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Medical treatment of infantile hypertrophic pyloric stenosis: should we always slice the "olive"?

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Abstract

Background/Purpose: Laparoscopic pyloromyotomy has recently gained wide acceptance as the optimum treatment of infantile hypertrophic pyloric stenosis (IHPS). However, medical treatment may be superior to laparoscopic surgery in invasiveness. The efficacy of our regimen of intravenous atropine therapy for IHPS was assessed in comparison with surgical treatment.

Methods: Medical treatment was initially chosen for 52 (61%) of 85 infants with IHPS at our institute between 1996 and 2004. Atropine was given intravenously at 0.01 mg/kg 6 times a day before feeding. When vomiting ceased and the infants were able to ingest 150 mL/kg per day of formula after stepwise increases in the feeding volume, they were given 0.02 mg/kg atropine 6 times a day orally, and the dose was decreased stepwise.

Results: Of the 52 patients, 45 (87%) ceased projectile vomiting with treatment using intravenous (median, 7 days) and subsequent oral (median, 44 days) atropine administration. The median hospital stay was 13 days (6-36), and no significant complications were encountered during atropine therapy. The remaining 7 patients required surgery. Of 40 who underwent surgery, 4 had wound infections and 1 with hemophilia had postoperative hemorrhagic shock. The patients who underwent successful atropine therapy had body weights comparable with those who underwent surgery at the age of 1 year.

Conclusions: The high success rate of intravenous atropine therapy for IHPS suggests that this therapy is an effective alternative to pyloromyotomy if the length of the hospital stay and the necessity of continuing oral atropine medication are accepted.

Fredet-Ramstedt pyloromyotomy is the optimal treatment of infantile hypertrophic pyloric stenosis (IHPS) [1]. With technological advances and the general increase in popularity of laparoscopic surgery even for small children, laparoscopic pyloromyotomy has come into vogue mainly in western countries [2]. However, its efficacy and benefits remain unclarified in comparison with the conventional open procedure [3]. On the other hand, the outcome was poor without surgical intervention for this condition because

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atropine given orally does not work consistently in infants with frequent projectile vomiting. However, recent studies regarding intravenous atropine therapy have shown significant success rates [4-6]. The current study assessed the efficacy and safety of our regimen of intravenous atropine therapy for IHPS in comparison with surgery.

1. Patients and methods

1.1. Patients

Since the introduction of intravenous atropine therapy in 1996, 87 patients with IHPS were treated at the Osaka Medical Center and Research Institute for Maternal and Child Health during the last 9 years. The diagnostic criteria for IHPS were as follows:

1. Repeated projectile vomiting more than twice a day.
2. Pyloric canal length ≥15 mm and pyloric muscle thickening ≥4 mm on ultrasonography.

When the measurement of pyloric hypertrophy was close to but did not fulfill the criteria, fluoroscopy was conducted, and patients were diagnosed with IHPS when characteristic string or umbrella signs were observed. Two patients who were subsequently diagnosed with associated malrotation or sliding hiatal hernia, respectively, were excluded from the study. The method of treatment of IHPS, medical or surgical, was determined according to the informed choice of the patients' guardians after ample explanation of each treatment, except for 1 patient. Medical treatment was chosen for a patient with an anorectal anomaly because surgery was difficult owing to his colostomy. Medical treatment with intravenous atropine therapy was initially chosen for 52 patients (61%). The remaining 33 patients chose surgery as the initial treatment at our hospital. Of them, 10 had undergone unsuccessful intravenous or oral atropine therapy before being referred to our hospital. The atropine therapy regimens for these patients were different from ours. Surgery was performed with pyloromyotomy using 2 surgical procedures: the supraumbilical skin-fold incision and the right upper quadrant incision. Before surgical and medical treatment, peripheral blood cell counts, electrolytes, and biochemical examination were conducted as a routine, whereas a coagulation test was not included in the routine test.

