Infantile Hypertrophic Pyloric Stenosis: Clinical, Biochemical, Radiologic Findings and Treatment: Review

İnfantil Hipertrofik Pilor Stenozu: Klinik, Biyokimyasal, Radyolojik Bulgular ve Tedavi

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ABSTRACT Infantile hypertrophic pyloric stenosis is a progressive gastric outlet obstruction, characterized with non-bilious projectile vomiting. In addition to high levels of gastrin, prostaglandin E2, prostaglandin F2α and several growth factors; various factors such as decreased levels of vasoactive intestinal polypeptide, neuropeptide Y, nitric oxide synthase and decreased count of enteric neuron supporting cells and Cajal cells in pyloric muscle are blamed in the etiology of infantile hypertrophic pyloric stenosis. Besides, the incidence of the disease has seasonal changes thus the environmental factors thought to have effect on etiology. Although the etiology is still unclear, the pyloric muscle thickens abnormally in time and causes the obstruction of gastric outlet. Depending on the duration of symptoms, dehydration and hypokalemic hypochloremic metabolic alkalosis may occur. A careful physical examination and if necessary ultrasonography are usually enough for diagnosis. Improving the fluid and electrolyte balance of the infant during the preoperative period is important. In the recent years, the patients with infantile hypertrophic pyloric stenosis have been reported to be referred earlier to the hospitals thus the metabolic disorders and dehydration are less encountered. Non-operative modalities such as atropine treatment and balloon dilatation of pylorus are rarely implemented. In modern era, the standardized treatment procedure for infantile hypertrophic pyloric stenosis is pyloromyotomy. Pyloromyotomy can be performed via laparoscopic or open surgical procedures. Oral intake of the patients can be started at postoperative 4 hours, full oral intake can be provided within 24 hours and patient can be discharged subsequently. The most severe complication due to pyloromyotomy is mucosal perforation of the duodenum. Bleeding, wound infection and insufficient pyloromyotomy are uncommon complications and the postoperative course is perfect.

Key Words: Pyloric stenosis; vomiting; hypokalemia; alkalosis; child

ÖZET İnfantil hipertrofik pilor stenozu, safrasız projektil kusma ile karakterize, progresif bir mide çıkışı obstrüksiyonudur. Gastrin, prostaglandin E2, prostaglandin F2α, bazı büyüme faktörlerinin yüksek olması yanında, vazoaktif intestinal polipeptid, nöropeptid Y, nitrik oksit sentaz seviyelerinin düşük olması, pilor kasında enterik sinir destek hücrelerinin azlığı ve Cajal hücrelerinin azlığı gibi faktörler etyolojide suçlanmaktadır. Mevsimsel olarak görülme sıklığının değişmesi nedeniyle, çevresel faktörlerin de etyolojide etkili olduğu düşünülmektedir. Etyolojisi halen tam bilinmemekle birlikte, pilor kası anormal bir şekilde giderek kalınlaşır ve mide çıkışında obstrüksiyona yol açar. Semptomların süresine bağlı olarak dehidratasyon ve hipokalemik, hipokloremik metabolik alkaloz gelişebilir. Dikkatli bir fizik muayene ve gerektiğinde ultrasonografi tanı için yeterlidir. Preoperatif dönemde bebeğin sıvı-elektrolit dengesinin sağlanması önemlidir. Son yıllarda infantil hipertrofik pilor stenozlu bebeklerin daha erken hastaneye getirildikleri, bu nedenle de dehidratasyon ve metabolik anormalliklerin daha az görüldüğü bildirilmektedir. Tedavide atropin ve balon kateter ile pilorun dilatasyonu gibi nonoperatif yöntemler nadiren kullanılmaktadır. Günümüzde infantil hipertrofik pilor stenozunda standart tedavi şekli piloromiyotomidir. Piloromiyotomi, açık veya laparoskopik cerrahiyle uygulanabilir. Hasta operasyondan 4 saat sonra oral beslenmeye başlanıp, 24 saat içerisinde oral tam beslenmeye geçilip, taburcu edilebilir. Operasyona bağlı en ciddi komplikasyon duodenal mukozal perforasyondur. Yara yerinde kanama, infeksiyon, yetersiz piloromyotomi gibi komplikasyonlar nadir görülür ve hastalığın postoperatif seyri mükemmeldir.

