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ORIGINAL ARTICLE

Efficacy of Medical Treatment for Infantile Hypertrophic Pyloric Stenosis: A Meta-analysis

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atropine;
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Background: Infantile hypertrophic pyloric stenosis (IHPS) is a common disease in infancy. Pyloromyotomy is universally considered the treatment for IHPS; however, oral or intravenous atropine has been reappraised for the treatment of IHPS in the past 20 years. We investigated the efficacy of atropine in the medical management of IHPS by using meta-analysis and investigated the sonographic changes of the pyloric canal, as well as the efficacy and adverse effects of atropine.
Methods: Information was retrieved from PubMed, Ovid, and MEDLINE. The efficacy and adverse effects of atropine treatment for IHPS were reviewed using the standard process of meta-analysis.
Results: Eleven articles were obtained. Five reports showed that 77 of 110 (70%) infants who were administered oral atropine benefitted by the induced remission of IHPS. Six reports showed that 288 of 345 (83.5%) patients who were treated initially with intravenous atropine then changed to oral atropine showed beneficial effects and had no serious side effects. Time to pyloric muscle normalization ranged from 5 weeks to 15 months.
Conclusion: The study results indicate that atropine is a possible alternative treatment for IHPS, particularly in infants with major concurrent disease, and is safe without obvious side effects.

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1. Introduction

Infantile hypertrophic pyloric stenosis (IHPS) showed a frequency of 3.9/10,000 live births between 1996 and 2004 in Taiwan.[1] The incidence declined to 3/10,000 live births in 2007 in Taiwan.[2] It is the most common cause of vomiting that requires surgical intervention in infants.[3] IHPS is an abnormal hypertrophy of the muscle of the pylorus. Pyloromyotomy, introduced by Dufur and Fredet[4] and Fredet[5] in 1908 and Ramstedt[6] in 1912, has become the first choice of treatment, as effective surgical intervention can easily be performed with minimal complications and rare mortality. In 1955, Corner[7] reported on medical treatment using methyl scopolamine nitrate. A group of workers from Osaka, Japan, reported a new regimen using intravenous (IV) methyl atropine nitrate since 1996[8]; thereafter, many studies have discussed the positive effects of atropine for treating IHPS. However, the sample size has been relatively small. Thus, we reviewed all published studies in a meta-analysis to assess the course and outcome of IHPS managed with atropine.

2. Materials and methods

2.1. Data sources

This search covered the period from January 1980 through March 2015. Data were independently extracted by the first two investigators and then cross-checked by all of the investigators to avoid any errors. The effects of medical treatment for IHPS were identified from PubMed, MEDLINE, and Ovid Medline using the following subject headings (MeSH) and text word terms: "(Infantile) hypertrophic pyloric stenosis, medical treatment, atropine therapy."

The diagnostic criteria for IHPS were repeated projectile vomiting, and pyloric muscle thickening $\geq$3–4 mm and pyloric canal length $\geq$14–18 mm on ultrasonography.

The selection criteria were as follows: (1) pediatric studies; (2) definite diagnosis of hypertrophic pyloric stenosis in infants using definite diagnostic standards; and (3) experiments analyzing the curative effect of atropine for pyloric stenosis. Case reports were excluded. The quality of each paper was evaluated using the modified Jadad scale[9] based on the adequacy of randomization, blinding, and follow up, with a maximum score of 8 points.

For each study, the date of publication, sample size, patient characteristics, treatment method, side effects, and outcomes were recorded. Successful treatment was defined as patients free from vomiting and steady weight gain.

2.2. Statistical analysis

Data for the successful proportion of medical treatment for IHPS in several studies covering the study period were pooled. The degree of heterogeneity among these studies was shown using the Q statistic and I^2 statistic. If the p value of the Q statistic was smaller than the significant level or if I^2 was >40%, then there was heterogeneity among the studies and the proportions were pooled using the random effect model. If there was homogeneity among studies, the fixed effect model was used to pool proportions. Significance was set at 0.05. Sensitivity analysis was conducted to explore the effect of excluding outliers on the pooled estimate. The funnel plot of the logit event rate against the standard error was assessed for publication bias. In addition, we reanalyzed the data by excluding studies with poor quality (modified Jadad score, $\leq$3). Formal statistical testing included an adjusted rank correlation test and a regression asymmetry test.[10,11] Meta-analysis was performed using the software Comprehensive Meta-Analysis (version 2.2.064; Biostat, Englewood, NJ, USA; 2005).

3. Results

Twelve articles[8,12–22] were obtained in the search (Figure 1). Table 1 summarizes the key characteristics of the 12 articles. Among them, the report of Kawahara et al[19] in 2005 included the same study participants recruited in the report of Kawahara et al[15] in 2002. As such, we excluded the study of Kawahara et al[15] published in 2002. Overall, a total of 11 studies were enrolled in this meta-analysis study. Three studies used oral atropine alone, whereas six studies used IV atropine initially, then substituted oral atropine. In two studies, atropine was given orally, then intravenously if ineffective. Oral atropine was given at an initial dose of 0.05 mg/kg/d and increased to a maximum dose of 0.1 mg/kg/d. The dose of IV atropine was started at 0.04–0.06 mg/kg/d and increased by 0.01 mg/kg/d until vomiting ceased. The IV atropine was then changed to oral atropine at twice the effective IV dose.

Treatment was discontinued under the following conditions: ultrasonography showed normalization of pyloric muscle thickness; passage of food through a wide channel on ultrasonography; the patient started gaining weight; vomiting ceased and then resumed for 2–3 weeks; or vomiting ceased and oral atropine was continuously used until the age of 10 weeks.

Five reports showed that in 110 patients receiving oral atropine, 77 (70%) patients showed beneficial effects in that treatment induced remission of IHPS whereas three cases converted to IV atropine. Six reports with a total of 345 patients who received IV atropine followed by oral atropine showed IHPS remission in 288 (83.5%) patients. The mean duration of medical therapy was 24–63 days.

The patients treated successfully with atropine showed steady weight gain. Three studies showed a mean weight gain of 17–30 g/d during the admission period in the groups with successful atropine therapy.[15,16,21] The body weight range on admission was from below the 3rd to the 25th percentile, and after 1 month of IV atropine treatment, the body weight range was from the 10th to 75th percentile in the study of Huang and Su.[16] Kawahara et al[15] reported a significant increase in body weight during atropine treatment by comparing body weight at 6 months of age with that at presentation. The adverse effects related to the use of IV atropine included flushing (7/184, 3.8%), tachycardia (14/184, 7.6%), and transient increase in serum alanine aminotransferase (ALT) level (12/184, 6.5%). There was no adverse effect related to the use of oral atropine.

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