



MESENTERIC ISCHEMIA CAUSED BY COCAINE USE: A REVIEW OF PATHOGENESIS, DIAGNOSIS AND TREATMENT

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Abstract

Mesenteric ischemia is a medical condition characterized by a reduction or loss of blood flow to the mesenteric arteries, which supply oxygen and nutrients to the intestines. This decreased blood flow leads to insufficient oxygen (hypoxia) and nutrient supply to the affected areas of the bowel, resulting in intestinal injury, inflammation, and, if untreated, tissue death (infarction). Mesenteric ischemia can occur as a result of arterial occlusion (blockage of blood vessels), venous thrombosis, or non-occlusive ischemia due to low blood pressure, and it is typically associated with severe abdominal pain, nausea, vomiting, and other gastrointestinal symptoms. If left untreated, it can lead to intestinal necrosis, sepsis, and multi-organ failure, requiring urgent medical intervention.

As the prevalence of vascular diseases increases globally, the incidence of mesenteric ischemia may also rise, making it important for both clinicians and public health systems to remain vigilant and proactive in managing this potentially devastating condition. The incidence of mesenteric ischemia is estimated to be around 1-2 cases per 100,000 people annually in the general population. However, this number may be underreported due to misdiagnosis or delayed diagnosis. Cocaine-induced mesenteric ischemia is a condition where the blood supply to the intestines is reduced or blocked due to the vasoconstrictive effects of cocaine. Cocaine causes the mesenteric arteries (which supply blood to the intestines) to constrict, leading to insufficient blood flow (ischemia) and potentially causing damage to the intestinal tissue. This can result in intestinal injury, necrosis (tissue death), and infarction (loss of blood supply), which can lead to bowel perforation, sepsis, and multi-organ failure if left untreated.

This condition is often seen in individuals with chronic cocaine use, though it can also affect those with acute intoxication. The symptoms typically include severe abdominal pain, nausea, vomiting, and signs of shock. Early diagnosis and intervention are crucial for improving outcomes and preventing long-term complications.

KEYWORDS

AMI- Acute Mesenteric Ischemia, CMI- Chronic Mesenteric Ischemia, CTA- CT Angiography, MRA- Magnetic Resonance Angiography, TPN- Total Parenteral Nutrition

INTRODUCTION

Mesenteric ischemia refers to a condition where there is a reduction of blood flow to the mesentery, the tissue that supports and supplies blood to the intestines. This diminished blood supply leads to inadequate oxygen and nutrients reaching the gastrointestinal (GI) organs, potentially resulting in tissue damage or death if not addressed promptly.^[1] The condition can range from mild to life-threatening, depending on the severity and speed at which blood flow is compromised. There are two

primary forms of mesenteric ischemia: acute and chronic. Acute mesenteric ischemia (AMI) is a medical emergency, often occurred by embolism, thrombosis, or other blockages in the area mesenteric arteries. Chronic mesenteric ischemia (CMI), in contrast, typically develops over time due to atherosclerosis, where the arteries supplying the intestines become gradually narrowed.^[2]

Risk factors for mesenteric ischemia include atherosclerosis, heart disease, atrial fibrillation, smoking, and certain medical conditions that affect blood flow or clotting. Symptoms of mesenteric ischemia often present with severe abdominal pain, nausea, vomiting, and bloating making early diagnosis challenging but crucial to prevent serious outcomes such as bowel necrosis.^[3] Mesenteric ischemia requires rapid intervention, including diagnostic imaging, medical therapy, and in some cases, surgical procedures to restore blood flow. The condition is associated with significant morbidity and mortality, underscoring the importance of awareness, early detection, and timely treatment.^[4]

