Intravenous atropine treatment in infantile hypertrophic pyloric stenosis

H Kawahara, K Imura, M Nishikawa, M Yagi, A Kubota

Aims: To assess the efficacy of a new regimen of intravenous atropine treatment for infantile hypertrophic pyloric stenosis (IHPS) with special reference to regression of pyloric hypertrophy.

Methods: Atropine was given intravenously at a dose of 0.01 mg/kg six times a day before feeding in 19 patients with IHPS diagnosed from radiographic and ultrasonographic findings. When vomiting ceased and the infants were able to ingest 150 ml/kg/day formula after stepwise increases in feeding volume, they were given 0.02 mg/kg atropine six times a day orally and the dose was decreased stepwise.

Results: Of the 19 infants, 17 (89%) ceased projectile vomiting after treatment with intravenous (median seven days) and subsequent oral (median 44 days) atropine administration. The remaining two infants required surgery. No significant complications were encountered. Ultrasonography showed a significant (p < 0.05) decrease in pyloric muscle thickness, but no significant shortening of the pyloric canal after completion of the atropine treatment. The patients exhibited failure to thrive at presentation, but were thriving at 6 months of age (p < 0.01).

Conclusions: This atropine therapy resulted in satisfactory clinical recovery. Pyloric muscle thickness was significantly reduced.

Treatment regimen
Atropine was administered intravenously at a dose of 0.01 mg/kg six times a day five minutes before feeding. During atropine infusion, the heart rate was continuously monitored by electrocardiography. Oral feeding was started at a volume of 10 ml formula, six times a day. The volume was increased day by day until patients tolerated 150 ml/kg/day (418 J/kg/day), unless vomiting occurred more than twice a day. Concentrated formula was not given. When patients were able to tolerate the full volume of formula without vomiting more than twice a day, 0.02 mg/kg atropine was administered orally six times a day before feeding. Intravenous atropine treatment was considered unsuccessful if patients failed to tolerate half of the full volume within a week or the full volume within two weeks. They were discharged from the hospital when vomiting was controlled with oral atropine. When patients were free of vomiting and showed steady weight gain, atropine was decreased in three steps (0.12 mg/kg/day, 0.06 mg/kg/day, 0.03 mg/kg/day). If patients vomited more than twice a day for three days after discontinuation of atropine treatment, oral administration was restarted.

Follow up
Successfully treated patients were followed up.

Clinical symptoms
Daily frequency of vomiting, recorded in medical charts during intravenous treatment and in guardians’ diaries during oral treatment, was examined at three weeks, three months, and six months after completion of oral atropine administration.

Physical development
Serial changes in body weight were examined at presentation and at the ages of 3 months, 6 months, 1 year, and 2 years. Weights were converted into standard deviation scores (SDS) using data from Japanese infants, published in the national survey for 1990 (Ministry of Health and Welfare, Japan).
Ultrasonographic evaluation of the pylorus
Ultrasonographic evaluations were conducted at presentation, at three weeks and six months after completion of oral atropine administration, and at 1 year of age. Ultrasonography was performed by the same paediatric radiologist (MN) using a Yokogawa Medical RT4600 and 7.5 MHZ linear probe. The patients were fasted for more than three hours before ultrasonographic examination and were not sedated. The examination was performed on several planes. The thickness of the pyloric muscle and the length of the pyloric canal were measured on transverse views, which showed the pylorus along its long axis. Transpyloric flow of gastric contents was also examined. All patients were followed up until 2 years of age.

Statistical analysis
All data are presented as median (range). Tests for statistically significant differences in weight SDSs and ultrasonographic measurements were analysed using the Kruskal-Wallis test. Categorical variables were compared using the Tukey test.

RESULTS
At the time of presentation, 12 patients had previously received infusions at other hospitals, and dehydration and/or electrolyte imbalance were not noted. Of the 19 patients, 17 became free from projectile vomiting during atropine treatment. The remaining two required surgery after 9 and 18 days of intravenous atropine. Total hospital stay was 13 (6–20) days for the 17 patients. The duration of intravenous and subsequent oral atropine administration was 7 (4–10) days and 44 (22–128) days respectively. Atropine was administered for 50 (28–136) days in total, and was completed at 93 (71–174) days of age.

Of the 17 patients, 13 experienced little vomiting three weeks after completion of oral atropine administration. The remaining four occasionally vomited once or twice a day three weeks after completion of oral atropine, but rarely vomited and atropine treatment was 7 (4–10) days for the 17 patients. The duration of intravenous and subsequent oral atropine administration was 7 (4–10) days and 44 (22–128) days respectively. Atropine was administered for 50 (28–136) days in total, and was completed at 93 (71–174) days of age.

