New Insights in Infantile Hypertrophic Pyloric Stenosis

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Infantile hypertrophic pyloric stenosis is a very common disease, occurring in 3 per 1,000 live births in the United States [1] and at a somewhat lower incidence in other countries [2]. The typical clinical features and the radiologic appearance of the pyloric channel are well established, as is the current gold standard of surgical treatment. When Rammstedt's pyloromyotomy operation was first described in 1912 the operative mortality was over 20%; today it should be nil.

Laparoscopic pyloromyotomy is currently advocated by many advanced centers [3,4]. Laparoscopic surgical approaches should not only decrease the risk of wound infections, but also shorten postoperative stay since feeding is tolerated within hours after surgery. Some authors also claim that the laparoscopic approach is more cost-effective than the open technique [5].

The last decade shed some light on the pathogenesis of infantile hypertrophic pyloric stenosis. IHPS is a developmental abnormality (erroneously called "congenital" in the past) in which the pyloric muscle hypertrophies after birth. There are sound data showing that the dimensions of the pyloric muscle at birth are the same in normal infants as in those destined to develop IHPS [6]. The hypertrophied muscle causes a time-dependent increase in mechanical obstruction; hence the clinical symptoms.

A decrease in substance P immunoreactivity, a potent member of the family of neuropeptides, in specimens taken from IHPS cases suggested possible involvement of peptidergic innervation in the pathogenesis of IHPS [7]. The mean fundic and antral somatostatin-like immunoreactivity concentrations were found to be significantly lower in IHPS children than in controls, and the significantly higher serum gastrin levels in response to standard breakfast also suggested a role in the pathogenesis of IHPS [8]. S-100 protein and D7 antigen (markers of peripheral Schwann cells) and GFAP (a marker of central-type nerve-supporting cells) were found to be either absent or markedly reduced within the hypertrophied circular and longitudinal muscle specimens taken from IHPS infants [9].

When NADPH diaphorase activity was found to be absent in the enteric nerve fibers in the hypertrophied circular musculature of patients with IHPS [10], it was assumed to represent lack of nitric oxide synthase and an explanation for the pylorospasm. Recently, subsets of patients with IHPS were found to have normal nitric oxide synthase activity in the pyloric muscle [11,12].

More confusing are recent reports on the success of medical treatment in IHPS. Until the mid-1960s, IHPS was often treated medically with either methyl scopolamine nitrate [13] or orally administered atropine. This approach was abandoned for more than three decades in favor of the surgical approach, which yielded prompt resolution of symptoms, efficacy, low associated morbidity and short hospital stay. Since 1996 a group of workers from Osaka, Japan [14] has revived the interest in medical treatment of IHPS with atropine. Only 2 of 23 infants reported by that group required pyloromyotomy, because of prolonged treatment or underdosing of oral atropine. All of the 21 infants who recovered after intravenous atropine without surgery had normalization of pyloric muscle caliber, as shown by ultrasonography 4–12 months after treatment. The disadvantages of the treatment noted by the authors were the length of stay in hospital and the need to continue atropine medication orally after discharge home. In a recent paper by the Osaka group [15], a protocol of intravenous atropine treatment was given 6 times a day before feeding in a fixed dose of 0.01 mg/kg to patients with IHPS for a median of 7 days until cessation of vomiting and achievement of 150 ml/kg/day oral intake. Subsequently the infants took oral atropine (0.02 mg/kg/dose) (median 44 days, range 22–128 days). Of the 19 infants 17 did not require surgery and all were thriving at 6 months of age. Atropine treatment was not associated with any significant adverse long-term effects. However, this renewed approach of atropine treatment for IHPS has not gained wide acceptance mainly because it requires a prolonged hospital stay and treatment at home.

Atropine sulfate is known to act peripherally as a competitive inhibitor of the muscarinic effects of acetylcholine, leading to increased gastrointestinal peristalsis. This action is believed to be important in IHPS cases.

Kawahara et al. [16] observed characteristic phasic and tonic contractile activity in the gastroduodenal junction that was uncoordinated with the antral contractions in IHPS patients. They postulated that such uncoordination may be a more important factor in the disturbed transpyloric flow in IHPS than the hypertrophy of the pyloric muscle. Fraser et al. [17] reported that in adult volunteers the entry of glucose or lipid into the duodenum increases the strength and number of contractions of the pylorus.

IHPS = infantile hypertrophic pyloric stenosis

This feeding-induced increased contraction of the pylorus was inhibited by administration of intravenous atropine. It might be that in IHPS the absence of nitric oxide inhibitory innervation of the pyloric smooth muscle results in unopposed contraction of the sphincter in response to muscarinic stimulation. Atropine may provide effective therapy for IHPS by weakening this inappropriately robust pyloric sphincter contraction. The author of this editorial (R.U.) is not aware of any group in Israel that has tried medical treatment in IHPS.

The wide availability of ultrasound services in the community in Israel and 24 hours/day service in Israeli hospitals was expected to change the clinical presentation of IHPS. In this issue of *IMAJ*, Shaoul and colleagues [18] compared the clinical presentation features of 70 infants with surgically confirmed diagnosis of IHPS in their hospital during the years 1990 to 2000 with historical data derived from the literature. Their study reflected a high index of suspicion and early seeking of medical advice, as evidenced by the lack of projectile vomiting history in a third of their patients and the rarity of peristaltic waves on physical examination. These data and the findings of dehydration in only 18% and electrolyte imbalance in less than 50% support their assumption. The classic baby who needs vigorous fluid and electrolyte resuscitation is seldom seen nowadays. These data are in accordance with a paper cited in their manuscript by Hulka et al. from Portland, Oregon [19], who compared data of 901 infants with IHPS during five periods from 1969 through 1994. They found that patients with IHPS present less frequently with the clinical hallmarks of the disease [19]. This has led to the diagnosis of IHPS before alkalosis has a chance to develop, a shorter clinical course, less morbidity, and a shorter postoperative hospital stay. The same group also reported [20] that the use of upper gastrointestinal series is more cost-effective than ultrasound, since fewer secondary studies were required and upper gastrointestinal series provided information regarding other pathologic conditions as compared with ultrasonography. A similar study has not been done in Israel and the common practice in Israel is to initiate an ultrasound study as the first line of investigation.

Shaoul et al. [18] report a low percentage of pyloric tumors palpated. In view of the easily available radiologic services in Israel this may not influence patients' outcome, but this declining clinical expertise is an alarming sign of the consequences of modern medicine.

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