

AN INTEGRATED APPROACH FOR MANAGEMENT OF IDIOPATHIC RECURRENT ACUTE PANCREATITIS (IRAP) WITH PERSISTENTLY INCREASED SERUM AMYLASE IN SPHINCTER OF ODDI DYSFUNCTION – A CASE REPORT

Soumya MS¹, Swathy S¹, Jwala Jayaram¹, Rajeshwari PN²

1. Final year PG Scholar, Department of Shalya Tantra (Surgery), Amrita School of Ayurveda, Amrita Vishwavidyapeetham, Coimbatore, India.

2. Associate Professor, Department of Shalya Tantra (Surgery), Amrita School of Ayurveda, Amrita Vishwavidyapeetham, Coimbatore, India.

Corresponding author

Dr Rajeshwari P N

drrajeshwariphd@gmail.com, dr.rajeshwaripn@ay.amrita.edu

ABSTRACT

Idiopathic Recurrent Acute Pancreatitis (IRAP) is a clinical entity portraying episodes of acute pancreatitis which occurs more than one occasion after the initial attack. The prevalence of Idiopathic Acute recurrent pancreatitis on acute pancreatitis varied from 10-30% depends on etiological factors. The cardinal symptoms include epigastric pain which may radiates to back, with nausea or vomiting. Careful review of patient's history and appropriate laboratory findings including raised serum amylase or lipase with radiological evidence confirms the diagnosis. The present case report highlights the efficacy of *Ayurvedic* treatment in, reducing the signs and symptoms of IRAP with significant changes in raised serum amylase and lipase. A 13year old girl, known case of Idiopathic Recurrent Acute pancreatitis after Acute pancreatitis management came to opd of Amrita School of Ayurveda with complaints of abdominal pain and nausea. On further evaluation Serum Amylase and Lipase were raised with USG showing bulky and hypoechoic uncinated process and head of pancreas. She was managed with internal medications like *Yaṣṭimadhu kṣīra pāka* (Licorice milk) and *Avipatti curṇam* for four months, by considering the treatment principles for *Amla Pitta* (Acid Reflux). In this case the combination of *Yaṣṭimadhu kṣīra pāka* and *Avipatti curṇam*, has shown a remarkable recovery from clinical symptoms and reduction in serum amylase and lipase. Acute Pancreatitis symptoms are having high morbidity and mortality rates with Multi organ dysfunction and hence this case report provides a new path to the clinicians and researchers for understanding and finding the medicinal option for the treatment of this challenging disorder. This case report indicates the potential of *Ayurveda* for safe and effective management of Post IRAP symptoms.

KEYWORDS

Idiopathic Recurrent Acute Pancreatitis (IRAP), *Yaṣṭimadhukṣīrapāka*, *Avipatti curṇam*, *Amlapitta*, Case Report

INTRODUCTION

Pancreatitis is an uncommon disease regulated by inflammation of the pancreas. It is a condition that proceeds abruptly and may be quite severe, whereas patients usually have a complete recovery from an acute attack. Pancreatic inflammatory disease may be classified as Acute Pancreatitis and Chronic Pancreatitis. Acute pancreatitis refers to an acute inflammatory process of the pancreas, usually accompanied by abdominal pain, elevations of serum pancreatic enzymes and imaging evidence of pancreatic and peripancreatic inflammation. This syndrome is generally a distinct episode, which may cause vacillating degrees of injury to the pancreas, also adjacent and distant organs. Acute recurrent pancreatitis on acute pancreatitis varied from 10-30% depends on etiological factors¹. The cardinal symptoms include epigastric pain which may radiates to back, with nausea or vomiting. As the known causes of AP are usually taken care of, RAP commonly occurs in the idiopathic group, which composes 20%– 25% of cases of AP². Idiopathic RAP (IRAP) is the failure to reveal the distinct etiology of pancreatitis in contempt of thorough history and conventional laboratory investigations. Despite, there is no unanimity on the duration of an “acute attack”, as pancreatic parenchymal changes being oedema and fluid collection may endure after the normalization of pancreatic enzymes and determination of patient’s symptoms³. The causes of IRAP can being together into mechanical, toxic– metabolic, anatomical, and miscellaneous. Sphincter of Oddi dysfunction is included under Mechanical causes and constitutes about 1/3 of all cases of IRAP. The mechanism of sphincter of Oddi dysfunction is not completely known but, in theory, when an individual has SOD, the sphincter goes into "spasm", causing temporary back-up of biliary and pancreatic juices, resulting in attacks of abdominal pain. The main cause of SOD dysfunction is papillary stenosis. There is a backup of bile and pancreatic juices, when the hole is overly tight, can result in abdominal pain and/or jaundice. Likewise, blockage to the pancreatic orifice can cause pancreatic pain or attacks of pancreatitis. The main symptom of SOD is abdominal pain and is mainly felt in mid- or right-upper abdomen. Other symptoms include Nausea, Vomiting, Fever, Chills and Diarrhoea.