Anahtar Kelimeler: Pilor stenozu; kusma; hipokalemi; alkaloz; çocuk

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Infantile hypertrophic pyloric stenosis (IHPS) is the most common cause of gastric outlet obstruction among the children, characterized by elongation and narrowing of pyloric canal due to the hypertrophy of pyloric muscle. In 1717, Blair reported the pyloric stenosis as an autopsy finding for the first time. Until Harald Hirschsprung reported 2 cases in 1888, IHPS had not been considered as a real disease. Formerly, in order to release pyloric muscle spasm, gastric lavage, electrical stimulation, dietary and drug treatments had been used. During this period gastroenterostomy which was performed as a desperate remedy, had a high mortality rate up to 50 percentages.[1]

In 1907, Henry Dufour and Pierre Fredet defined the surgical correction including splitting of pyloric muscle until submucosa with transverse closure of the muscle.[1,2] In 1910, Fredet and Guillemot reported the clinical signs of pyloric stenosis enclosing pyloric tumor, increased gastric peristalsis, projectile vomiting and weight loss, as well as, the high frequency of the pyloric stenosis in boys. Additionally they recommended reducing oral intake, gastric lavage and atropine usage for the initial treatment, and suggested surgery for refractory disease.[1]

In 1912, Conrad Ramstedt reported that there was no need to close pyloric muscle after splitting of hypertrophic pyloric muscle until submucosa. "Ramstedt" operation had been commonly accepted in USA and mortality rate had been reported as 7.1% during 1920s. Better understanding of fluid and electrolyte imbalance related disorders among these patients had decreased the mortality rate below 1% during 1950s.[1]

EPIDEMIOLOGY

The incidence of IHPS is 1.5 to 4 per 1000 live births.[2] In a recent study of Pedersen et al. IHPS incidence in 7 region of Europe had been evaluated between 1980 and 2002 and found 0.86 to 3.96 per 1000 live births.[3] Although IHPS is a more common disease among western countries, the incidence has been reported to decrease gradually in recent years.[4] In this study, mothers under the age of 20 have been reported to have 40% more risk of having a child with IHPS than the older ones. Additionally breast feeding infants have been reported to have lower risk of IHPS.[5] A recently published study has indicated that IHPS risk 4.6-folds higher among bottle-feeding infants.[6]

While most of the infants with IHPS are term, 11% are preterm. IHPS is 4 folds more common in boys than girls. Familial IHPS cases have been reported and heredity is supposed to be polygenic.[2,4]

Seasonal factors are also believed to be effective on the development of IHPS. The first study on this topic has been conducted by Kwok et al. and they have found the incidence of IHPS is highest between April and May, October and November.[7] Additionally, a recent study from our country has indicated that IHPS incidence in terms of seasonal distribution is the highest during spring and autumn, thus, they have suggested that some seasonally changing environmental factors may be effective on the pathophysiology of disease.[8]

ETIOLOGY

The pylorus has a high-pressure zone that relaxes with the peristalsis of antrum and contracts as a response to duodenal stimulation thus prevents regurgitation of duodenal contents back to stomach. Pyloric sphincter works under the control of some kind of hormones such as gastrin, cholecystokinin, and secretin. Today, etiology of IHPS is still unclear. Formerly, the reason of pyloric hypertrophy was thought to be due to high gastrin levels, subsequent studies suggested that hypergastrinemia and high acidity of stomach were developed as a result of gastric outlet obstruction.[9] Increased levels of prostaglandins E2 and F2α in IHPS which effect muscle contraction are also suggested to be secondary to increased acid secretion.[2,9]

Inability of pyloric muscle relaxation is supposed to be effective on IHPS development. The levels of vasoactive intestinal polypeptide and neuropeptide Y, which are responsible from pep-

tidergic innervation, as well as, nitric oxide (NO) synthase which produces the nitrergic innervations mediator NO that all have relaxation effect on pyloric muscle, are found to be decreased in patients with IHPS.[10,11] Also expression of neural cell adhesion molecule that has an important role in the initial conduct between neural and muscle cells, has been found significantly low in IHPS.[2,9]