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Ultrasonographic measurements were made before and three weeks after atropine administration. IV, Intravenous atropine administration.

Figure 1

Serial changes in weight standard deviation scores (SDS) in patients successfully treated with atropine. Box, interquartile range; horizontal bar, median; whiskers, 10th and 90th centile. *p < 0.01, **p < 0.05.

but not at 3 months (<0.6 (−3.1–0)), compared with that at presentation (<1.4 (−4.1–0.2)). There was no further significant change at 1 year (0.2 (−1.7–2.1)) and 2 years of age (−0.4 (−1.2–2.4)).

Ultrasonography showed significant (p < 0.01) changes during atropine treatment. Figure 2 shows serial changes in pyloric muscle thickness and pyloric canal length. Pyloric muscle thickness decreased significantly (p < 0.05) from 5 (4–6) mm at presentation to 3 (2–5) mm three weeks after completion of oral atropine. Pyloric canal length was 19 (15–25) mm at presentation and 15 (12–20) mm three weeks after completion of oral atropine (not significant). Transpyloric flow of intragastric fluid was not observed by ultrasound in any patient before treatment, but was detected in all three weeks after completion of oral atropine. Pyloric muscle thickness was 2 (2–4) mm six months after completion of oral atropine and 2 (2–3) mm at 1 year of age, both of which were significantly (p < 0.01) less than at presentation. Pyloric canal length
**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 was associated with a successful short term outcome. The clusters of tonic and phasic pyloric contractions characteristic of IHPS recently reported are transiently abolished by an intravenous atropine injection of 0.01 mg/kg. We thought that this dose of atropine would improve transpyloric flow by inhibiting the contractions. We therefore used this as a fixed dose before feeds six times a day. This was in contrast with the regimen of Nagita et al., in which the dose of atropine was increased until projectile vomiting was controlled. In that study, the dose of atropine actually given was 0.07 (0.04–0.11) mg/kg/day, and 12 of 22 patients received a dose greater than that used in our study. The success rate in our regimen (89%) was similar to that reported by Nagita et al. The duration of intravenous atropine administration was slightly longer in our study (7–10 days) than in theirs (5–8 days) (p < 0.05; Mann-Whitney U test). No special characteristics were evident in the two patients for whom atropine treatment failed. During subsequent oral atropine treatment, we used double the intravenous dose as described by Nagita et al.

During the intravenous administration, heart rate was maintained in a safe range and there were no serious clinical problems. The adverse events in the series of Nagita et al. included mild facial flushing, increased alanine aminotransferase, and tachycardia. No serious complications occurred with intravenous atropine, but it may be both safer and more convenient to use a fixed dose as in our regimen.

In this study, we attempted to reach half the full volume of formula within a week and the full volume within two weeks. Although prolonged intravenous atropine was given for a couple of days at the guardians’ request in two patients, they did not improve and required surgery. In contrast, projectile vomiting was controlled within 10 days in 17 patients.

Long term outcome has not been compared in patients with IHPS treated medically and surgically. The patients treated successfully with atropine showed failure to thrive at presentation. They had all recovered when reviewed at 6 months of age. They were all free from symptoms without atropine. All were well at their two year follow up. These findings indicate that atropine treatment is not associated with any significant adverse long term effects.

Regression of pyloric muscle hypertrophy has been investigated ultrasonographically in patients treated surgically and medically. Sauerbrei and Paloschi reported that pyloric muscle thickness and the diameter and length of the pyloric canal were normal within six weeks of pyloromyotomy. In patients with IHPS treated with atropine, Nagita et al. reported that the time to normalisation of pyloric muscle thickness ranged from four to 12 months. Yamataka et al. reported that the normalisation of pyloric muscle thickness was not significantly different between patients undergoing pyloromyotomy (3.8 (2.0) months) and those treated with atropine (3.4 (2.3) months). The present study indicated that pyloric muscle thickness was significantly less on completion of oral atropine treatment, and preceded normalisation of pyloric canal length.

The value of intravenous atropine as a treatment for IHPS remains controversial. It has not gained wide acceptance mainly because it requires a prolonged hospital stay and treatment at home. Although pyloromyotomy has been regarded as the optimum treatment of IHPS, the actual and potential consequences of surgery cannot be ignored. The patient has an abdominal scar, and there is a small long term risk of complications due to adhesion. Expert paediatric surgery is not universally available. A randomised controlled trial comparing the outcomes and cost effectiveness of intravenous atropine versus surgery is required.

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**REFERENCES**


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**Figure 2** Serial changes in pyloric muscle thickness (A) and pyloric canal length (B) of patients successfully treated with atropine. Box, interquartile range; horizontal bar, median; whiskers, 10th and 90th centile. *p < 0.01, **p < 0.05.