

## Infantile hypertrophic pyloric stenosis: a study of feeding practices and other possible causes

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We carried out a case-control study of the hospital charts of 91 infants with infantile hypertrophic pyloric stenosis (IHPS) to determine the feeding practices at the time of discharge from the neonatal nursery. We excluded infants whose feeding might have been influenced by confounding factors. The infants were matched with controls for gestational age. The mean birth weight of the IHPS group was 3501 g and of the control group 3543 g. The male:female ratio for the IHPS group was 5.5. The odds ratio of male predominance was 4. We found that bottle-feeding was 2.9 times more prevalent among the infants with IHPS than among the control subjects. We speculate that the recently observed decrease in the incidence of IHPS is due to the decline in bottle-feeding.

On compare les dossiers de 91 nourrissons traités pour sténose hypertrophique du pylore (SHP) avec ceux de témoins appariés quant à l'âge gestationnel sous le rapport de leur mode d'allaitement à la sortie de la maternité. On exclut les nourrissons chez qui certains facteurs auraient pu avoir une influence sur le choix de l'allaitement. Le poids moyen de naissance est de 3501 g chez les malades et 3543 g chez les témoins. Le rapport des sexes (masculin:féminin) chez les malades est de 5,5 et le rapport de probabilité d'une prédominance masculine de 4. Nous trouvons 2,9 fois plus de bébés nourris au biberon parmi les malades que parmi les témoins. On peut penser que la diminution notée récemment dans la fréquence de survenue

de la SHP provient du déclin de l'alimentation au biberon.

We have reported a decrease in the incidence of infantile hypertrophic pyloric stenosis (IHPS) in Saskatchewan in 1978-85 as compared with 1970-77 (see pages 395 to 398 of this issue). Several authors<sup>1-4</sup> reported an increased rate in Britain in the 1970s and 1980s, and some<sup>2,5,6</sup> have speculated that this might be related to the increased prevalence of breast-feeding there. Because breast-feeding is also being practised more frequently in Saskatchewan,<sup>7</sup> we decided to investigate the feeding practices of mothers of children with IHPS. We also examined other possible causes of IHPS that have been implicated in other studies; these include sex distribution (males have consistently been affected more often than females have<sup>5,6,8-10</sup>), birth order (some authors<sup>1,5</sup> have considered that the condition is more common among first-born children) and maternal blood groups (Dodge<sup>11,12</sup> found an increased prevalence of blood group B and a decreased prevalence of blood group A; Adelstein and Fedrick<sup>8</sup> could not confirm this but found an excess of mothers who were Rhesus [Rh] negative).

### Methods

In the summer of 1987 we reviewed the charts of 333 patients with IHPS who had been admitted to University, Saskatoon City and St. Paul's hospitals, Saskatoon, from 1970 to 1985. We excluded 228 nonresidents, because we wished to match the cases with control subjects who had been born in the same hospital and resided in the same city to avoid bias due to local feeding practices. Native Indians were excluded because of the difficulty in matching for race and the feeling that their feeding practices may have differed from those of non-

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Indians. We also excluded children whose feeding might have been influenced by other factors; these included infants with severe congenital anomalies, premature infants (born before 37 weeks' gestation) and those who required admission to a neonatal intensive care unit. This left 91 infants. All cases of IHPS were confirmed at operation.

The control subjects were selected by examining the charts of the two children born immediately before and the two immediately after each index patient. The same exclusion criteria were applied. The infant who was closest in gestational age to the index case was chosen as the control, because feeding can be affected by gestational age.

The neonatal charts were examined to determine the birth weight, sex, birth rank, blood group, maternal blood group and method of feeding used at the time of discharge from the nursery. In addition, the feeding method used at the time of admission because of IHPS was noted.

Statistical analysis was done with McNemar's test and the paired *t*-test for matched data.