Cocaine-induced mesenteric ischemia is a rare but potentially life-threatening condition caused by the use of cocaine, which can disrupt blood flow to the intestines.^[5] Cocaine is a potent stimulant that exerts various physiological effects, including vasoconstriction, increased blood pressure, and changes in blood clotting. These effects can lead to the narrowing or blockage of the mesenteric arteries, the blood vessels responsible for supplying oxygenated blood to the intestines, resulting in ischemia (reduced blood flow).^[6] In the case of mesenteric ischemia, the lack of adequate blood supply to the intestines leads to tissue injury, and, if left untreated, can cause bowel necrosis, perforation, and even death. Cocaine-induced mesenteric ischemia typically presents with sudden-onset of severe abdominal pain, nausea, vomiting, and sometimes gastrointestinal bleeding, often in individuals who have a history of cocaine use.^[7] This condition is considered as an acute medical emergency, as the effects of cocaine on the vascular system can be rapid and devastating. Cocaine-induced mesenteric ischemia is more commonly seen in young, otherwise healthy individuals without traditional risk factors for ischemic bowel disease, such as atherosclerosis. Treatment may involve supportive care medications to reverse vasoconstriction, and surgical procedures to restore blood flow to the affected bowel tissue.^[8,9] The occurrence of this condition highlights the serious vascular consequences of cocaine abuse, especially in terms of gastrointestinal health.

PREVALENCE OF ASTHMA

According to the World Health Organization (WHO) it does not provide a specific global prevalence rate for mesenteric ischemia.^[10] However, studies indicate that the condition is relatively rare but serious, with an incidence of about 2 to 3 cases per 100,000 people per year in the general population. The prevalence is higher in older adults, particularly those over the age of 60, due to the increased likelihood of conditions like atherosclerosis, atrial fibrillation, and other cardiovascular risk factors.^[11] Mesenteric ischemia can be classified as acute or chronic, with acute cases being more emergent and less common. Chronic mesenteric ischemia, which develops over time due to atherosclerosis, may be underreported because its symptoms can be subtle and may not always result in hospitalization.^[12] Because mesenteric ischemia is a condition that often requires timely diagnosis and intervention, its relatively low prevalence may still have a significant impact on healthcare systems, especially in populations with high rates of risk factors such as cardiovascular diseases and smoking.^[13]

The World Health Organization (WHO) does not provide a specific prevalence rate for cocaine-induced mesenteric ischemia, as this is a rare and relatively under-researched condition. Cocaine-induced mesenteric ischemia is considered an uncommon complication of cocaine use and is not extensively tracked in global health statistics.^[14]

However, it is known that cocaine can cause various vascular complications due to its vasoconstrictive properties, including mesenteric ischemia, but the actual incidence remains difficult to determine due to the relatively low number of reported cases. Most of the data on cocaine-induced mesenteric ischemia comes from case reports and small studies rather than large-scale epidemiological studies.^[15,16]

In general, mesenteric ischemia is a rare condition, and when it is caused by cocaine, it is likely to occur in younger individuals with a history of cocaine use, in overdose or high-dose use. The overall occurrence of cocaine-induced mesenteric ischemia is considered much lower than that of other forms of mesenteric ischemia (such as atherosclerotic or thrombotic causes).^[17]

PATHOGENESIS AND PATHOPHYSIOLOGY OF COCAINE INDUCED MESENTRIC ISCHEMIA

Cocaine-induced mesenteric ischemia occurs due to the vasoconstrictive effects of cocaine on the mesenteric arteries, which supply blood to the intestines. The pathogenesis of this condition is complex and involves a combination of vascular spasm, thrombosis, increased sympathetic tone, and direct endothelial injury.^[18] Here's a detailed explanation of how cocaine causes mesenteric ischemia:

1. Cocaine's Effect on Vascular Tone and Blood Flow

- **Vasoconstriction:** Cocaine is a powerful sympathomimetic drug that inhibits the reuptake of catecholamines (such as norepinephrine, dopamine, and serotonin) at nerve synapses. This results in increased sympathetic nervous system activity. The overactivation of the sympathetic nervous system leads to widespread vasoconstriction, particularly in smaller arteries like the mesenteric arteries. The mesenteric arteries supply blood to the intestines, and when they constrict, blood flow to the intestines is severely restricted, leading to ischemia.^[19]
- **Direct Effect on Smooth Muscle:** Cocaine also has a direct effect on the vascular smooth muscle by promoting calcium influx into the smooth muscle cells, which further exacerbates vasoconstriction. This leads to the narrowing or even complete occlusion of the mesenteric vessels.