1.2. Treatment regimen for intravenous atropine therapy

The details of the regimen of intravenous atropine therapy were reported previously [5]. Atropine was intravenously administered at 0.01 mg/kg 6 times a day, 5 minutes before feeding. During atropine infusion, the heart rate was continuously monitored with electrocardiography. Oral feeding was started at 10-mL formula, 6 times a day. The volume was increased day by day until each patient tolerated 150 mL/kg per day, unless vomiting occurred more than twice a day. When the patient was able to tolerate the full volume of formula without vomiting more than twice a day, 0.02 mg/kg atropine was orally administered 6 times a day before feeding. Patients with IHPS who did not respond to the medical treatment underwent open pyloromyotomy. The patients who underwent successful medical treatment were discharged when their vomiting was controllable with oral atropine. When a patient was free of vomiting and showed steady weight gain, atropine was decreased in 3 steps of 0.12, 0.06, and 0.03 mg/kg per day. If the patient vomited more than twice a day for 3 days after the discontinuation of atropine therapy, oral administration was recommenced.

1.3. Follow-up

The guardians of patients who were treated with atropine therapy or surgery were asked for permission to review the patient at the age of 1 year. The clinical condition and body weight were recorded in medical charts, and weights were converted into SD scores using data from Japanese infants published in the national survey of 1990 (Ministry of Health and Welfare, Japan).

1.4. Statistical analysis

All data are presented as median values and ranges. Tests for significant differences were analyzed using the Mann-Whitney U test unless otherwise specified. Data on the hospital stays of 4 patients who were admitted owing to other pathological conditions since birth were excluded when analyzed.

2. Results

Intravenous atropine therapy was chosen for 52 patients with IHPS with a median age of 40 (10-132) days. Their median body weights were 2981 (626-4430) g at birth and 3730 (2323-5410) g at the time of presentation. Among them, 45 (87%), including 1 with colostomy, were successfully treated with our atropine therapy regimen. The details of those who were successfully and unsuccessfully treated with atropine therapy are shown in Table 1. Body weight at the time of presentation was significantly different between the 2 groups (P = .04). The durations of subsequent oral atropine administration and total atropine therapy were 44 (23-128) days and 51 (29-137) days, respectively. Significant complications were not encountered during therapy. Urinary tract infection, upper respiratory tract infection, and a transient increase in serum aspartate aminotransferase were observed in 1 patient each.

In total, 40 patients, including 7 who had received unsuccessful atropine therapy at our hospital, underwent surgery at the median age of 42 (17-135) days. Their median body weight was 3085 (1414-3838) g at birth and

Table 1 Characteristics of patients who underwent successful and unsuccessful atropine therapy

	Successful	Unsuccessful	*P*
Age at presentation (d)	41 (10-132)	38 (16-75)	.56
Body weight (g)			
At birth	2982 (626-4430)	2880 (2138-3430)	.98
At presentation	3885 (2323-5410)	3230 (2615-4175)	.04
Ultrasound findings (mm)			
Pyloric thickness	5 (3-7)	5 (3-7)	.98
Pyloric length	18 (12-25)	18 (17-20)	.83
Duration (d)			
Hospital stay[a]	13 (6-36)	15 (7-28)	.41
Intravenous atropine	7 (2-20)	7 (2-11)	.90

[a] Hospital stay: 4 patients who were admitted owing to other pathological conditions since birth were excluded.

3573 (2505-4895) g at the time of presentation, both of which were not significantly different from that of patients who were successfully treated with atropine therapy (P = .32, P = .10). The duration of the hospital stay of patients for whom initial surgical treatment was chosen was significantly shorter than that of the successful atropine group (5 [4-29] vs 13 [6-36] days, P < .001). A supraumbilical skin-fold incision was used on 31 patients and a right upper quadrant incision on 9. Wound infection occurred in 4 patients (10%) who underwent the supraumbilical skin-fold approach. Among them, 3 required readmission to treat wound abscesses, and 1 had undergone unsuccessful intravenous atropine therapy before surgery. The incidence of wound infection was not significantly increased by the preceding intravenous atropine therapy (P = .43, Fisher's Exact probability test). Mucosal perforation during pyloromyotomy occurred in 1 patient with a supraumbilical skin-fold incision. In addition, 1 patient with hemophilia had postoperative hemorrhagic shock that caused hypoxic encephalopathy. He died of brain hemorrhage at the age of 18 months.

Of 85 patients, 30 who were successfully treated with atropine and 18 who were surgically treated were reviewed at the age of 1 year. One patient showed occasional emesis and failure to thrive and was subsequently diagnosed with antral web by endoscopy. The remaining patients did not show any symptoms related to IHPS. There was no significant difference for the weight SD scores between the atropine and surgical groups (+0.04 [−1.7 to +2.1] vs −0.22 [−2.1 to +1.8], P = .86).