## Results

The mean birth weight of the infants with IHPS was 3501 g, and the mean length of gestation was 40 weeks. The corresponding figures for the control subjects were 3543 g and 40 weeks. The differences in birth weight were not statistically significant.

The male:female ratio for the IHPS group was 5.5 and for the control group 1.2 (Table I). The odds ratio of male predominance was 4 ( $p < 0.0001$ ; confidence limits 1.8 and 9.8).

First-born children accounted for 39 of the 90 infants with IHPS and 41 of the 90 controls (one pair had insufficient information for analysis). The result of the McNemar's test for birth rank was not statistically significant.

Of the 81 patients and matched controls whose charts listed maternal blood group 35 and 39 respectively had mothers with blood group A; this was not found to be significant. The maternal Rh factor was recorded for 86 matched pairs: the mothers of 9 patients and 15 control subjects were found to be Rh negative; this again was not significant.

The methods used for feeding are shown in Table II. The odds ratio for the infants with IHPS having been bottle-fed at the time of discharge from the nursery was 2.9 ( $p < 0.002$ ; confidence limits 1.3 and 6.6).

## Discussion

A preponderance of males has also been observed in other studies.<sup>5,6,8-10</sup> Bottle-feeding was used significantly more often in the IHPS group than in the control group at the time of discharge from the nursery. Furthermore, although 37 of the

infants with IHPS had been breast-fed at discharge from the nursery, only 15 were being exclusively breast-fed, and 11 were being breast-fed and fed by other means at the time of admission because of IHPS. We could not obtain comparable information on the control subjects.

Although the evidence of a genetic component to IHPS is strong<sup>8,13,14</sup> the recent changes in the incidence rates in different regions<sup>1-5</sup> suggest that environmental factors also play a role. The period studied here has been associated with significant changes in infant feeding practices.<sup>15</sup> Results of a study by Myres<sup>16</sup> and of the Nutrition Canada survey<sup>17</sup> showed that very few infants in Canada were breast-fed in the early 1970s. Since then there has been a marked increase in breast-feeding across Canada.<sup>18</sup> The preliminary findings of a survey being conducted by Ross Laboratories, Montreal, have demonstrated that in the prairie provinces the proportion of mothers who breast-feed in hospital increased from 46% in 1973 to 83% in 1986; the respective figures at 2 months after discharge were 29% and 74% (Suzanne Hendricks: personal communication, May 1986). Fig. 1 depicts the changes in the incidence rates of IHPS in Saskatchewan (based on the results of our other study in this issue) and in bottle-feeding practices in the prairie provinces (based on the preliminary findings of the Ross Laboratories survey). In Saskatchewan in 1980 Kilcher, Harasym and Havelock<sup>7</sup> found that 77% of mothers breast-fed at first and that 63% continued to breast-feed at 6 weeks. In a similar survey in 1977<sup>19</sup> the figures were 58% and 41% respectively.

There has also been a marked change in the

Table I — Results of matched-pair analysis of sex distribution of infants with infantile hypertrophic pyloric stenosis (IHPS) and control subjects

Sex; no. of infants with IHPS	Sex; no. of controls		
	Male	Female	Total
Male	41	36	77
Female	9	5	14
Total	50	41	91

\*Chi-squared = 15.0, 1 degree of freedom (df),  $p < 0.0001$ .

Table II — Results of matched-pair analysis of methods of feeding infants with IHPS and control subjects

Method; no. of infants with IHPS	Method; no. of controls		
	Breast	Bottle	Total
Breast	26	11	37
Bottle	32	22	54
Total	58	33	91

\*Chi-squared = 9.3, 1 df,  $p < 0.002$ .

practice of introducing solid foods at an early age. Tanaka, Yeung and Anderson<sup>20</sup> reported that during 1984 and 1985 in Toronto less than 5% of infants were receiving solids at 1 month of age, as compared with over 60% during 1977 and 1978.