2. Endothelial Dysfunction

- **Endothelial Injury:** Cocaine can damage the endothelium (the inner lining of blood vessels), contributing to increased vascular permeability and promoting thrombosis (formation of blood clots). This injury impairs the ability of the vessels to dilate appropriately, further compromising blood flow to the intestines.
- **Inflammation:** Cocaine-induced endothelial dysfunction can also provoke a local inflammatory response in the mesenteric vasculature, contributing to the progression of ischemia and increasing the risk of clot formation (thrombosis) or embolism.^[20]

3. Increased Sympathetic Tone and Vasoconstriction

- **Decreased Mesenteric Blood Flow:** As a consequence of the vasoconstriction, mesenteric blood flow is reduced, and the bowel tissue becomes hypoxic, which can lead to ischemia. In severe cases, this ischemia can progress to bowel infarction (tissue death) if blood flow is not restored.

4. Thrombosis and Embolism

- **Increased Risk of Thrombosis:** Cocaine use is associated with an increased risk of thrombosis (formation of blood clots). The vasoconstriction caused by cocaine may lead to endothelial damage, creating a surface where blood clots can form. This increases the risk of mesenteric artery thrombosis, in which a clot obstructs the artery and further reduces blood flow to the bowel.
- **Embolism:** Cocaine-induced arrhythmias, particularly atrial fibrillation, can increase the risk of embolism. Clots or debris from the heart can travel to the mesenteric arteries, blocking blood flow and contributing to ischemia.^[20]

5. Reduced Oxygen Supply to the Bowel

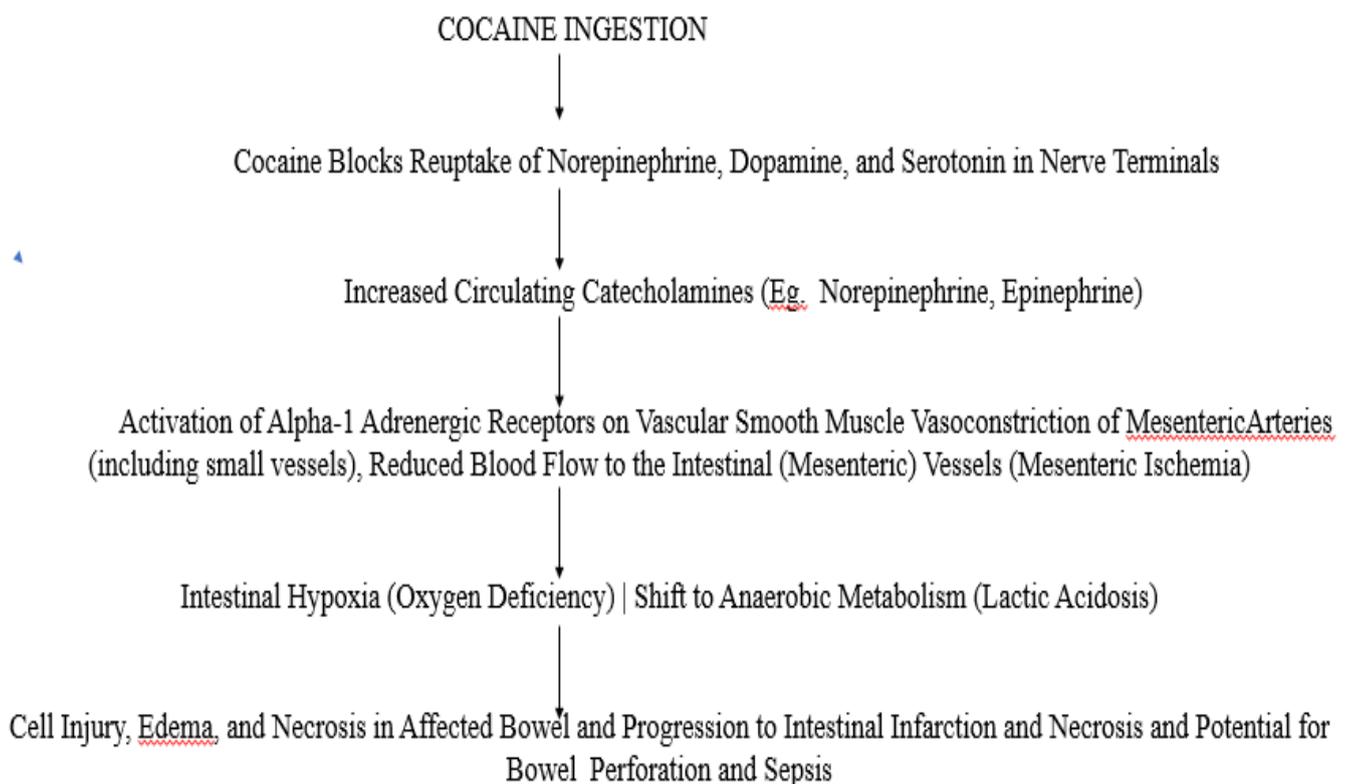
- **Hypoxia and Cellular Injury:** As the blood flow to the intestines decreases, oxygen supply to the intestinal tissue becomes inadequate. The oxygen deprivation leads to tissue hypoxia, which in turn results in cellular injury and lactate accumulation (a byproduct of anaerobic metabolism). If the ischemia persists, bowel cells may undergo necrosis, leading to permanent tissue damage.
- **Metabolic Changes:** Prolonged ischemia results in the production of toxic metabolites like lactate, which can exacerbate the damage to the bowel and lead to systemic acidosis (low blood pH), worsening the clinical picture.