In Ayurvēda, the condition was assessed based on the dōṣa concept as the detailed disease description is unavailable. Among three dōṣa (Bodily humors), pitta is responsible for digestion, metabolism, production of heat and other forms of energy. Pācaka pitta (subtype of pitta) described by ācārya can be compared with the wide variety of digestive secretions viz. Trypsin, Chymotrypsin, Carboxypolypeptidase, Pancreatic amylase, Pancreatic lipase, Cholesterol esterase, Phospholipase, Maltase, Pepsin, Gelatinase, Urase, bile, pancreatic juice and intestinal secretions⁴. It performs its function with the help of samāna vāyu, and klēdaka kapha. In sphincter of Oddi dysfunction when samāna vāyu gets vitiated by nidāna, simultaneously khavaiguṇya takes place due to mārḡavarōdha. Which in turn vitiates the pācaka pitta where tīkṣṇa and uṣṇa guṇa of pitta are aggravated because of the involvement of tēja and ap mahābhūta⁵. This heat originated through pancreatic secretion leads some inflammatory responses. It can be assumed that amylase and lipase are the enzymes which are liable to increase in double the quantity, means destruction of pancreatic cells. samāna vāyu, pācaka pitta and klēdaka kapha may involve in sthānasamśraya at āmāśaya also in pittadharā kala (ḡrahaṇī) where simultaneously khavaiguṇya takes place⁶. These changes produce the symptoms of pitta-kapha āvruta vāta like, arōcaka, chardi, avipāka, klama, utklēśa, amlōdgāra, gaurava and hrtkaṇṭha. According to Shrikanta datta commendator of Susruta samhita, Amlapitta is a disease mainly due to vitiation of Pitta (pācaka) but Kapha (klēdaka) and vāta (samāna) are associated. Hence Amlapitta is the disease condition which we can co relate to pitta-kapha āvruta vāta⁷. The understanding of disease pathology as per Ayurveda was the steppingstone for the management. The integrated approach was essential initially to know the prognosis of the disease condition.

PATIENT INFORMATION

On September 4, 2019, a 13-year-old girl, known case of Idiopathic Recurrent Acute pancreatitis after Acute pancreatitis management came to OPD of Amrita School of Ayurveda with complaints of abdominal pain and nausea. History revealed that, on 28/07/2019 she had developed pain in abdomen and nausea, and the pain relived on bending forwards. She was taken to an allopathic hospital and took symptomatic treatment. However, the symptoms persisted, hence she was referred to higher center. There she was diagnosed as Acute pancreatitis with increased serum amylase and serum lipase level. She was admitted and treated with Enzyme replacement therapy. The Serum amylase and Lipase reduced but the abdominal pain, nausea persisted with occasional episodes of vomiting. As these symptoms were not reducing with the given medicines, on 04/09/2019 she came to our hospital for the alternative remedy. Patient has the similar episode of Acute pancreatitis occurred four years before and were managed symptomatically. No evidence of familial history and she is with optimum growth & developmental milestones. Immunized as per the schedule with no relevant family history to the present illness.

