

CASE REPORT

Pain Management with IV and Oral Ketamine in a Child with Acute on Chronic Pancreatitis: Old Wine in New Bottle—A Case Report

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ABSTRACT

A 13-year-old male child, a known case of chronic pancreatitis with acute exacerbation, presented with severe abdominal pain. The pain was dull aching type associated with burning sensation present all over the abdomen with VAS score–9/10. He was treated with paracetamol, Non-steroidal anti-inflammatory drugs, and opioids. Despite this multimodal analgesia, he had inadequate pain relief. Since the child exhibited both nociceptive and neuropathic elements, ketamine was considered as the analgesic of choice. He was successfully treated with subanesthetic low dose intravenous (IV) ketamine infusion followed by oral ketamine therapy for 15 days till he underwent proposed surgery. We have been unable to find any previous reports of oral ketamine use for this condition.

Keywords: Acute pain, Chronic pancreatitis, Ketamine, Neuropathic pain, Oral administration, Pediatric pain

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INTRODUCTION

Chronic pediatric pain has been an increasingly significant problem known to be common, under-recognized, and under-treated.¹ Main challenges we face in children is, diagnosing the pain and it's severity, as they fail to express. Untreated pain in children incurs a high risk for the subsequent development of pain and psychological disorders later in life.² Acute pancreatitis remains an uncommon cause of abdominal pain during childhood, chronic pancreatitis (CP) even rare. Its prevalence within pediatric hospitals and the community is largely unknown. It is a potentially debilitating disorder as the

pathogenesis of the condition is not fully understood and forms an important cause of morbidity and occasionally mortality in this group.³ We describe an uncommon case of a 13-year-old male child who presented with intractable abdominal pain secondary to chronic pancreatitis for pain management.

CASE REPORT

A 13-year-old male child who was a known case of chronic pancreatitis since past 1 year, presented with acute exacerbation and was admitted under the pediatric surgery unit with a tentative plan for surgery. He was referred to the pain clinic for pain management. The child complained of severe pain in the abdomen for the past 15 days. The pain was gradual in onset, intermittent in nature, diffuse, dull aching type, non-radiating associated with constant burning sensation present all over the abdomen with VAS score: 9/10. The pain was aggravated by food and decreased to some extent with analgesics (Inj. tramadol), curling posture provided some relief. There was no diurnal variation. The pain was affecting his psychological health and disturbing his daily routine. Other symptoms included disturbed sleep, decreased appetite leading to low weight and depressed mood. The child was fully conscious, oriented but was restless and agitated due to pain. He was not able to sit comfortably and kept attaining the curling position. On examination, he was poorly built and severely malnourished with height: 142 cm and weight: 18 kgs. Hemodynamic vital parameters were within normal limits. Abdominal examination showed diffuse tenderness with guarding and rigidity, and other systems were normal. computed tomography (CT) scan showed features suggestive of acute on chronic pancreatitis, mild ascites, left pleural effusion, small left kidney and hepatomegaly. The diagnosis of chronic calcific pancreatitis with atrophic pancreas was confirmed on magnetic resonance imaging (MRI).

MANAGEMENT

The child was treated with oral omeprazole and pancreatic enzymes. For analgesia, he was receiving intravenous (IV) Paracetamol 300 mg thrice daily (TID), IV diclofenac

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1 mg/kg and IV Tramadol 25 mg intermittently, for which he had inadequate pain relief. Since he was on irregular and inadequate analgesic treatment, we replaced with a more potent opioid analgesic—IV fentanyl infusion in the dose of 1 mcg/kg/hr. After this treatment, the child had some relief, but he continued to complain of burning type of pain. Since the child exhibited elements of both nociceptive and neuropathic pain, after thorough deliberations we decided to start the child on IV Ketamine therapy for the pain management as per the guidelines.^{4,5} Initially, a loading dose of 0.25 mg/kg IV ketamine was administered for which the child had 80% pain relief. This was immediately followed by low dose infusion of IV ketamine in the dose of 1.5 mcg/kg/min given for 8 hours via infusion pump under standard monitoring in the operation theatre area. After the infusion, the child was sent to the ward with regular assessment of pain, vitals and psychotropic effects. On assessment VAS score was decreased to 4/10 and vitals remained stable, but the child had intermittent attacks and exacerbation of pain for which rescue analgesic IV Fentanyl 20 mcg was given three times. No psychomimetic effects due to ketamine were noted. The next day, ketamine infusion was again started in the same dose and continued for 8 hours. At the end of infusion on the second-day child had better pain relief with VAS score 1/10 which continued even after stopping it. His mother reported that he had slept well for the first time in two months. Over the next two days, the same dose of infusion was continued for 8 hours after which VAS score was reduced to 0/10. No other rescue analgesic was required. The child was cheerful with a dramatic improvement in his mood which may explain the antidepressant effect of ketamine. No any adverse effects were noted. IV paracetamol 300 mg TID was continued throughout along with ketamine infusion. Since the child was confined to bed for IV ketamine infusion, we decided to switch over from IV to oral ketamine. We used the injectable preparation orally, as separate oral preparation of ketamine is not available and literature supports the substitution of IV preparation for oral use. Oral ketamine in the dose of 10 mg (0.5 mg/kg)^{1,2} mixed with fruit juice was given 8th hourly in the ward for the next 10 days. The child continued to have very good pain relief with a VAS score of 0/10, was able to sleep and eat well. Occasional episodes of lightheadedness were reported by the child, which was neither unpleasant nor discomforting to him but still we tapered the dose to 5 mg 8th hourly. Since the quality of pain relief was not good after decreasing the dose, his mother requested to increase the dose. Hence, we resumed to oral ketamine 10 mg 8th hourly, keeping a watch on the adverse effects. The child was maintained pain-free for 15 days after which he underwent pancreaticojejunostomy uneventfully.