6. Bowel Injury and Necrosis

- **Intestinal Ischemia and Infarction:** The reduction in blood flow can cause the bowel to become progressively more ischemic, leading to intestinal infarction (tissue death) if left untreated. This infarction can progress to perforation, where the dead tissue bursts, releasing intestinal contents into the peritoneal cavity, causing peritonitis (inflammation of the lining of the abdomen) and sepsis (systemic infection).
- **Bowel Dysfunction:** As a result of ischemia, the affected bowel may become non-functional, leading to severe abdominal pain, bloating, and distension. If necrosis develops, the bowel may no longer be able to absorb nutrients, leading to systemic complications like septic shock. ^[21]

7. Autonomic Dysfunction

- **Exacerbation of Vasoconstriction:** The increase in sympathetic tone due to cocaine use not only promotes vasoconstriction but also reduces parasympathetic (vagal) influence on blood vessels. The balance between the sympathetic and parasympathetic systems is disrupted, which further exacerbates vascular spasm and impairs normal bowel motility, exacerbating the ischemia.



DIAGNOSIS OF COCAINE INDUCED MESENTERIC ISCHEMIA

The diagnosis of this condition requires a careful combination of clinical evaluation, imaging studies, and laboratory tests, especially since its symptoms often overlap with other causes of abdominal pain. Here's how it is diagnosed:

1. Clinical Evaluation

- **History:** A critical aspect of diagnosing cocaine-induced mesenteric ischemia is identifying recent cocaine use. The patient may present with:
 - Acute or severe abdominal pain, often disproportionate to physical examination findings.
 - Nausea, vomiting and sometimes diarrhoea.
 - History of cocaine use, particularly if the patient had used large amounts or a history of overdose.
- **Physical Examination:** The abdomen may be mildly tender, but signs of peritonitis (such as rebound tenderness or guarding) may not be present in the early stages. This is why clinical suspicion is vital, especially in individuals with known cocaine use.

2. Imaging Studies

- **CT Angiography (CTA):** The most widely used diagnostic tool. It can show:
 - Mesenteric artery occlusion or narrowing, often caused by vasoconstriction due to cocaine use.
 - Signs of bowel ischemia, such as bowel wall thickening or absence of contrast in the mesenteric vessels.
- **Magnetic Resonance Angiography (MRA):** Another imaging modality to visualize mesenteric artery flow, though CTA is typically preferred in acute settings.
- **Doppler Ultrasound:** This can assess blood flow in the mesenteric arteries but is less sensitive than CTA or MRA in acute cases of ischemia.

In cocaine-induced mesenteric ischemia, CTA or MRA may reveal vascular spasm or reduced blood flow due to the effects of cocaine on the blood vessels, potentially causing embolism or thrombosis in the mesenteric arteries.