Nerve supporting cells of enteric neuronal system between hypertrophied circular and longitudinal muscle fibers of pylorus are absent or extremely rare. The decrease of neuron supporting cells may also be due to absence of or decreased of peptidergic, nitrergic, cholinergic and adrenergic neural fibers. Interstitial cells of Cajal (ICC), generates a network among all gastrointestinal tissues. ICC is pacemaker of gastrointestinal smooth muscles, provides effective distribution of electrical activities and mediates neurotransmission. Furthermore, ICC helps inhibitory neurotransmission by producing NO. Absence or scarcity of ICC within IHPS resulting in abnormal motility, secondary to decrease in slow wave occurrence, has been blamed.[9,12,13]

Increase of type-I procollagen synthesis within circular muscle fibers and connective tissue septa between fibers has been demonstrated in IHPS and this composition forms the characteristic "firm" structure of pyloric tumor. Electron microscope studies engendered the division of IHPS into two groups as primarily myogenic and predominantly neurogenic types. Degenerative/regressive changes of hypertrophied pyloric smooth muscle cells have been determined in myogenic type.[14] Advancement of molecular biology in the recent years has provided the demonstration of various increased growth factors in IHPS such as insulin-like growth factor-I, platelet-derivated growth factor-BB and transforming growth factor-β. Growth factors have been thought to be responsible from smooth muscle hypertrophy.[9,15,16]

Some kind of environmental factors such as putting to sleep the infant in prone position, Helicobacter pylori infection, maternal smoking, and usage of erythromycin which is motilin agonist have been blamed in the etiology of IHPS.[2,4,5]

PATHOLOGY

Muscular tunica of stomach is composed of muscle fibers organized in three different directions. Muscle fibers are distributed longitudinal in peripheral layer, circular in middle and oblique in the inner layer. Circular muscle layer in pyloric region thickens and forms pyloric sphincter. This muscle complex becomes hypertrophied in IHPS and causes luminal obstruction. By the time, in addition to muscle hypertrophy, submucosal edema and lymphocyte infiltration causes more narrowing of pyloric channel.[9,13]

CLINICAL PRESENTATION

Clinical signs of IHPS are related to the duration of symptoms. The most evident symptom in IHPS is vomiting. In a study conducted by Schärli et al. on 1215 patients with IHPS, they have revealed the initiation of vomiting after delivery in 20%, 1 to 2 weeks of age in 60% and after 4 weeks of age in 20% of the patients.[17,18] Vomiting is defined as "projectile", forced and non-bilious. Bloody vomiting may be encountered due to esophagitis or gastritis development.[2] Vomiting is usually shortly after feeding and the infant is persistently hungry. Bilious vomiting is rare and caused by transient relaxation of pylorus during vomiting. This situation may cause diagnostic faults during upper gastrointestinal contrast studies (UGI). Piroutek et al. have reported that 1.4% of infants with IHPS have bilious emesis.[19]

Continuous vomiting of gastric content in IHPS causes dehydration resulting in urine decrease and constipation. Delay in diagnosis deepens malnutrition of infant and causes lethargy. Jaundice is encountered in 2-5% of infants with IHPS, and characterized with indirect hyperbilirubinemia due to glucuronyl transferase deficiency.[2,18] Severe metabolic alkalosis caused by vomiting in IHPS may result in apnea-like events.[20] During postoperative course sufficient calorie intake increases the enzyme activity and jaundice improves.[2,18]

LABORATORY FINDINGS

Continuous vomiting of gastric content in IHPS results in dehydration and metabolic disorders. Gastric fluid of infant includes 60-90 mEq/L of sodium, 100-130 mEq/L of chloride and 10-15 mEq/L of potassium. Prolonged vomiting causes electrolyte loss, which is rich from hydrogen, chloride and poor from sodium and potassium. As a result, hypochloremic metabolic alkalosis develops. Renal compensation mechanisms start as a response to metabolic alkalosis. Renal tubules excrete sodium and potassium to ensure the maintenance of hydrogen ions within the body. As the vomiting goes on, hypovolemia activates renin-angiotensin system resulting in aldosterone secretion. Aldosterone provides sodium and water absorption through renal tubules, stimulates potassium and hydrogen excretion. Amount of chloride is also decreased via gastric fluid loss resulting in bicarbonate absorption from renal tubules with sodium and this situation deepens metabolic alkalosis. As a result, hypochloremic hypokalemic metabolic alkalosis emerges. When hypokalemia is increased, renal tubules tend to keep potassium and excrete hydrogen ion from renal tubules. Thus, development of paradoxical aciduria is an indicator of deepened hypokalemia in an infant with IHPS. In case of delayed diagnosis, hypoglycemia and hypoalbuminemia may also be encountered.[21,22]

