

Iron poisoning in young children: association with the birth of a sibling

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Abstract

Background: Iron is a leading cause of death due to poisoning in young children. Because perinatal iron therapy is common, the presence of these tablets, which have a candylike appearance, in the home may pose a hazard to a mother's other young children. We explored the association between iron poisoning in young children and the birth of a sibling.

Methods: We conducted a population-based case-control study linking health care databases in Ontario. Health care records for the mothers of children less than 3 years of age admitted to hospital with iron poisoning between Apr. 1, 1991, and Mar. 31, 2000, were compared with those for the mothers of age- and sex-matched control children without iron poisoning.

Results: We studied records for 40 children admitted to hospital for iron poisoning. Seventeen cases (42%) occurred within a year (before or after) a sibling's birth. Children whose mothers had given birth to a sibling were almost twice as likely as children whose mothers had not given birth to a sibling to be admitted for iron poisoning within 6 months of birth (adjusted odds ratio [OR] 1.9, 95% confidence interval [CI] 0.9 to 3.9). The postpartum year was associated with a consistently elevated risk, including an almost 4-fold increase in the risk of iron poisoning during the first postpartum month (adjusted OR 3.6, 95% CI 0.8 to 16.5).

Interpretation: Pregnancy is a major risk factor for iron poisoning in young children, and the period immediately after delivery is associated with the greatest risk. Almost half of all hospital admissions for iron poisoning in young children could be prevented by keeping iron supplements safely out of reach in the year before and after the birth of a sibling.

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Iron tablets are available without a prescription and may be perceived as health supplements with minimal toxic potential.¹ When taken in excess, however, iron is far more dangerous than most prescription medications.² As few as 10 ferrous sulfate tablets (total of 600 mg elemental iron) can kill a small child.^{3,4} Indeed, iron is one of the leading causes of poisoning-related death in children.⁴⁻¹⁰

Many of the millions of women who give birth each year have other children at home. We hypothesized that pediatric iron poisoning might be associated with the birth of a sibling for several reasons. Treatment with iron during and

after pregnancy is common,^{11,12} and typical prenatal products contain 60 mg of elemental iron per tablet. To promote adherence, the container may be left in a visible (and therefore accessible) area of the home. Finally, children may be attracted by the resemblance of some iron tablets to coloured candy (Fig. 1).^{2,4,13}

We sought to determine if the birth of a sibling was associated with an increase in risk of iron poisoning for other young children in the home.

Methods

We used a population-based case-control design linking multiple administrative databases in Ontario. The study interval encompassed the 13-year period from Apr. 1, 1988, to Mar. 31, 2001, representing 9 complete years for case identification (1991 to 2000) and 13 complete years for maternal health care analysis (1988 to 2001). The study was approved by the Institutional Review Board of Sunnybrook and Women's College Health Sciences Centre.

We used the discharge abstract database of the Canadian Institute for Health Information to identify all hospital admissions for iron poisoning (International Classification of Diseases, 9th revision [ICD-9], code 964.0) in children under 3 years of age occurring between Apr. 1, 1991, and Mar. 31, 2000. Children under 3 years of

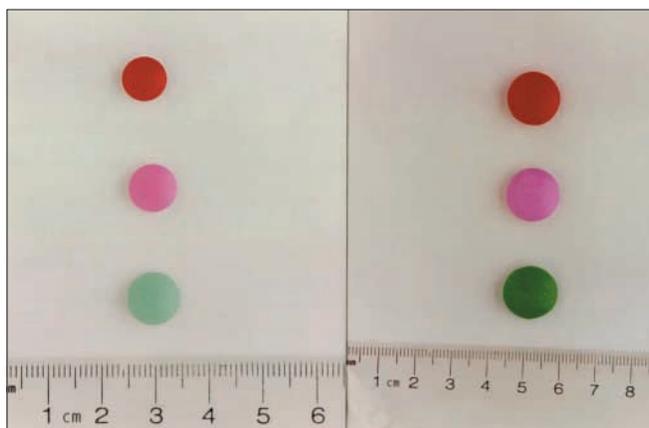


Fig. 1: Resemblance of iron tablets to candy. At left, from top, ferrous sulfate 300 mg, ferrous fumarate 200 mg and ferrous gluconate 300 mg. These tablets contain 60, 66 and 36 mg of elemental iron respectively. Ingestion of as few as 10 ferrous sulfate tablets has been fatal in children.^{3,4} At right, popular candy-coated chocolates with similar appearance.