3. Laboratory Tests

Several laboratory tests can aid in confirming the diagnosis and assessing the severity of ischemia:

- **Elevated Lactate Levels:** Elevated lactate in the blood is a common marker of tissue hypoxia and ischemia. This is a key indicator of mesenteric ischemia.
- **Complete Blood Count (CBC):** May show an elevated white blood cell count (leukocytosis) due to inflammation or ischemia.
- **Renal Function Tests:** Elevated blood urea nitrogen and creatinine levels may indicate systemic effects from ischemia, such as hypoperfusion or shock.
- **Arterial Blood Gases (ABGs):** These may show metabolic acidosis, a result of anaerobic metabolism due to lack of oxygen in the affected bowel.
- **Cocaine Toxicology Screening:** A urine or blood test for cocaine and its metabolites (like benzoylecgonine) can confirm recent cocaine use, which is crucial in identifying the cause of mesenteric ischemia in this context. ^[25]

4. Electrocardiogram (ECG)

Since cocaine use is associated with increased risk of arrhythmias (such as atrial fibrillation), an ECG may be performed to check for any arrhythmias that could contribute to embolic mesenteric ischemia.

5. Mesenteric Angiography

- Angiography is considered the gold standard for diagnosing mesenteric ischemia, especially if other imaging results are inconclusive or if therapeutic intervention (e.g., clot removal or stenting) is needed.
- This procedure involves the direct visualization of the mesenteric arteries and can help assess the extent of vascular occlusion or narrowing caused by cocaine-induced vasoconstriction.

6. Differential Diagnosis

Cocaine-induced mesenteric ischemia should be differentiated from other causes of acute abdominal pain, including:

- Atherosclerotic mesenteric ischemia (more common in older patients).
- Bowel perforation or infection (e.g., appendicitis, diverticulitis, peritonitis).
- Acute pancreatitis, which may present with similar symptoms.
- Other thromboembolic events that may cause mesenteric ischemia.

Early diagnosis and intervention are critical in preventing severe complications like bowel infarction, necrosis, or perforation, which may occur rapidly in cocaine-induced mesenteric ischemia. ^[26]

MANAGEMENT OF COCAINE INDUCED MESENTERIC ISCHEMIA

Cocaine-induced mesenteric ischemia is a rare but life-threatening condition caused by the vasoconstrictive effects of cocaine on the mesenteric arteries. The condition can cause reduced blood flow to the intestines, leading to ischemia and potentially bowel necrosis if not treated promptly. The management of this condition requires a combination of supportive care, medical interventions, and possibly surgical procedures, depending on the severity of the ischemia.

1. Immediate Supportive Care

- **Hospitalization:** Most patients require hospitalization, often in an intensive care unit (ICU), due to the severity of cocaine-induced mesenteric ischemia.
- **Fluid Resuscitation:** IV fluids (e.g., normal saline or lactated Ringer's) are administered to restore circulatory volume, maintain blood pressure, and prevent shock.
- **Oxygen Therapy:** Supplemental oxygen is provided to ensure adequate oxygenation, especially if there is systemic hypoxia due to bowel ischemia.
- **Pain Management:** Strong analgesics (e.g., opioids) may be necessary to manage severe abdominal pain, but care should be taken to avoid masking worsening symptoms (e.g., peritonitis or bowel perforation).

2. Reversal of Cocaine's Effects

- **Vasodilators:** Since cocaine induces vasoconstriction, the use of vasodilators is a key part of treatment. Medications such as nitroglycerin or nitroprusside may be administered to counteract the vasoconstrictive effects of cocaine, helping to restore blood flow to the mesenteric arteries.
 - Calcium channel blockers (e.g., diltiazem or verapamil) may also be used in some cases to help relax the blood vessels and restore mesenteric circulation.

- Benzodiazepines: Medications like lorazepam or diazepam may be given to help reduce sympathetic stimulation and manage agitation or seizures caused by cocaine use.

3. Anticoagulation Therapy

- Heparin or low-molecular-weight heparin (e.g., enoxaparin) may be initiated in cases where thrombosis (blood clots) is suspected to be contributing to mesenteric ischemia, particularly if embolism or clot formation is secondary to cocaine use. However, this must be closely monitored due to the risk of bleeding, especially in patients with compromised bowel tissue. ^[27]

4. Endovascular Intervention

For patients with severe or persistent mesenteric ischemia, endovascular procedures are often used as a first-line treatment to restore blood flow without the need for open surgery.