DIAGNOSIS

Infants having weight loss with non-bilious projectile vomiting should be considered for IHPS. On physical examination abdominal distention and gastric peristaltic waves due to gastric outlet obstruction may be visible on left upper quadrant (Figure 1). Palpation of mobile ovoid mass called "the olive" on the epigastrium or right upper quadrant may solely enough for the diagnosis of IHPS. A careful examination may be sufficient for diagnosis in 75% of the patients.[2,23] In cases that the mass is not palpable, radiologic studies should be done. Over feeding vomiting, gastroesophageal reflux, antral web, pyloric duplication, ectopic tissue in pylorus, external pressure to stomach, increased intracranial pressure and adrenogenital syndromes should be considered in differential diagnosis.[2]

A plain abdominal X-ray demonstrates a large gastric gas image (Figure 2). If the olive is not palpated, the most sensitive test is ultrasonography (US). "Target sign" or "bull's eye sign" are typical demonstrative signs for hypertrophied pylorus in transverse sections on US examination. Diagnostic criteria for IHPS on US are; pyloric muscle thickness ≥4 mm, pyloric channel length ≥16 mm and

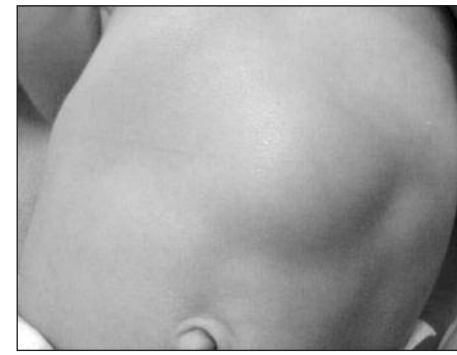

FIGURE 1: Gastric peristaltic waves moving from left to right side of abdomen in an infant with IHPS.

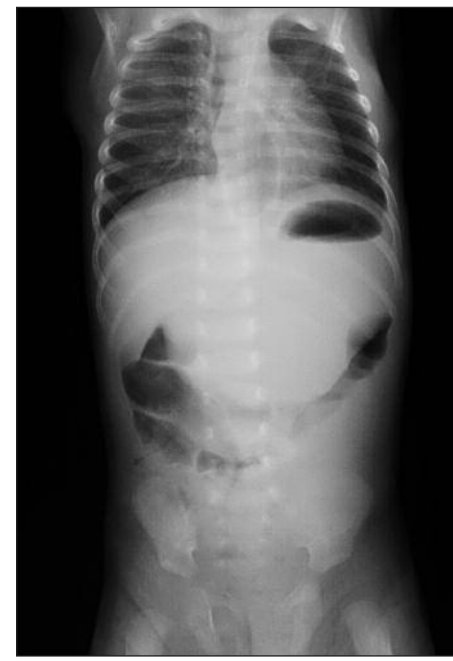

FIGURE 2: Plain abdominal X-ray demonstrates a distended stomach pushing bowel segments.

pyloric diameter more than 14 mm (Figure 3).[2] For the infants younger than 30 days, 3 mm pyloric muscle thickness is assumed as threshold.[24] US has a reported sensitivity rate of 98% and specificity rate of 100% when diagnosing IHPS.[25]

UGI may be used following a non-diagnostic US (Figure 4). UGI may demonstrate elongation and narrowing of pyloric channel called as "string sign" and an extrinsic impression of hypertrophied muscle on antrum called as "shoulder sign". UGI can also demonstrate other reasons of non-bilious vomiting such as antral web, gastric atonia, prolonged gastric emptying and gastroesophageal reflux.[2] The diagnosis of IHPS may be delayed when there is a coexisting gastrointestinal anomaly such as esophagus atresia.[26]