Although these temporal changes in feeding practices are not necessarily causally related to the decline in the incidence of IHPS, the method of feeding may be a factor in the development of IHPS in a genetically susceptible child. Lynn<sup>21</sup> proposed that milk curds propelled through a spastic pyloric canal cause edema of the mucosa and submucosa and produce further narrowing of the canal. Webb, Lari and Dodge<sup>1</sup> argued that low-osmolar foods, such as those in the "humanized" formulas introduced in the 1970s in Britain, could lead to incoordination in gastric emptying and predispose to IHPS. They found that the increased incidence of IHPS occurred mainly among bottle-fed infants. Another possible explanation for the decreased occurrence of IHPS among breast-fed babies could be that this mode of feeding protects against an infectious trigger; however, attempts to demonstrate a viral cause have

failed,<sup>22</sup> and bacterial cultures of pyloric tissue have always been sterile.<sup>23</sup>

We could not confirm the findings of Dodge<sup>11,12</sup> that fewer mothers of affected infants had blood group A than other blood groups or those of Adelstein and Fedrick<sup>8</sup> that many of the mothers were Rh negative. However, the power of our study was too weak to rule out a significant difference; we would have had to include at least 259 matched pairs to measure a difference of 10% with 90% power. A similar problem with the power of the study makes our finding regarding birth rank open to challenge.

## Conclusions

We believe that this is the first case-control study of IHPS. The increased prevalence of bottle-feeding in the IHPS group at the time of discharge from the nursery suggests that the decrease in this condition observed in Saskatchewan in recent years is related in part to a decline in bottle-feeding.

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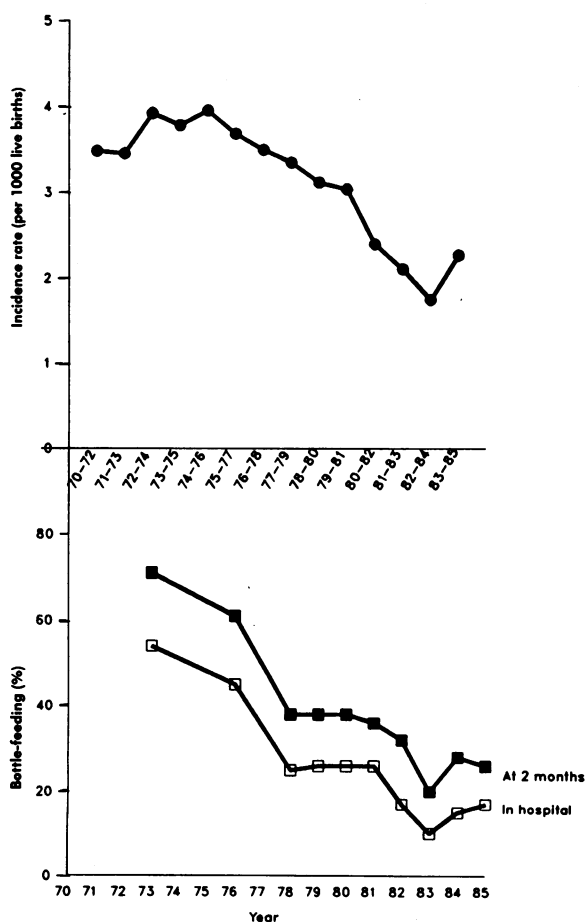


Fig. 1 — Three-year moving averages of incidence rates of infantile hypertrophic pyloric stenosis in Saskatchewan from 1970 to 1985 and proportion of mothers bottle-feeding in hospital (white squares) and 2 months after infant's discharge from nursery (black squares) during same period.

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**Drug Interactions:** No interactions have been observed between nizatidine and theophylline, chlorthalidone, lorazepam, lidocaine, and warfarin. Nizatidine does not inhibit the cytochrome P-450-linked drug-metabolizing enzyme system; therefore, drug interactions mediated by inhibition of hepatic metabolism are not expected to occur.