- Embolus Removal: If an embolism is present (e.g., from atrial fibrillation or clot formation), catheter-based techniques may be used to remove the embolus.
- Thrombolysis: Tissue plasminogen activator (tPA) or other thrombolytic agents can be administered to dissolve blood clots that are blocking the mesenteric arteries.
- Angioplasty and Stenting: If there is significant narrowing or blockage of the mesenteric arteries, angioplasty (balloon dilation) and stent placement can be performed to restore normal blood flow. ^[28]

5. Surgical Management

In cases of severe ischemia or if there is bowel necrosis, surgical intervention may be required. This is particularly true if endovascular methods are ineffective or if the bowel is at risk of perforating.

- Exploratory Laparotomy: A surgeon may perform a laparotomy to assess the extent of bowel ischemia or necrosis. During surgery, the affected portion of the bowel may need to be resected if necrosis is present.
- Bowel Resection: If significant bowel infarction or necrosis is found, the damaged portion of the intestine is removed to prevent sepsis.
- Restoration of Blood Flow: In rare cases, a mesenteric artery bypass may be performed if the mesenteric arteries are severely occluded or damaged.
- Stoma Creation: If bowel resection is extensive, a temporary or permanent colostomy or ileostomy may be created to allow for healing. ^[29]

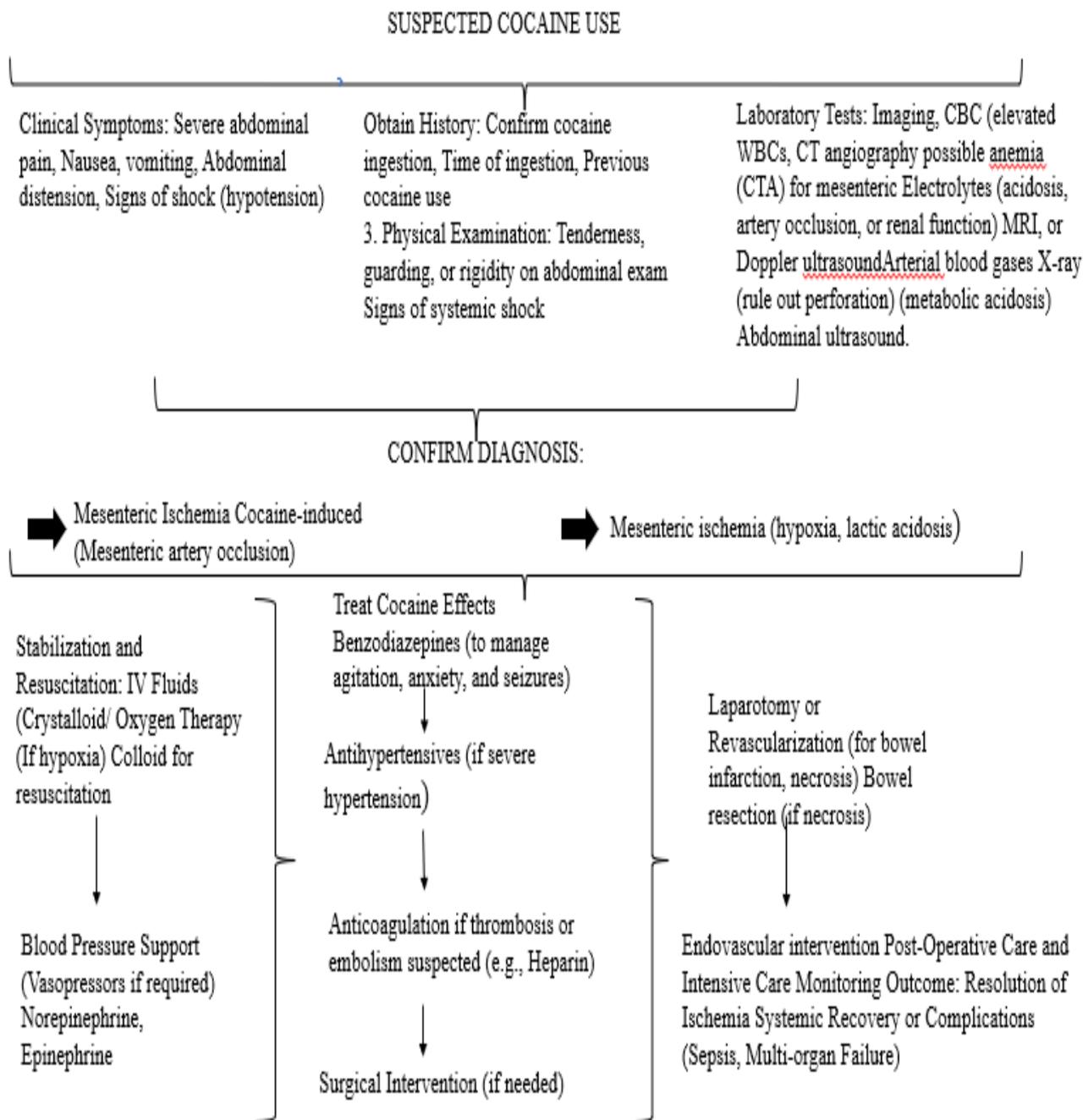
6. Post-Treatment Monitoring and Long-Term Care