age account for almost all serious cases of pediatric iron poisoning.⁴ For each case, we randomly selected 50 control children, matched on birth date and sex, from the general population of Ontario using the Ontario Registered Persons Database (RPDB). We chose a 50:1 matching ratio to ensure cell sizes of at least 5 for exposures with a prevalence rate of 10% or higher to reduce bias due to small samples in the conditional logistic regression.¹⁴

We determined the mother of each child by identifying the woman who delivered a newborn on the child's date of birth at the health care facility where the child was born. The mother-child relationship was confirmed by the exact concordance of maternal and newborn postal codes in the RPDB. The health care record of each child's mother was then analyzed over a 13-year period (Apr. 1, 1988, to Mar. 31, 2001) to identify sibling deliveries. Socioeconomic status for each mother was determined indirectly from the home postal code, according to the median household income for that area as determined by the 1996 population census of Canada.

We defined exposure as the delivery of a sibling, and the date of delivery served as the index date for exposure. If a mother delivered 2 or more children within a year (before or after) the poisoning date, the most proximate delivery served as the date of exposure. To test whether our findings extended to another common childhood poisoning, we replicated our analyses in children less than 3 years of age admitted to hospital with acetaminophen poisoning (ICD-9 code 965.4) during the same period.

The primary analysis considered iron poisoning within 6 months of delivery of a sibling. Sensitivity analyses examined admissions within 12 months and within 3 months of a delivery. Intervals in the postpartum period (1, 3 and 12 months) were then compared with corresponding intervals in the antepartum period. We used Mantel-Haenszel methods to estimate the odds ratio of iron poisoning at each interval, and we used conditional logistic regression to adjust for maternal age and socioeconomic status, both of which are potential predictors of childhood injury.¹⁵⁻¹⁹

Results

We identified 49 admissions for iron poisoning in children younger than 3 years, and 41 of these children could be linked to their mothers. We excluded one 60-day-old child whose poisoning could not have represented independent ingestion. The mean age for the 40 remaining cases was 2.1 years; 30 (75%) of the children were boys.

Almost half (17 [42%]) of the children with iron poisoning had a sibling born within a year of their admission. The corresponding sibling birth rate in the control group was 27%. The adjusted odds ratio of iron poisoning within 6 months of a sibling's delivery was 1.9 (95% confidence interval [CI] 0.9 to 3.9). Sensitivity analyses revealed a somewhat higher risk of iron poisoning nearer delivery (Table 1). The risk was consistently elevated throughout the postpartum period, with an almost 4-fold increase in the first postpartum month (Table 1).

We identified 162 children admitted to hospital for acetaminophen poisoning during the same period and also found an increase in the risk of this poisoning within 6 months of a sibling's delivery (Table 2). However, we did not find a consistently elevated risk of acetaminophen poisoning nearer delivery or throughout the postpartum period.

Consistent with previous research,²⁰ we found that advancing maternal age was associated with a lower risk of hospital admission for both types of poisoning. Every 10-year increase in maternal age was accompanied by an almost 2-fold reduction in the risk of iron poisoning (odds ratio 0.45, 95% CI 0.24 to 0.87) and acetaminophen poisoning (odds ratio 0.52, 95% CI 0.38 to 0.71). Median household income was not associated with hospital admission for either type of poisoning.

Table 1: Hospital admissions for iron poisoning in relation to birth of a sibling

Analysis*	Birth of sibling within 1 year; no. (and %) of children		Odds ratio (and 95% CI)	
	Cases <i>n</i> = 40	Controls <i>n</i> = 2000	Crude†	Adjusted‡
Primary analysis (within 6 months)	10 (25)	284 (14)	2.0 (1.0-4.2)	1.9 (0.9-3.9)
Secondary analyses§				
<i>Within 12 months</i>	17 (42)	537 (27)	2.0 (1.1-3.8)	1.8 (1.0-3.5)
<i>Within 3 months</i>	6 (15)	124 (6)	2.7 (1.1-6.5)	2.6 (1.1-6.3)
<i>Poisoning before delivery</i>				
1 month	0	17 (1)	NA	NA
3 months	2 (5)	57 (3)	1.8 (0.4-7.6)	2.0 (0.5-8.6)
12 months	5 (12)	282 (14)	0.9 (0.3-2.2)	0.8 (0.3-2.1)
<i>Poisoning after delivery</i>				
1 month	2 (5)	26 (1)	4.0 (0.9-17.4)	3.6 (0.8-16.5)
3 months	4 (10)	68 (3)	3.2 (1.1-9.1)	2.7 (0.9-7.9)
12 months	12 (30)	255 (12)	2.9 (1.5-5.8)	2.7 (1.3-5.5)

Note: CI = confidence interval, NA = not applicable.