CLINICAL FINDINGS

Systemic Examination-

- Central nervous system- child was conscious and oriented.
 1. Higher Mental Function: INTACT
 2. Motor and Sensory system: NAD
- Respiratory system- Normal breath sounds heard and chest was clear.
- Cardiovascular system- Heart was clinically normal.
- Gastrointestinal system-
 1. Abdomen – Soft
 2. Distension – Absent
 3. Guarding – Present on epigastric region.
 4. Tenderness – Present on epigastric region.
 5. Abdominal mass- No palpable abdominal mass.
 6. Organomegaly – Absent
 7. Evidence of free fluid- Absent
 8. Neurological deficits – Nothing detected.
- Musculoskeletal system – NAD
- Genitourinary system – NAD

Specific examination: Examination of Epigastric and Lt hypochondrium region showed, Pain and tenderness. Muscle rigidity is slightly present over these quadrants of abdomen

TIMELINE

29/07/2019

Onset of symptoms
(raised *S.amylase*, *S. lipase*)

04/9/2019 (*S.amylase* in normal range)

06/01/2020

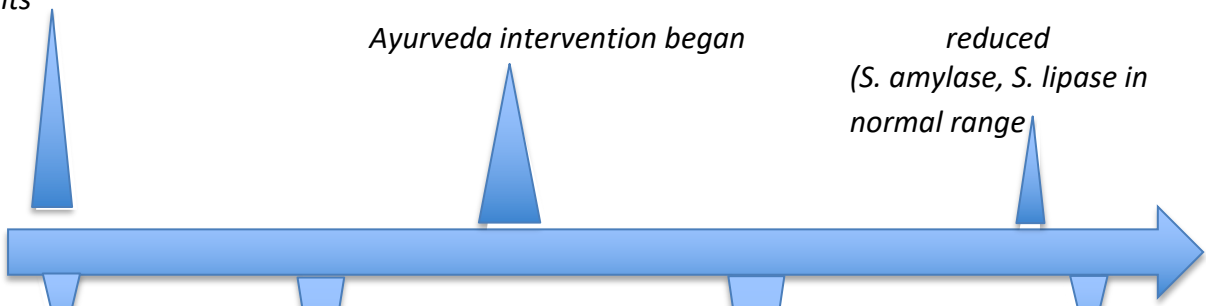
Treated symptomatically
complaints

abdominal pain, nausea persists

chief

Ayurveda intervention began

reduced
(*S. amylase*, *S. lipase* in
normal range)



01/08/2019

Diagnosed with USG

03/08/2019

Not responding to the treatment
S. amylase raised –
referred to specialty center
Allopathy treatment started

21/11/2019

chief complaints
began to reduce
S. amylase, *S. lipase*
in normal range

30/01/2020

USG showed
normal pancreas
without
calcification

DIAGNOSTIC ASSESSMENT

An abdominal ultrasound was performed on her initial presentation to her local hospital showed bulky head of pancreas & features of acute Pancreatitis. There were no calculi in Gallbladder, Common bile duct and peripancreatic fluid collection. Laboratory investigation showed raised *S. amylase* & *S. lipase*. Laboratory investigations drawn on arrival at the tertiary hospital were significant with raised Amylase & Lipase, but CBC, LFT, RFT, *S. electrolytes*, Urine analysis remained within normal range. Ultrasonography impression marked elevation of Amylase (265.0U/L) & Lipase (489.7U/L) confirmed the diagnosis of Acute pancreatitis. The patient had a history of two episodes in past 4years and no specific aetiology was found hence, it was classified under idiopathic recurrent acute pancreatitis. Ayurveda diagnostic tool was not adopted to diagnose the condition.

THERAPEUTIC INTERVENTION

The patient was managed conservatively with enema and followed by administration of Laxopeg to relieve constipation. Nil per oral was maintained supported with IV fluids in the Tertiary hospital. She was improved with this treatment in 10days and started a soft diet without many symptoms. She patient was stable hemodynamically at the time of discharge. The dischargemedication includes Cap Creon 10000 U, 1TID with food, Tab Zincovit 1 OD, Cap Laxopeg 1daily with water, Tab Udiliv 300 g 1-0-1. These medications were prescribed for one month. Serum amylase and lipase levels dropped to 96 IU/L and 178 IU/L, respectively, after 1month of intake of medicines. But the symptoms such as abdominal pain and nausea persists, and she seeks supportive treatment from Ayurveda. Initially

she was administered with Yaṣṭimadhu kṣīrapāka (Liquorice milk decoction) 50ml morning on empty stomach, Avipathi cūrna ½ tsp twice daily before food with ½ glass warm water for 7days and continued for 2months when patient began to respond to the treatment. During the Ayurveda interventions Cap Creon 10000 U was continued to complete its 2-month course as advised by consulting gastroenterologists. Other medications were withdrawn from the schedule. Ayurveda medicine were selected considering the treatment of principles of Amla pitta and aruci and these are easily dispersible and gives maximum benefit to the patients in short span of time. Yaṣṭimadhu kṣīrapāka reduces acid reflux symptoms and provides nutritive benefits to the patient where as Avipathi cūrna improves taste in mouth.