**Indications:** Nizatidine is indicated in the treatment of conditions where a controlled reduction of gastric acid secretion is required for ulcer healing and/or pain relief. Conditions include acute duodenal ulcer, acute benign gastric ulcer, and prophylactic use in duodenal ulcer.

**Contraindications:** Patients with known hypersensitivity to the drug.

**Precautions:** Gastric ulcer: Where gastric ulcer is suspected the possibility of malignancy should be excluded before therapy with nizatidine is instituted.

**Pregnancy and Lactation:** Safety of nizatidine during pregnancy has not been established. Reproduction studies performed in rats and rabbits at doses up to 300 times the human dose have revealed no evidence of impaired fertility or teratogenicity. If the administration of nizatidine is considered to be necessary, its use requires that the potential benefits be weighed against possible hazards to the patient and the fetus. Nizatidine is secreted in the milk of lactating rats, it is assumed to be secreted in human milk and caution should be exercised when nizatidine is administered to nursing mothers.

**Impaired Renal Function:** As nizatidine is excreted via the kidney, dosage should be adjusted in patients with moderately or severely impaired renal function (see Dosage).

**Hepatic Dysfunction:** Nizatidine is partially metabolized in the liver; however, in patients with uncomplicated hepatic dysfunction, disposition of nizatidine is similar to that of normal subjects.

**Geriatrics:** Ulcer healing rates in elderly patients are similar to those in younger age groups. The incidence rates of adverse events and laboratory test abnormalities are also similar to those seen in other age groups. Age alone is not an important factor in the disposition of nizatidine. Elderly patients may have reduced renal function (see Dosage).

**Children:** Safety and effectiveness of nizatidine in children has not been established.

**Adverse Effects:** In double-blind, placebo-controlled clinical trials in over 2,300 patients, the overall incidence of adverse events reported by patients treated with nizatidine was no greater than in the placebo group. Clinical pharmacology studies and controlled clinical trials showed no evidence of antiandrogenic activity or other adverse hormonal effects.

Headache, asthenia, chest pain, myalgia, abnormal dreams, somnolence, rhinitis, pharyngitis, cough and pruritus were reported with a slightly higher frequency by nizatidine-treated patients than by the placebo group. A relationship to nizatidine administration has not been established. Excessive sweating may be related to administration and has been reported by 1.1% of patients.

**Laboratory Values:** Patients treated with placebo and those receiving nizatidine therapy had mild, transient, asymptomatic elevations of transaminases; rare instances of marked elevations (>500 IU/L) occurred in nizatidine-treated patients, although causality has not been established. These abnormalities were asymptomatic and readily reversible after discontinuation of the drug. Other laboratory variables which were statistically different from placebo in the nizatidine-treated group, include serum cholesterol, serum uric acid, platelet count, serum creatinine, and white blood cell count. The clinical significance of these differences is not clear.

**Laboratory Tests:** False positive tests for urobilinogen with Multistix® may occur during therapy with nizatidine.

**Overdose:** Treatment: There is no clinical experience with deliberate overdosage of nizatidine in humans. Should overdosage occur, the usual measures to remove unabsorbed material from the gastrointestinal tract should be employed along with clinical monitoring and supportive therapy. The amount of nizatidine absorbed from the gastrointestinal tract can be reduced by activated charcoal.

**Dosage:** Duodenal or Gastric Ulcer: One 300 mg capsule or two 150 mg capsules once daily at bedtime. Treatment should be given for 4 to 8 weeks, but the duration of the treatment may be shortened if healing can be documented. Healing occurs within 4 weeks in most cases of duodenal ulcer.

**Maintenance Dosage in Duodenal Ulcer:** One 150 mg capsule once daily at bedtime for 6 to 12 months depending on the severity of the condition. Antacids may be given concomitantly if needed.

#### Dosage Adjustment in Renal Impairment:

Renal Function	Creatinine Clearance (mL/min)	Dosage	
		Acute	Maintenance
Normal	>50	300 mg/day	150 mg/day
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