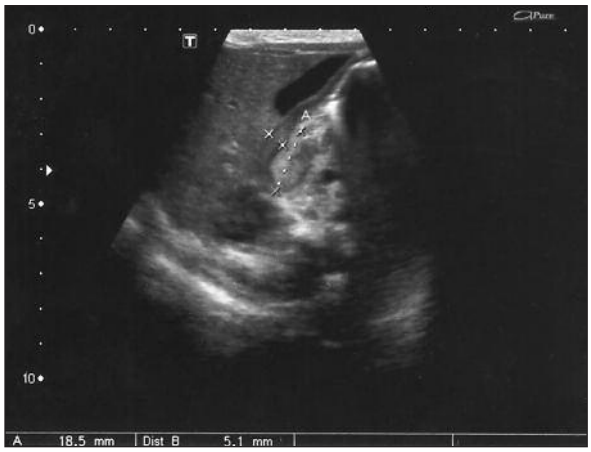

FIGURE 3: Elongated and narrowed pyloric channel on US (length of pyloric channel was measured 18.5 mm and wall thickness was measured 5.1 mm).

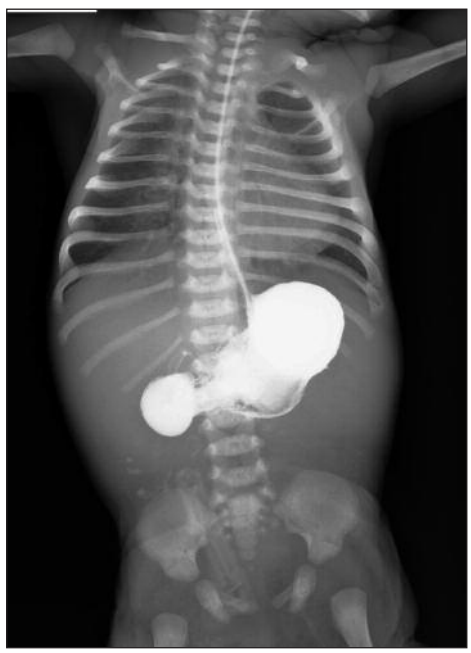

FIGURE 4: UGI study demonstrating delayed gastric emptying.

PREOPERATIVE PREPARATION

If there is a dehydration level under 5% and serum electrolytes are in normal values, preoperative preparation is not needed. In the recent years patients with IHPS have been reported to have earlier diagnosis and metabolic disorders have been less encountered.[27] The duration of preoperative preparation depends on fluid-electrolyte deterioration degree. Generally there is no complete obstruction in IHPS, thus infant may tolerate its own gastric secretion. Nasogastric intubation may cause additional fluid and hydrochloric acid loss, thus nasogastric tube is not needed whether infants with IHPS that do not vomit following oral intake is stopped.[2]

If the infant has dehydration and laboratory signs of hypochloremic hypokalemic metabolic alkalosis, initially 10-20 cc/kg normal saline is administered and subsequently 0.45 normal saline with 5-10% dextrose infusion is started at a dosage 1.25 to 2 folds higher than infants normal requirement (depending on the severity of dehydration). When urinary output of infant becomes sufficient, 20-40 mEq/L of potassium chloride is added to the fluid treatment. Fluid treatment is preceded under control of urine output of the infant and serum electrolyte values repeated in 6-12 hours periods. The aims of fluid treatment are improving dehydration and achieving potassium and chloride values close to normal.[2,22]

Bicarbonate values higher than 30 mEq/L may cause myocardial dysfunction and central respiratory depression. Apnea due to metabolic alkalosis in IHPS has been reported.[20] Usage of H2-receptor antagonists have been reported to improve metabolic alkalosis more quickly in IHPS.[28,29] Chemoreceptors in central nervous sys-

tem are sensitive to pH or PCO_2 changes in brain.[30] Carbon dioxide sensitivity of respiratory center is decreased in these patients, thus increasing carbon dioxide concentration following anesthesia do not stimulate respiratory center and spontaneous respiration is disturbed.[31] For this reason, improving alkalosis during preoperative course is aimed. Decreasing of serum bicarbonate value less than 30 mEq/L represents improvement of alkalosis.[2]

