Ineffectiveness of dietary folic acid supplementation on the incidence of lipomyelomeningocele: pathogenetic implications

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Object. Periconceptual folic acid supplementation is effective in myelomeningocele prevention. The relationship between folic acid and lipomyelomeningocele (LMM) and the overall incidence of this occult form of spina bifida has never been studied. The objectives of this study were to determine the impact of dietary folic acid supplementation on the incidence of LMM and to measure its overall incidence.

Methods. In a retrospective population-based study the authors calculated the incidence of LMM in Nova Scotia between 1985 and 2001. Because of changes in public policy during this period, there are three intervals defined in relation to the treatment of the food supply with folic acid: 1) prior to folic acid fortification (1985–1994); 2) postsupplementation but prefortification (1995–1998); and 3) postfortification.

The overall incidence of LMM in Nova Scotia between 1985 and 2001 was 16 per 100,000 live births or one case per 6121 live births. Its incidence between 1985 and 1994 was 15 per 100,000 live births, and between 1995 and 1998 it was 12 per 100,000 live births (relative risk [RR] 0.82, 95% confidence interval [CI] 0.31–2.22; p = 0.7). Between 1999 and 2001, the incidence of LMM was 29 per 100,000 live births, which was not significantly different from that between 1995 and 1998 (RR 2.41, 95% CI 0.79–7.36; p = 0.11) or between 1985 and 1994 (RR 1.98, 95% CI 0.86–4.56; p = 0.1).

Conclusions. The overall incidence of LMM between 1985 and 2001 in Nova Scotia was 16 per 100,000 live births and has not been reduced by dietary folic acid supplementation. This finding provides epidemiological evidence that the embryogenesis of LMM is fundamentally different from that of myelomeningocele.

KEY WORDS • spina bifida occulta • epidemiology • folic acid • lipomyelomeningocele • pediatric neurosurgery

A N LMM is a congenital lesion that is generally considered a form of OSD. This lesion consists of a caudally located and dysmorphic conus medullaris infiltrated by fat. This fat is continuous with a skin-covered subcutaneous lipoma through dural, osseous, and fascial defects and is typically found in the lumbosacral region.14,15,17

There is now ample evidence demonstrating that periconceptual folic acid supplementation is effective in preventing open NTDs.3,6,10 In 1994, the Canadian Task Force on Periodic Health Examination recommended that women of childbearing age increase their consumption of folic acid through diet or supplementation to 0.4 mg/day beginning 1 month before pregnancy and ending at the start of the second trimester.2 Subsequently, the US Food and Drug Administration and Health Canada ordered fortification of all enriched grain products. Fortification was to be implemented no later than January 1, 1998, in the US4 and November 5, 1998, in Canada.5 In a recent study investigators from our institution demonstrated that folic acid fortification has indeed been effective in reducing the incidence of open NTDs.16

The relationship between open NTDs and occult forms of spina bifida including LMM is uncertain.7 The role of dietary folic acid supplementation in the prevention of OSD has never been studied. Finally, the overall incidence of LMM is not known with certainty.14

The objectives of this study were to determine the overall population-based incidence of LMM and to measure the impact of dietary folic acid supplementation and fortification on the incidence of this form of OSD.

Clinical Material and Methods

A population-based retrospective study design was used. Information concerning the total number of live births was obtained from the Division of Vital Statistics of the Department of Service and Municipal Relations of the Province of Nova Scotia (Halifax, Nova Scotia, Canada). Nova Scotia’s population in 2001 was 942,691.1

Abbreviations used in this paper: CI = confidence interval; LMM = lipomyelomeningocele; NTD = neural tube defect; OSD = occult spinal dysraphism; RR = relative risk.
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graphically, the province consists of a peninsula attached to mainland Canada by a narrow isthmus. Pediatric neurosurgery services in Nova Scotia are provided at a single institution, the IWK Health Centre in Halifax. All patients in whom LMM is diagnosed are seen at this center, and findings in these cases are entered into the Spina Bifida Clinic database. This database began recording all diagnoses of spinal dysraphism at the IWK Health Centre in 1985 and it was used to identify our LMM cases. The patient’s date of birth was used as the index year in which the case occurred.

