**ORIGINAL ARTICLE**

Intravenous atropine treatment in infantile hypertrophic pyloric stenosis

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**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.

**PATIENTS AND METHODS**

**Patients**

Ethical approval was obtained from the departmental committee, and informed consent was obtained from the patients' guardians. The study population consisted of 19 consecutive infants (male/female 16:3) with IHPS, who were in Osaka Medical Centre and Research Institute for Maternal and Child Health in the period November 1996 to March 1998. All fulfilled the following diagnostic criteria for IHPS:

1. Repeated projectile vomiting more than twice a day;
2. Gastric outlet obstruction and characteristic narrow, long pyloric canal on upper gastrointestinal series;
3. Pyloric canal length ≥ 15 mm and pyloric muscle thickening ≥ 4 mm on ultrasonography.

Table 1 shows the patient characteristics. The median (range) age was 40 (22–85) days at admission. Their median (range) weights at birth and admission were 3086 (2480–4430) g and 3970 (3200–5410) g respectively.

**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 SDs 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. Figure 1 shows 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.

Table 1 Characteristics of subjects

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<th>Hospital stay (days)</th>
<th>Weight at admission (g)</th>
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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 2 (2–3) mm at 1 year of age, both of which were significantly (p < 0.01) less than at presentation. Pyloric canal length...
maintained in a safe range and there were no serious clinical
injection of 0.01 mg/kg.

We therefore used this as a fixed dose before feeds six
would improve transpyloric flow by inhibiting the contrac-
al
failed. During subsequent oral atropine treatment, we used
Mann-Whitney U test). No special characteristics were
reported by Nagita et al.

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.

During the intravenous administration, heart rate was
significantly (p < 0.01) less than that at presentation.

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.
cluded mild facial flushing, increased alanine aminotrans-
ferase, 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 cou-
ples of days at the guardians’ request in two patients, they did
not improve and required surgery. In contrast, projectile vom-
itng was controlled within 10 days in 17 patients.

Long term outcome has not been compared in patients with
IHPS treated medically and surgically.\textsuperscript{8} The patients treated
successfully with atropine showed failure to thrive at presen-
tation. 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.\textsuperscript{11}

Regression of pyloric muscle hypertrophy has been investi-
gated ultrasonographically in patients treated surgically\textsuperscript{12} and
medically.\textsuperscript{8,11} Sauerbrei and Paloschi\textsuperscript{12} reported that pyloric mus-
cle 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\textsuperscript{11} reported that the
time to normalisation of pyloric muscle thickness ranged from
four to 12 months. Yamataka et al\textsuperscript{3} reported that the normalisa-
tion 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.\textsuperscript{11} It has not gained wide acceptance
mainly because it requires a prolonged hospital stay and treat-
ment at home. Although pyloromyotomy has been regarded as
the optimum treatment of IHPS, the actual and potential con-
sequences of surgery cannot be ignored.\textsuperscript{3,15} The patient has an
abdominal scar, and there is a small long term risk of complica-
tions due to adhesion. Expert paediatric surgery is not uni-
versally available. A randomised controlled trial comparing
the outcomes and cost effectiveness of intravenous atropine
versus surgery is required.

**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.\textsuperscript{4,5} 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.\textsuperscript{10} We thought that this dose of atropine
would improve transpyloric flow by inhibiting the contrac-
tions. 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,\textsuperscript{1} 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 (91%).\textsuperscript{1} The duration of intravenous
atropine administration was slightly longer in our study (7
to 10 days) than in theirs (5–18 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.

Atropine was 14 (11–19) mm six months after completion of oral atro-
pine and 12 (9–19) mm at 1 year of age, both of which were
significantly (p < 0.01) less than that at presentation.

Significant complications were not encountered. One
patient had a urinary tract infection and one a transient slight
increase in serum aspartate aminotransferase and alanine
aminotransferase (< 60 IU/l) during intravenous atropine
administration. Facial flushing was not reported during treat-
ment. The resting heart rate remained less than 160
beats/min.

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