DISCUSSION

Ketamine is a phencyclidine derivative that has been available for over six decades. For many years, it has been used to provide analgesia and anesthesia in battlefield and emergency room settings, not to mention in veterinary medicine. Though its role as an anesthetic agent in the operating room is well known, its use has arguably been on the decline, in part because of its psychotropic and sympathomimetic adverse effects. Nevertheless, a resurgence in its use is now being seen for treating pain in its various forms—acute, chronic, neuropathic and cancer-related pain as well as for addressing treatment-resistant depression.⁶ Pancreatitis is an uncommon condition in a pediatric patient. CP has a complex pathophysiology which includes damage to nociceptive neurons and neuropathic features. Recently, evidence from experimental human pain research has indicated that in many of these patients pain processing in the central nervous system is abnormal and mimics that of neuropathic pain disorders.⁷ Pain treatment for this condition begins with medical management and also there is a role of interventional blocks—Coeliac or splanchnic nerve block in adults.⁷ The pain in acute as well as chronic pancreatitis is often severe and difficult to manage as the pathogenesis of the condition is not fully understood in children. It is poorly responsive to medication in most cases and addiction to pain medication, the excessive number of missed school days and restriction in sports activities are common as seen in our case. Our patient was receiving medical management of pancreatitis. Analgesics like paracetamol, non-steroidal anti-inflammatory drugs and opioids were given for which he did not have much pain relief. The literature showed no evidence of interventions performed in the pediatric age group for chronic pancreatitis. Besides, surgical intervention was being planned. Since the child was suffering from intractable pain with minimal response to opioids and he persistently complained of burning pain which is a typical feature of neuropathic pain, ketamine was considered as the analgesic of choice. As the child was in the acute phase, oral neuropathic drugs would not have been appropriate. IV ketamine bolus followed by infusion was given for rapid onset of action. Once good analgesia was ensured, we considered switching over to the oral route. The rationale for using ketamine in chronic as well as acute pain is different. For chronic pain, ketamine is purported to reverse central sensitization and enhance descending modulatory pathways; hence, the use of higher cumulative dosages and serial infusions are often advocated. Ketamine's analgesic properties in acute pain likely derive from its reversible antagonism of the N-methyl-D-aspartate (NMDA) receptor. It also leads to decreased

levels of several proinflammatory mediators beneficial in the acute phase. Ketamine also acts on a multitude of other non-NMDA pathways that play integral roles in pain and mood regulation, including its effect on μ -opioid receptors, nicotinic, muscarinic cholinergic, γ -aminobutyric acid receptors, the blockade of sodium and potassium channels, activation of high-affinity D2 dopamine receptors and L-type voltage-gated calcium channels.⁴

For oral ketamine, a recommended starting dosage in ketamine naïve patients is 0.5 mg/kg racemic ketamine or 0.25 mg/kg S-ketamine as a single oral dose. The dosage is increased by the same amount if required. For a continuous analgesic effect, it is usually given three to four times daily. The injection fluid can be taken orally. When parenteral ketamine is switched to oral administration, the daily dosage can be kept equal and, depending on clinical effect and/or adverse effects is slowly increased. The pharmacologically active metabolite nor ketamine is believed to contribute to the analgesic effect of oral ketamine.¹ Although the use of ketamine as an analgesic is now generally accepted, the evidence base remains poor. Little formal research has been performed on the efficacy and safety of ketamine in chronic pain management, especially concerning long-term oral administration.²

CONCLUSION

Ketamine can be considered as an alternative analgesic option for acute and chronic pain conditions in children. Oral ketamine can be safely used in managing paediatric pain. We found that ketamine offered an effective and well-tolerated means of pain control in acute pain secondary to chronic pancreatitis. This drug should be

used with caution and the development of potential side effects should be carefully monitored.

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