotic resistance. The use of secretory inhibitors and enzyme modulators shows promise in preventing pancreatic autodigestion, though the efficacy of these agents varies and requires further investigation through clinical trials.

Non-pharmacological management is equally essential, particularly in the initial phases of treatment, as it emphasizes pancreatic rest, fluid resuscitation, and nutritional support. Aggressive fluid resuscitation with isotonic crystalloids, particularly Ringer's lactate, is crucial to maintaining hemodynamic stability and preventing organ failure, though caution is warranted to avoid fluid overload. Early enteral nutrition, ideally initiated within 24-72 hours, has been shown to maintain gut integrity, lower infection risk, and improve outcomes compared to parenteral nutrition, highlighting its importance in both mild and severe cases. Lifestyle modifications, including alcohol abstinence and dietary adjustments, are critical in preventing recurrent episodes, especially for patients with alcohol-induced pancreatitis. Minimally invasive procedures, such as endoscopic retrograde cholangiopancreatography (ERCP) for biliary pancreatitis and endoscopic necrosectomy for infected necrotizing pancreatitis, have shown efficacy in reducing morbidity and improving survival rates when conservative measures fail. These interventions represent significant advancements over traditional open surgeries, offering reduced recovery times and fewer complications, though they require expertise and careful patient selection. Furthermore, the use of diagnostic tools like CT and MRI has refined prognostic scoring, enabling better prediction of disease severity and informing treatment decisions.

Despite advancements in understanding and treating acute pancreatitis, challenges remain in establishing universally effective protocols due to the variability in patient responses and disease severity. A multidisciplinary, patient-centered approach that combines tailored pharmacological and non-pharmacological strategies is critical in optimizing outcomes. Future research should focus on refining prognostic tools, exploring novel therapeutics, and establishing clear guidelines for early intervention and management of severe cases.

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