*In this context, "within" means poisoning occurred in the specified period before or after the birth of a sibling.

†Mantel-Haenszel estimates of odds ratio.

‡Adjusted for maternal age and median household income.

§Shorter time intervals are subsets of longer intervals.

Interpretation

Using population-based health care records we identified an association between hospital admission for iron poisoning in young children and the birth of a sibling. This provides empirical evidence implicating perinatal iron therapy as a risk factor for childhood iron poisoning. We also found a significant but inconsistent association between acetaminophen poisoning and birth of a sibling. Our findings support the previously hypothesized relation between household stressors and childhood poisoning.²⁰

The risk of iron poisoning followed a plausible temporal gradient, with a particularly high risk in the immediate postpartum period, when parents may be fatigued and distracted by the needs of a newborn. However, lack of attention to other children in the household does not fully explain this finding, because a similar phenomenon was not observed for acetaminophen. Indeed, the point estimates of the odds ratio of iron poisoning were consistently greater than those for acetaminophen poisoning. The difference in risk may reflect the more regular use of iron products in the perinatal period, the misperception that iron is a non-toxic substance or the resemblance of some iron tablets to candy (Fig. 1).

The almost 4-fold higher risk of iron poisoning immediately after delivery may reflect the household dynamics of caring for a newborn. Alternatively, it may relate to the different nature of maternal iron therapy after delivery, when treatment may be specifically intended to treat postpartum anemia. Whereas daily prenatal multivitamins are typically large, unappealing tablets, postpartum anemia is more likely to be treated with colourful

single-agent preparations taken several times a day.

Some limitations of this research should be noted. We studied only children with poisoning who were admitted to hospital; presumably these represent more serious cases, but less serious episodes were not available for analysis. The sample sizes in our analyses were relatively small, and many of the estimates are imprecise. Finally, we have no direct measure of socioeconomic status, and our databases did not identify adoptions, home deliveries or births that took place outside Ontario, relatively infrequent events that might cause our analysis to underestimate risks.

Childhood poisonings are preventable, and suggestions to prevent iron poisoning have been published previously.² Calls to modify the candylike appearance of iron tablets have been issued for more than half a century.^{2,13,21,22} However, access to a poison is a prerequisite for poisoning, and children who cannot gain access to iron cannot poison themselves with it. Physicians and pharmacists can assume an active role in the prevention of childhood iron poisoning by reminding parents about the drug's potential toxicity.² The most opportune moment for this intervention may be at the time iron is recommended.²³

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Table 2: Hospital admissions for acetaminophen poisoning in relation to birth of a sibling

Analysis*	Birth of sibling within 1 year; no. (and %) of children		Odds ratio (and 95% CI)	
	Cases <i>n</i> = 162	Controls <i>n</i> = 8100	Crude†	Adjusted‡
Primary analysis (within 6 months)	35 (22)	1156 (14)	1.7 (1.1–2.4)	1.5 (1.0–2.2)
Secondary analyses§				
<i>Within 12 months</i>	59 (36)	2148 (27)	1.6 (1.2–2.2)	1.4 (1.0–1.9)
<i>Within 3 months</i>	10 (6)	610 (8)	0.8 (0.4–1.5)	0.7 (0.4–1.4)
<i>Poisoning before delivery</i>				
1 month	2 (1)	126 (2)	0.8 (0.2–3.2)	0.8 (0.2–3.1)
3 months	5 (3)	305 (4)	0.8 (0.3–2.0)	0.8 (0.3–1.9)
12 months	23 (14)	1027 (13)	1.1 (0.7–1.8)	1.0 (0.7–1.6)
<i>Poisoning after delivery</i>				
1 month	3 (2)	103 (1)	1.5 (0.5–4.7)	1.3 (0.4–4.2)
3 months	3 (2)	202 (2)	0.7 (0.2–2.3)	0.7 (0.2–2.1)
12 months	36 (22)	1123 (14)	1.8 (1.2–2.6)	1.6 (1.1–2.3)

*In this context, "within" means poisoning occurred in the specified period before or after the birth of a sibling.

†Mantel-Haenszel estimates of odds ratio.

‡Adjusted for maternal age and median household income.

§Shorter time intervals are subsets of longer intervals.