3. Discussion

Medical treatment with atropine has been reappraised as an option for IHPS treatment using a step-up dosage technique with intravenous atropine administration and is associated with a successful short-term outcome [4,6]. On the other hand, we devised our original regimen with a fixed dose of intravenous atropine and a gradual increase in oral intake to reduce the frequency of emesis [5]. It was aimed in this regimen to simplify the treatment by avoiding considerable variation in the dose of intravenous atropine, which required much medical supervision and careful monitoring for the toxic effects of the drug. The dose of intravenous atropine used in the current study was determined by the manometric finding that clusters of tonic and phasic pyloric contractions characteristic of IHPS were transiently abolished by the intravenous injection of 0.01 mg/kg of atropine [7]. Our preliminary report suggested the efficacy of this regimen of intravenous atropine therapy [5]. The success rate of intravenous atropine therapy of 87% shown in the current study with a reasonably large number of patients supports the consideration that this therapy is an effective alternative to pyloromyotomy.

It is important to delineate the patient selection criteria to determine which infants are likely to respond to medical therapy [8]. Comparing successful and unsuccessful patients, there was a statistical difference only in body weight at the time of presentation. Therefore, it is difficult to predict the outcome of atropine therapy with pretreatment data. Through our clinical experience, the result was predictable by looking at changes in intestinal gas shown in abdominal x-rays taken during atropine therapy.

The disadvantages of intravenous atropine therapy are the length of hospital stay required and the necessity of continuing oral atropine medication after discharge. Continuous frequent oral administration of atropine at home may require a lot of effort for the patients' guardians. The data of medical cost were not included in this study because the fees for surgery and anesthesia of small infants and for hospital stay were greatly diverse among countries. Despite a longer hospital stay, there was no significant difference in medical cost between the atropine and surgical groups.

Surgical treatment is associated with various complications, although they are infrequent. In the current series, wound infection occurred in 4 (13%) of 31 patients who underwent a supraumbilical skin-fold incision. Mucosal perforation was also encountered in 1 using this approach. Supraumbilical skin-fold incision produces an almost undetectable scar and has definitive cosmetic advantages. This method is a reliable alternative to the laparoscopic approach because of its financial and technical advantages [9] but is associated with more complications compared with the conventional right upper quadrant approach [10]. The most serious complication that occurred in the current series was postoperative hemorrhagic shock that caused hypoxic encephalopathy in 1 patient with hemophilia. A coagulation test had not been performed before pyloromyotomy as a routine, and the bleeding tendency was not recognized during pyloromyotomy in this patient. Surgery is always associated with risks caused by such unpredictable

conditions. In particular, for pyloromyotomy for IHPS, the various complications reported previously cannot be ignored [11-13].

Our preliminary data demonstrated that patients with IHPS treated with intravenous atropine therapy showed failure to thrive at presentation but recovered by the age of 6 months [5]. There have been no studies comparing the long-term outcome of intravenous atropine therapy and surgery. The data obtained in the current study indicate that patients with IHPS treated with intravenous atropine therapy or by surgery show comparable and adequate physical development. A previous histologic study showed that the enteric nervous system is normalized during the regression of pyloric hypertrophy after the healing of the pyloromyotomy [14]. However, in adults who had pyloromyotomy for IHPS during infancy, patterns of pyloric motility were reported to be abnormal [15]. The cause of this abnormality in pyloric motility has not been clarified, but the disconnection of the neural network by pyloromyotomy may be responsible. The long-term effects of atropine therapy on pyloric motility need to be investigated to clarify the functional value of medical treatment in comparison with surgery.

Intravenous atropine therapy has not gained wide acceptance in western countries because of the uncertainty of the results and the long duration of treatment [8]. Although pyloromyotomy is the optimum treatment of IHPS, the actual and potential consequences of surgery cannot be ignored. An aseptic surgical setting and expert pediatric surgeons are not universally available from a global point of view. Intravenous atropine therapy can be performed when infusion with meticulous atropine injection can be safely carried out on small infants. Recently, this therapy has tended to become popular in certain geographic settings where surgery on small infants is not necessarily safe [16,17]. This therapy is worthwhile in patients who have difficulty in undergoing surgical treatment of IHPS, such as patients with colostomy in the upper abdomen. However, it must be kept in mind that skilled nursing care is mandatory to conduct the repeated injection of small doses of atropine during this therapy.

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