FOLLOW-UP AND OUTCOMES

Patient was observed after 7days to know the improvements and adverse effects. In the first follow up the nausea reduced and mild improvement in the abdominal pain was observed. Patient was comfortable and was able to take soft foods without the episodes of nausea and vomiting. The medicines were continued for period of 3weeks and looked for S. amylase and S. lipase. They remained 98 IU/L & 39.3 IU/L, respectively. Again, medicines were continued for 1more month & S. amylase & S. lipase remained 95 IU/L & 43.9 IU/L, respectively. At the end of 2months patient was completely relieved with signs and symptoms. She was advised to stop the medication and observe for the relapse of symptoms. But there was not much relapse of symptoms except few episodes of constipation occasionally. On abdominal palpation the tenderness over epigastric region was completely relieved. After 2months of follow up USG was done, and it showed normal size and echo pattern of pancreas without calcification. The patient has maintained her health and had not experienced a recurrence of acute in past 9months.

DISCUSSION

Ayurvedic treatment principles incorporated and prioritized by understating the pathogenesis in management of IRAP, put forward an effective strategy for treating the disease without any untoward side effects in a short time. The results after treatment shows reduction in symptoms with normal texture of pancreas without calcifications in ultrasonography. Ailment was initially treated with allopathic management and the symptoms not subsided with the same were effectively managed later with Ayurvedic formulations.

Idiopathic Recurrent Acute pancreatitis (IRAP) among children is mainly diagnosed with most common gastrointestinal complaints like abdominal pain and nausea. In this presenting case, IRAP was clinically diagnosed with abdominal pain and nausea with a supportive evidence of increased S.Amylase and S.lipase level along with an abnormal abdominal USG . In IRAP, recurrent repeated inflammatory responses may occur with the involvement of Sphincter of Oddi Dysfunction with a doubled level of S.Amylase and S.Lipase, which in turn usually produces the symptoms of *pitta-kapha āvruta vāta* like *arōcaka* (nausea), *chardi* (vomiting), *avipāka* (indigestion), *amlōdgāra* (belching) and *ruja* (abdominal pain). Hence *amlapitta is having similar features, its treatment principles* can reduce the symptoms that results in brisky recovery of clinical symptoms in IRAP

According to *bhāvaprakāśā*, *Yasthimadhu* is a *pittaśāmaka* drug (pacifying *Pitta*). In *Amlapitta*, it can be used effectively administered due to the *dāha śāmaka* (pacifying burning sensation) and *Pitta śāmaka* properties of *Yasthimadhu*. *Yaṣṭimadhu* pacifies aggravated *vāta* by the integrity of its *guru* (heavy), *snigdha* (unctuous) and *madhura* (sweet) qualities⁸. *Yaṣṭimadhu kṣīra*

pāka also found to be effective in reducing epigastric pain due to its *Pitta- vāta śāmaka* property⁹. It pacifies the *pitta* dosha by the virtue of its *madhura* (sweet) and *śīta* (cold) qualities. Due to its *Pitta- vāta śāmaka* property, it could work in *samprāpti vighaṭṭana* of *Amlapitta*.

Glycyrrhizin, a main active component in this *ksheera paka* by the activation of NF-kappaB and STAT-3, reduces the development of acute inflammation. *Yaṣṭimadhu kṣīra pākam* has been specifically indicated in conditions such as ulcer, inflammation, abdominal pain, poison, nausea, vomiting, thirst, tiredness, and diminution of tissues. Glycyrrhizic acid molecule in the extract is the cause of sweetener activity in *Yaṣṭimadhu kṣīra pāka*. During its hydrolysis, 18-beta-glycyrrhetic acid is released, which is responsible for anti-inflammatory, antispasmodic, and cytoprotective activity, also it regulates the exocrine functions of pancreas. Glycyrrhizin, a triterpenoid saponin in *Yaṣṭimadhu kṣīra pāka*, is found to be decreasing production of serum amylase and lipase, which are the important mediators in IRAP. The drug *Yaṣṭimadhu kṣīra pāka* prevented the damage of the pancreatic cells which could be caused by the excessive enzyme secretion and thus, it provided a good pancreatic echopattern.