- Intensive Monitoring: Patients who undergo surgery or endovascular procedures require intensive monitoring in an ICU setting for signs of complications such as infection, sepsis, or recurrent ischemia.
- Nutritional Support: Patients who have undergone significant bowel resection may require total parenteral nutrition (TPN) or enteral feeding until their bowel function returns.
- Psychiatric Support: Since cocaine use is a substance abuse issue, it is important to provide psychiatric or addiction support to address the underlying drug dependency. Counseling, rehabilitation, or detoxification programs may be recommended to prevent recurrence of cocaine use.

8. Prevention of Recurrence

- Addressing Cocaine Use: Long-term prevention focuses on addressing cocaine addiction through rehabilitation programs, counseling, and possibly medications to manage withdrawal symptoms.
- Management of Risk Factors: Patients may need to manage cardiovascular risk factors (e.g., hypertension, arrhythmias) that could exacerbate mesenteric ischemia. [30]

ALGORITHM



SIGNIFICANCE

The significance of cocaine-induced mesenteric ischemia lies in its potential for life-threatening complications, the challenges associated with its early diagnosis and management, and its growing relevance in the context of rising cocaine abuse worldwide. Early recognition, prompt medical intervention, and a multi-disciplinary approach are essential for improving

outcomes. The significance of this condition has grown with the ongoing global issue of cocaine abuse, and the increasing prevalence of related health complications. Despite its devastating potential, early diagnosis and intervention can significantly improve patient outcomes, particularly when management is multidisciplinary and includes fluid resuscitation, vasopressors, anticoagulation, and, in severe cases, surgical revascularization or bowel resection.

Additionally, enhancing public awareness, improving healthcare provider education, and conducting further research are vital steps toward addressing this serious and often fatal condition.

CONCLUSION

Cocaine-induced mesenteric ischemia is a serious and potentially life-threatening condition that occurs when cocaine's vasoconstrictive effects reduce blood flow to the intestines, leading to ischemia, bowel infarction, and systemic complications. The condition represents a significant challenge due to its rapid progression, often presenting with nonspecific symptoms such as abdominal pain, nausea, and signs of shock, which can delay diagnosis and treatment.

However, challenges remain in terms of recognition, timely diagnosis, and effective treatment, particularly given the condition's subtle onset and the need for advanced imaging and multidisciplinary expertise. Public health initiatives aimed at reducing cocaine use, along with better educational efforts for both healthcare providers and the general public, are essential to decrease the burden of cocaine-induced mesenteric ischemia.

Ultimately, cocaine-induced mesenteric ischemia highlights the significant cardiovascular risks associated with illicit drug use, and its management underscores the importance of prompt, coordinated care to prevent irreversible damage and improve patient survival. Continued research into its pathophysiology, improved diagnostic tools, and treatment strategies are necessary to further optimize outcomes for individuals affected by this severe condition.

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