NON-OPERATIVE TREATMENT

Although non-operative treatment is not accepted all around the world, it had been used in some European countries for a period.[2] In this modality metoclopramide or atropine may be used. Kawahara et al. have conducted a study concerning 52 IHPS cases, they have treated the infants with initial administration of intravenous atropine 0.01 mg/kg 6 times a day followed by oral atropine and reported an 87% success rate. Hospitalization time of these patients ranged 6 to 36 days, and duration of atropine treatment ranged 29 to 137 days.[32] Another similar study revealed that atropine was only able to respond after 6th to 7th days of treatment and the success rate was 75%. Additionally due to atropine usage of these patients, 24% had transient tachycardia and 6% had flushed skin.[33] Today, this way of treatment is only considered for the patients who cannot be operated due to other medical conditions and therefore this modality requires long hospital stay and long duration of treatment.

Balloon dilatation of pyloric channel has been tried for non-operative treatment. In the first study with balloon dilatation that had tried on 6 patients with IHPS, only in one, dilatation of pyloric channel has succeeded but mucosal rupture has been reported in this patient.[34] Afterwards, an infant that had developed IHPS following closure of a giant omphalocele, was reported to have improved after 2 pyloric dilatations.[35] There are some articles suggesting balloon dilatation of pyloric channel for recurrent pyloric stenosis after IHPS operation and for the hypertrophic pyloric stenosis that have late-onset.[36,37]

OPERATIVE TREATMENT

Pyloromyotomy for IHPS is one of the most important operations of the 20th century. For the first time in 1907, Pierre Fredet who was a surgeon from Paris performed Heinecke-Mickulicz pyloroplasty (a longitudinal cut through both muscle and mucosa that was then sutured in a horizontal fashion) on an infant suffering from vomiting for one-month period. The infant died due to abundant hematemesis one day after operation, thus later he performed pyloroplasty by extramucosal fashion. In 1911, Conrad Ramstedt, performed extramucosal pyloroplasty on an infant with IHPS but did not closed the muscular layer and leaved open.[1] This technique is still in use for the surgical treatment of IHPS and called as Fredet-Ramstedt pyloromyotomy (Figure 5, 6). For the open surgical approach many type of incisions such as lateral oblique muscle-splitting incision, transverse right upper quadrant incision, right semicircular umbilical incision and supraumblical semicircular incision have been defined. In Fredet-Ramstedt pyloromyotomy, following a longitudinal incision on the anterior wall of hypertrophied pylorus, hypertrophied muscles are separated to each side until the mucosal prolapse is achieved.[1,2]

Alain et al. defined laparoscopic pyloromyotomy for the first time in 1991.[38] The only superiority of laparoscopic pyloromyotomy to open surgical approach is better cosmetic result. In a recently published randomized prospective study, operation time and recovery period of the patients have been found similar in both open and laparoscopic pyloromyotomies.[39] In another study that 457 pyloromyotomies, in which 232 were laparoscopic, have been evaluated and complication rates of both techniques have been found to be similar (4.4% open vs. 5.6% laparoscopic). In this study, mucosal perforation was more common in open surgical technique and incomplete pyloromyotomy was more common in laparoscopic technique.[40] Laparoscopic and open surgical techniques have been reported to be similar, in terms of, operative time, postoperative vomiting, time of full oral intake and duration of hospitalization.[2]

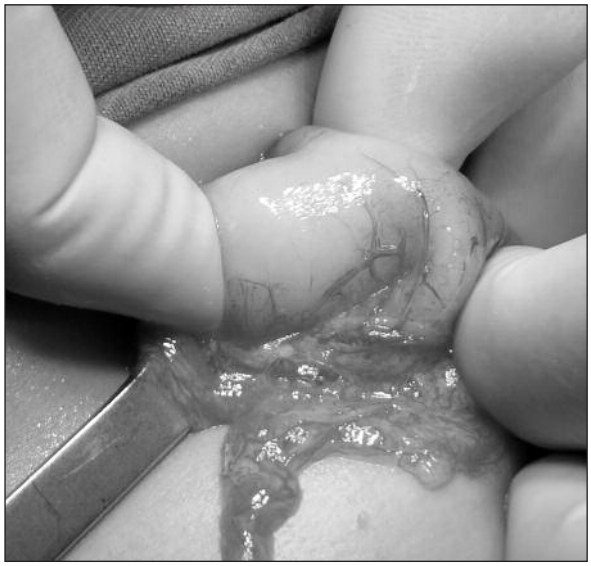

FIGURE 5: Intraoperative appearance of "olive".