Inclusion criteria required the diagnosis of LMM confirmed by operative findings. Patients were included if they were born in Nova Scotia between January 1, 1985, and December 31, 2001.

Incidence rates and CIs were calculated using the total number of patients born with an LMM during a given period and the total number of live births during that epoch. We considered the years 1985 to 1994 to be the period prior to the recommendation of folic acid supplementation; the years 1995 to 1998 to be the period during which dietary supplementation was being recommended, but prior to its fortification in the food supply; and finally, the years 1999 to 2001 to be the period after fortification was instituted.

Statistical calculations were performed using SPSS for Windows (version 11.0.1; SPSS, Inc., Chicago, IL). Descriptive statistics were tabulated, and comparisons of means between groups were performed and expressed as RR ratios with 95% CIs. Chi-square analysis was used to calculate statistical significance. Results were considered significant at a probability value less than 0.05.

Results

During the overall study period (1985–2001), there were 31 cases of LMM identified and 189,752 live births recorded in the province of Nova Scotia, yielding an overall incidence of 16 per 100,000 live births, or one case per 6121 live births (Table 1). In this cohort, 20 (65%) of 31 patients were female.

The mean annual incidence of LMM between 1985 and 1994 was 15 per 100,000 live births, and between 1995 and 1998 it was 12 per 100,000 live births (RR 0.82, 95% CI 0.31–2.22; p = 0.7). During the period from 1999 to 2001, the mean annual incidence of LMM was 29 per 100,000 live births, which was not significantly different from that during the period 1995 to 1998 (RR 2.41, 95% CI 0.79–7.36; p = 0.11) or from 1985 to 1994 (RR 1.98, 95% CI 0.86–4.56; p = 0.1). There was in fact a trend toward increasing incidence of LMM over time, which did not reach statistical significance.

Discussion

In the present study we demonstrated for the first time that public policies encouraging periconceptual folic acid supplementation and eventually mandating fortification of the food supply have not had a significant impact on the incidence of LMM. The relationship between occult forms of spina bifida and open NTDs remains uncertain.7 The embryogenesis of LMM is not known with certainty but may involve premature focal dysjunction of neural ectoderm from cutaneous ectoderm during the process of primary neurulation.13,14 This would allow migration of periaxial mesoderm into the developing neural tube and lead to posterior myeloschisis. The finding that dietary folic acid supplementation does not reduce the incidence of LMM is evidence that the pathogenesis of LMM is fundamentally different from that of myelomeningocele.

The overall incidence of LMM in Nova Scotia during the study period (1985–2001) was 16 per 100,000 live births. To our knowledge, this is the first population-based study to calculate the incidence of this condition. Other authors have estimated the incidence as approximately one case per 4000 births.11,14 This estimate appears to be based on the known incidence of myelomeningoceles (one case/1000 births) coupled with the observation that LMM seemed to occur with an incidence of 25% that of myelomeningoceles.17 The preponderance of affected female patients in our study has been noted in previous series.8,11

12,17 Documentation of the epidemiology of LMM is likely to be useful to future investigators conducting studies of this condition.

The strengths of this study include Nova Scotia’s unique geography and the nature of healthcare delivery in this province. Accurate population statistics are readily available, and all pediatric neurosurgery services are located at a single institution. This provides us with the unique opportunity of obtaining accurate population-based information. The limitation of this study is that identification of LMM cases was dependent on patient referral to neurosurgical care. It is possible that some asymptomatic patients are never referred for neurosurgical attention. Improving access to magnetic resonance imaging and increasing awareness of this problem may be responsible for the trend toward the higher incidence of LMM over time noted in the present cohort of patients.

Conclusions

The overall incidence of LMM in Nova Scotia between 1985 and 2001 was 16 per 100,000 live births (one case per 6121 live births). This incidence has not been reduced by public policies encouraging dietary folic acid supple-
mentation or by mandatory fortification of the food supply. That the incidence of LMM has not been reduced following dietary folic acid supplementation provides epidemiological evidence to support the view that its pathogenesis is fundamentally different from that of myelomeningocele.

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