Contributors: Dr. Juurlink conceived of the project and, along with Dr. Redelmeier, collected the data. Drs. Juurlink, Tenebein, Koren and Redelmeier contributed to the study design and the analysis and interpretation of the data. Dr. Juurlink wrote the first draft of the manuscript, and all authors contributed to successive critical revisions.

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References

1. Anderson AC. Iron poisoning in children. *Curr Opin Pediatr* 1994;6(3):289-94.
2. Tenenbein M, Rodgers GC. The four A's of decreasing the toll of childhood iron poisoning deaths. *Arch Fam Med* 1994;3:754-5.
3. Reynolds LG, Klein M. Iron poisoning — a preventable hazard of childhood. *S Afr Med J* 1985;67(17):680-3.
4. Fine JS. Iron poisoning. *Curr Probl Pediatr* 2000;30(3):71-90.
5. Shannon M. Ingestion of toxic substances by children. *N Engl J Med* 2000;342(3):186-91.
6. Litovitz TL, Felberg L, White S, Klein-Schwartz W. 1995 annual report of the American Association of Poison Control Centers Toxic Exposure Surveillance System. *Am J Emerg Med* 1996;14(5):487-537.
7. Litovitz TL, Smilkstein M, Felberg L, Klein-Schwartz W, Berlin R, Morgan JL. 1996 annual report of the American Association of Poison Control Centers Toxic Exposure Surveillance System. *Am J Emerg Med* 1997;15(5):447-500.
8. Litovitz TL, Klein-Schwartz W, Dyer KS, Shannon M, Lee S, Powers M. 1997 annual report of the American Association of Poison Control Centers Toxic Exposure Surveillance System. *Am J Emerg Med* 1998;16(5):443-97.
9. Litovitz TL, Klein-Schwartz W, Caravati EM, Youniss J, Crouch B, Lee S. 1998 annual report of the American Association of Poison Control Centers Toxic Exposure Surveillance System. *Am J Emerg Med* 1999;17(5):435-87.
10. Litovitz T, Manoguerra A. Comparison of pediatric poisoning hazards: an analysis of 3.8 million exposure incidents. A report from the American Association of Poison Control Centers. *Pediatrics* 1992;89(6 Pt 1):999-1006.
11. Menard MK. Vitamin and mineral supplement prior to and during pregnancy. *Obstet Gynecol Clin North Am* 1997;24(3):479-98.
12. Beard JL. Effectiveness and strategies of iron supplementation during pregnancy. *Am J Clin Nutr* 2000;71(5 Suppl):1288S-1294S.
13. Toddler deaths resulting from ingestion of iron supplements — Los Angeles, 1992–1993. *MMWR Morb Mortal Wkly Rep* 1993;42(6):111-3.
14. Greenland S, Schwartzbaum JA, Finkle WD. Problems due to small samples and sparse data in conditional logistic regression analysis. *Am J Epidemiol* 2000;151(5):531-9.
15. Hippisley-Cox J, Groom L, Kendrick D, Coupland C, Webber E, Savelyich B. Cross sectional survey of socioeconomic variations in severity and mechanism of childhood injuries in Trent 1992-7. *BMJ* 2002;324(7346):1132-4.
16. Laing GJ, Logan S. Patterns of unintentional injury in childhood and their relation to socio-economic factors. *Public Health* 1999;113(6):291-4.
17. Faelker T, Pickett W, Brison RJ. Socioeconomic differences in childhood injury: a population based epidemiologic study in Ontario, Canada. *Inj Prev* 2000;6(3):203-8.
18. Bobak M, Pikhart H, Koupilova I. Maternal socioeconomic characteristics and infant mortality from injuries in the Czech Republic 1989-92. *Inj Prev* 2000;6(3):195-8.
19. Scholer SJ, Mitchel EF, Jr, Ray WA. Predictors of injury mortality in early childhood. *Pediatrics* 1997;100(3 Pt 1):342-7.
20. Sibert R. Stress in families of children who have ingested poisons. *BMJ* 1975;3(5975):87-9.
21. Spencer I. Ferrous sulphate poisoning in children. *BMJ* 1951;2:112-7.
22. Berkovitch M, Matsui D, Lamm SH, Rosa F, Koren G. Recent increases in numbers and risk of fatalities in young children ingesting iron preparations. *Vet Hum Toxicol* 1994;36(1):53-5.
23. Battle CU, Miller G. Acute iron poisoning: obstetrician's opportunity. *Am J Obstet Gynecol* 1970;108(3):485-6.

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