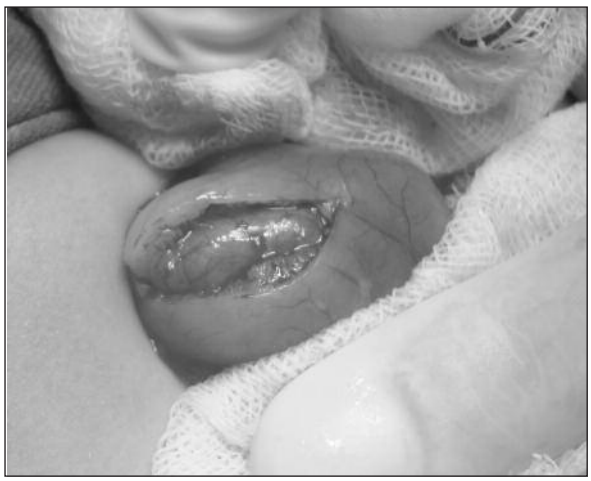

FIGURE 6: Fredet Ramstedt pyloromyotomy (hypertrophied muscle fibers are separated in midline to both sides in a fashion allowing for mucosal prolapse).

POSTOPERATIVE CARE

After pyloromyotomy in the first 24 hours existence of ineffective gastric peristalsis has been demonstrated and only after the first week of surgery, gastric emptying could come back to normal. However, oral feeding in IHPS can be started in 4-6 hours after surgery, and complete oral intake can be achieved within 24 hours. First oral feeding may be delayed to 12 hours for the infants having hematemesis during preoperative course due to gastritis. Oral intake starts with 30 cc parenteral fluid including electrolytes and dextrose, three hours later 30 cc formula is given and full oral intake is achieved by increasing the amount of formula 15 cc for every three hours periods. Infants adopting this feeding regimen are generally discharged within 24-48 hours.[2,39]

COMPLICATIONS

Today, mortality after pyloromyotomy is almost not encountered and morbidity is also extremely rare.[1,2] Rupture of duodenal mucosa is the most severe complication due to surgery. Mucosal perforation risk is reported to be between 0.4 and 10% in laparoscopic surgery and between 0 and 6% in open surgery.[2,40] In case of mucosal perforation, perforation area is repaired with absorbable sutures and covered with muscles in two layers and by turning pylorus than a new pyloromyotomy from a safe distance is performed or mucosal repair area may be covered with omental patch.[2]

During postoperative 24 hours, vomiting due to gastric atonia may be encountered and vomiting caused by pyloric edema may be prolonged to three to 10 days. For vomiting continuing after 48 hours of surgery incomplete myotomy should be considered. Incomplete myotomy is generally caused by insufficient splitting of muscle fibers of pylorus on gastric side. If passage is interrupted on UGI study, balloon dilatation of pylorus may be tried or pyloromyotomy is repeated.[36,37]

The ratio of postoperative wound infection is reported to be 0 to 6% in laparoscopic group, and 0 to 7 in open surgical approach.[2,27,39,41] Postoperative hemorrhage, wound dehiscence and incisional hernia are rare complications.[27,39,41] A recently published meta analysis concerning IHPS has indicated major complication rates respectively 4.9% for laparoscopic surgery and 2% for open surgery.[42]

In conclusion, IHPS is a progressive gastric outlet obstruction, characterized with non-bilious projectile vomiting resulting in serious biochemical

abnormalities. Improving the fluid and electrolyte imbalance of the infant during the preoperative period is crucial. IHPS has an excellent clinical course with early diagnosis, appropriate medical and surgical treatment. For about a century, Fredet- Ramstedt pyloromyotomy has been the primary surgical procedure for IHPS and the postoperative course is perfect.

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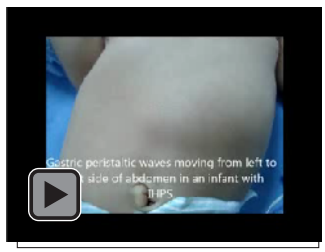

Video 1