Aetiology

Review: schizophrenia is associated with premature rupture of membranes, gestational age <37 weeks, and use of an incubator or resuscitation

Geddes JR, Verdoux H, Takei N, et al. *Schizophrenia and complications of pregnancy and labor: an individual patient data meta-analysis*. *Schizophr Bull* 1999;25:413–23.

QUESTION: What are the associations between schizophrenia and specific complications of pregnancy and labour that, individually, are of low prevalence?

Data sources

Published case control studies were identified by a Medline search, by scanning the bibliographies of relevant papers and previous review articles, and by contacting researchers.

Study selection

Studies were selected if they had a case control design comparing patients with schizophrenia with normal controls and if the Lewis-Murray scale was or could be applied.

Data extraction

Published and unpublished individual patient data were obtained for those patients with a Research Diagnostic Criteria, ICD-9, or DSM-III-R criteria diagnosis of schizophrenia and for normal controls. Data were collected on 15 specific obstetric complications rated by the scale of Lewis and Murray.

Main results

12 studies met the selection criteria. Raw data were obtained on 700 patients with schizophrenia and 835 normal controls. No evidence of heterogeneity was noted among study specific estimates for any of the abnormalities of pregnancy and labour, except for pre-eclampsia. Associations were detected between schizophrenia and premature rupture of membranes, gestational age <37 weeks, and use of resuscitation or incubator (table). A borderline association existed between schizophrenia and birth weight <2500 g (table). No association existed between these complications and sex.

Conclusions

Premature rupture of membranes, prematurity, and use of an incubator or resuscitation are risk factors for the

subsequent development of schizophrenia. A borderline association also exists between schizophrenia and birth weight <2500 g.

COMMENTARY

It seems obvious that the associations found in the review by Geddes *et al* are all related to aspects of immaturity of the fetus. The suggestion that cases of schizophrenia could be prevented by improved perinatal care might be true, but how to accomplish this is not easy to understand. How also can we accommodate results from high risk studies, such as the finding that the effect of birth complications is related to genetic risk of schizophrenia?¹ What about the conflicting evidence from child schizophrenia, with 1 study showing an association with obstetric complications and another showing no such association?^{2,3} What about conflicting results from 2 recent, population based, case control studies?^{4,5} In the first study, indices of immaturity and brain damage were strongly related to schizophrenia.⁴ In the second, larger study, this relation was only found for boys.⁵ Instead, multiparity and maternal bleeding during pregnancy seemed to be significant risk factors.

Research into risk factors for possibly aetiologically heterogeneous diseases has not been a success story. The search for environmental risk factors for schizophrenia is no exception. Results of aetiological studies may not help the practising clinician today, but may help us to understand the disorder and may point to interventions in the future.

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- 2 Matsumoto H, Takei N, Saito H, *et al*. Childhood-onset schizophrenia and obstetric complications: a case-control study. *Schizophr Res* 1999;38:93–9.
- 3 Nicolson R, Malaspina D, Giedd JN, *et al*. Obstetrical complications and childhood-onset schizophrenia. *Am J Psychiatry* 1999;156:1650–2.
- 4 Jones PB, Rantakallio P, Hartikainen AL, *et al*. Schizophrenia as a long-term outcome of pregnancy, delivery, and perinatal complications: a 28-year follow-up of the 1966 north Finland general population birth cohort. *Am J Psychiatry* 1998;155:355–64.
- 5 Hultman CM, Sparén P, Takei N, *et al*. Prenatal and perinatal risk factors for schizophrenia, affective psychosis, and reactive psychosis of early onset: case-control study. *BMJ* 1999;318:421–6.

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Association of individual complications of pregnancy and labour with schizophrenia

Complications	Number of studies	Weighted average odds ratio (95% CI)	p Value	Attributable fraction (CI)
Premature rupture of membranes	10	3.1 (1.4 to 7.0)	0.006	0.07 (0.03 to 0.12)
Gestational age <37 weeks	5	2.4 (1.1 to 5.3)	0.023	0.05 (0.02 to 0.07)
Incubator or resuscitation	11	2.2 (1.4 to 3.5)	0.001	0.06 (0.03 to 0.09)
Birth weight <2500 g	12	1.5 (1.0 to 2.3)	0.056	0.03 (0.0 to 0.07)