Avipatti curṇam acts mainly by its *dīpana* (improving appetite), *pācana* (improving digestion) and *Sara Guna* (stool loosening property), which normalizes the vitiated *Pitta* and eliminates the excess *Pitta* (bile/acid) from the body by its laxative action. Research evidences shows that the ingredients of *Avipatti curṇam* possess significant gastroprotective and antisecretory activity. Other cytoprotective effects of *marīca* (*Piper nigrum*), *pippalī* (*Piper longum*), *harītakī* (*Terminalia chebula*) can also positively acts on the gastric mucosa. *śuṅṭi* (*Zingiber officinale*) decreases the gastric secretion, increases the mucosal resistance and potentiates the defensive factors of the gastric mucosa. *Lavanga* helps in maintaining the basal gastric mucosal blood flow and it increases the mucus secretion¹⁰. *Avipatti curṇam* also helps in correcting the *agni māndhyam* at *kōṣṭha* and *dhātu* level thereby brings the *samāna vāyu* to the *prakruta avastha*¹¹. The *prakruta samāna vāyu* helps in reducing the spasmodic pain and normalize the metabolism. *Avipatti curṇam* contains drugs with *uṣṇa vīrya*, *kaṭu vipāka* and does the *rasa dhatvagni dīpana*. Which in turn reduces the level of increased serum amylase and lipase. Also the drugs in *Avipatti curṇam* helps in the *klēda śōṣaṇa* and *karṣaṇa* of *mēdō dhātu* thereby helping in relieved the symptoms of *amlapitta*¹². Thus overall effect of *Yaṣṭimadhu kṣīra pāka* and *Avipatti curṇam* are found to be effective in this case of IRAP with Sphincter of Oddi Dysfunction

The studies have shown that active principles in *Yaṣṭimadhu* decrease the swelling of mucous membrane in inflammatory gastric conditions. Pharmacological studies also revealed about the action of the ingredients of *Avipatti curṇam* exhibit antiulcer properties with *harītakī*, *marīca* and *pippalī* exhibits cytoprotective action on the gastric mucosa. *śuṅṭi* decreases the gastric secretion, increases the mucosal resistance, and potentiates the defensive factors of the gastric mucosa¹³. The integrated approach in this case was maintained throughout the observation as enzymatic replacement therapy cannot be discontinued/ stopped without completing its course and focused on prevailing associated symptoms with Ayurveda medicines. Thus, the judicious selection of these drugs resulted in alleviation and complete cure of symptoms.

PATIENT'S PERSPECTIVE

I was anxious and had a dilemma to begin with Ayurveda treatments. We were aware with the disease, ongoing medication, and child's health status. Abdominal pain and nausea were disturbing to the child than episodes of constipation and Vomiting. Hence, we wanted a supportive care. Consulting doctor assured to take medicine for a week and update the prognosis. Periodical monitoring and discussion related to relief of symptoms in terms of Severe, moderate, and mild increased the confidence among the family members. As S. amylase and S. lipase remained within

normal limits during treatment gained the confidence to complete the course of treatment. Am explained about the treatment modalities, complications and its documentation for Publication.

LEARNING POINTS/TAKE HOME MESSAGES 3-5 bullet points

- Understanding of the disease as per Ayurveda concepts and contemporary system of medicine helps us to plan the treatment than just considering the Diagnosis already made.
- Selection of suitable medicine and dosage forms helps to achieve maximum benefit to the patient.
- Short follow ups and repeating the necessary laboratory investigations helps to assess the prognosis
- Treating doctor should be aware of ongoing medications their merits, demerits, the early, delayed complications of the disease and should be explained to the patient/caretaker.

INFORMED CONSENT

Informed consent was obtained from the patient for publication of this case report and the document has been made available for examination by the editors.

AUTHOR CONTRIBUTIONS

Soumya M S - Prepared the case report coordinating with parents of the patient

Swathy. S - Collected and Documented the previous treatment details, laboratory, USG reports and documented them in a chronological order

Jwala Jayaram - Literary work related to the subject is referred, analysed, and discussed with the consultant

Rajeshwari PN - Doctor who treated the case and summarised the case report

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CONFLICT OF INTEREST

NIL

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