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Does avoidance of breast feeding reduce mother-to-infant transmission of hepatitis C virus infection?

Report by

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You are the doctor or midwife reviewing a newborn infant whose mother is infected with hepatitis C virus (HCV; but not infected with human immunodeficiency virus (HIV)). She wishes to breast feed but is concerned about whether this would affect the risk of her infant acquiring HCV infection. You would like your advice to be based on the best evidence available.

Structured clinical question

In newborn infants of mothers with [HCV] infection [patients], does avoidance of breastfeeding [intervention] reduce mother-to-infant transmission of HCV [outcome]?

Search strategy and outcome

Medline 1966–2006 and EMBASE 1980–2006 (using OVID interface).

The Cochrane Library [2006, issue 3].

Search terms: hepatitis “C” (MeSH term) AND “breastfeeding”/“breastmilk” (MeSH term) AND “transmission, vertical” (keyword).

We found 44 articles in Medline and EMBASE and none in The Cochrane Library. Altogether, 33 articles were irrelevant. All of the relevant articles were observational studies (cohort studies or case-series). We did not find any systematic reviews or randomised controlled trials.

Eight of the observational studies were small with data reported for less than about 100 mother–infant pairs.^{1–8} Three were large cohort multicentre studies undertaken by clinical networks.^{9–11} Table 2 describes the large cohort studies.

Commentary

HCV infection is a major worldwide cause of chronic liver disease, including hepatic fibrosis, cirrhosis and hepatocellular carcinoma.^{12 13} Mother-to-infant transmission is now the principal route of infection in childhood. The rate of mother to infant transmission of HCV is about 6%.^{14 15}

HCV is a bloodborne virus but has been detected in colostrum and breast milk in low levels.³ We wished to determine whether any evidence exists showing that avoiding breast feeding reduces the risk of mother-to-infant HCV infection. We did not find any randomised controlled trials of this intervention. We did find several observational studies. Most of them were small single-centre studies (less than about 100 mother–infant pairs) and therefore underpowered to assess whether the transmission was affected. We found three larger multicentre cohort studies in which a total of 1854 mother–infant pairs participated.^{9–11} None of these studies found a relevant

Table 2 Large cohort studies

Author, date and country	Patient group	Study type (level of evidence)	Outcome	Key results	Study weaknesses
European Paediatric HCV network 2001 Europe, 7 countries	971 mother–child pairs. Mothers seropositive for HCV but not for HIV. Breastfeeding status known in 887 pairs. 319 infants were breast fed.	Observational cohort. (2b)	HCV infection in children diagnosed by PCR and antibody testing on follow-up until 18 months.	Proportion of infected children among those who breast fed (6.6%) was not statistically significantly different to that among the non-breast fed infants (6.3%).	Maternal viremic load (quantitative PCR) and clinical status (symptomatic liver disease or not) not known.
Gibb 2000 UK and Eire	441 mother–child pairs (but 22 mothers known to be coinfecting with HIV and HIV status not known in 91 mothers). Breast feeding status known in 414 pairs. 59 infants were breast fed.	Observational cohort. (2b)	HCV infection in children diagnosed by PCR and antibody testing on follow-up until 24 months.	Proportion of infected children among those who breast fed (7.7%) was not statistically significantly different to that among the non-breast fed infants (6.7%).	Maternal viremic load (quantitative PCR) not known in most cases. Unknown HIV status in 20% of mothers.
Resti <i>et al</i> 1998 Italy	442 mother–child pairs. Follow-up of infants of 275 mothers who were HCV RNA positive (and HIV negative). Breast feeding status known for all infants: 87 were breast fed.	Observational cohort (2b)	HCV infection in children diagnosed by PCR and antibody testing on follow-up until 24 months	Proportion of infected children among those who breast fed (7%) was not statistically significantly different to that among the non-breast fed infants (4%).	Drop out: 39 pairs

HCV, hepatitis C virus; PCR, polymerase chain reaction.

difference in the rate of transmission between infants fed with breast milk and those fed with formula. This is consistent with evidence from other cohort studies which indicate that most infants who acquire HCV infection do so in utero or in the peripartum period.^{11 16}

The studies were all undertaken in European countries during the past 10 years. They were generally of good methodological quality with valid definitions of inclusion criteria and outcomes and near-complete cohort follow-up. Only one of the studies specifically examined the effect of breast feeding avoidance in mothers with HCV viraemia. Because transmission from a mother with no RNA detectable at delivery is extremely rare,¹⁷ this may have been a confounding variable in the other studies where the HCV viral status was not assessed. We specifically aimed at evaluating the evidence in women who were not coinfecting with HIV. This was possible for two studies but not for the third where 5% of participants were HIV positive. A subgroup analysis of mothers who were not infected with HIV was not possible. HIV coinfection is a contraindication to breast feeding in high-income countries.

CLINICAL BOTTOM LINE

- Approximately 6% of babies born to hepatitis C (HCV) infected mothers will develop HCV infection (grade A).
- Avoidance of breast feeding is not an effective intervention for preventing mother-to-infant transmission of HCV (grade B).

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Should children under treatment for juvenile idiopathic arthritis receive flu vaccination?

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A 12-year-old girl with rheumatoid factor negative polyarticular juvenile idiopathic arthritis (JIA) attends an outpatient appointment with her mother. Her disease has been controlled by subcutaneous methotrexate, but over the past month, she has stopped taking medication because of adverse effects—in particular, nausea and vomiting after administration of methotrexate injection. On examination, she is found to have a flare of her disease with 10 swollen inflamed joints and early morning stiffness for 2 h/day. You apply for funding for anti-tumour necrosis factor (TNF) treatment and, in the meantime, plan to treat her disease flare with a course of prednisolone. On discussion during the consultation, her mother tells you that she has had a letter from the general practitioner asking her child to attend for a flu vaccination and asks your advice.

Structured clinical questions

Do children with JIA [patient] who become infected with influenza [intervention] have a more prolonged illness [outcome] than healthy children [comparison]? In children with JIA [patient], should flu vaccinations be given [intervention] to prevent flu [outcome]? Do children with JIA respond to flu vaccination [does the vaccination have the required effect]? Does flu vaccination [intervention] cause a flare of JIA [adverse event]?

Search strategy and outcomes

Search terms used for all searches (search date 13 September 2006) were: {vaccine OR vaccination} AND {arthritis}, AND {child OR childhood OR children or juvenile} AND {influenza}.

Primary sources: Medline via Pubmed; 20 papers identified, 3 relevant. Embase: 58 articles identified, 6 relevant to vaccination but only 3 specific to influenza vaccine in JIA (table 3).

Secondary sources: Cochrane Library. Nil relevant. One review identified for influenza vaccination in healthy children (2006), but not for children immunosuppressed by disease or drugs. TRIP: 59 evidence-based articles identified, 1 relevant. Twelve guidelines were identified, 1 of which was relevant. Ten query answers, 3 e-textbooks and 1 patient information leaflet were identified, but none of these were relevant. Seventy Medline articles were identified through TRIP, but duplicated primary searches.

Commentary

Currently, there is variation in practice regarding immunisation of children with JIA owing to a lack of available published evidence.^{4 5} Existing guidelines suggest that influenza may cause severe disease in patients immunocompromised by disease or drugs, and predisposes to bacterial infection.^{6–9} It is therefore recommended that, each autumn, influenza vaccination should be given widely to this patient population, their family contacts and their care givers. The decision as to whether children with JIA should be vaccinated against influenza currently rests with individual doctors who balance the risk of influenza and influenza vaccination in individual patients with JIA. The present threat of an influenza pandemic,