An effective and feasible approach to prevention of primary cytomegalovirus infection in pregnancy

In the absence of a cytomegalovirus (CMV) vaccine, other strategies for prevention of primary infection in pregnancy should be considered. Behavioural interventions have been reported to significantly decrease seroconversion rate among seronegative pregnant women. We report here on a recently completed controlled study in which seronegative women at high risk of infection because of close contacts with children <36 months, were identified and informed about risky and protective behaviours. Informed women seroconverted at a significantly lower rate than non-informed women.

When in 1974 Elek and Stern published their paper with the committing title ‘Development of a vaccine against mental retardation caused by cytomegalovirus infection in utero’ they could not imagine that 40 years later the CMV vaccine would still be an elusive target, and the hope that ‘...the use of such a vaccine in adolescent girls would reduce the incidence of primary cytomegalovirus infection in pregnancy and thus eliminate fetal brain damage due to this cause’ would remain unmet. Although considered top priority, the availability of a CMV vaccine is not foreseen for the near future. Sadly, nowadays, seronegative pregnant women are at the same risk of acquiring a primary CMV infection as they were decades ago. Congenital CMV is perpetuated by the lack of public awareness, serologic screening, unavailability of an effective vaccine and of effective therapeutic treatments.

On the other hand, our knowledge about the epidemiology of the virus and its ways of transmission, together with the availability of reliable serology assays have the potential, when properly used, to markedly reduce the incidence of primary infection in pregnant women and, ultimately, of congenital infection.

In two small studies conducted in Virginia, US, in 1996 and 2004 the group of S. Adler reported that: (1) behavioural interventions such as frequent hand washing and avoiding close contacts with young children had the potential of reducing the risk of primary CMV infection; and (2) pregnant women were more motivated to follow behavioural interventions than were nonpregnant women. In other words, four conditions had to be satisfied for hygiene recommendations to be effective, namely the woman had: (1) to be pregnant; (2)
know to be at risk (i.e. seronegative); (3) to be informed about hygiene measures; and (4) to comply with behavioural recommendations. Although the above studies were not powered to answer the key questions and suffered from substantial methodological limitations, they were important pilot studies and they were instrumental to the design of subsequent larger studies. More recently, a French study conducted among more than 5000 pregnant women at a single hospital in Paris showed a reduction from 0.4% to 0.2% in the seroconversion rate following CMV counseling. However, the control group appeared questionable from the methodological point of view because seroconversions diagnosed prospectively in the informed group in the second and third trimester of gestation, were compared to primary infections retrospectively diagnosed as having occurred in the first trimester (0–12 weeks’ gestation) on the basis of presence of IgM and IgG avidity results. Behavioural interventions have been reported to be highly successful for the prevention of other infectious diseases transmitted via contaminated hands. Presently, however, quite a degree of uncertainty remains that a behavioural intervention can effectively encourage pregnant women to consistently follow CMV recommendations.

Inspired by the above studies, we designed a controlled study to investigate the actual effectiveness and feasibility of an intervention, based on: (1) identification of seronegative pregnant women at high risk of primary infection (i.e. having frequent contacts with children <36 months because of personal or occupational reasons); and (2) CMV counseling about risky and protective behaviours to reduce the risk of primary infection. The study is reported in detail elsewhere. Briefly, the study comprised an intervention arm and an observational control group. In the intervention arm, CMV-seronegative women, identified at the maternal serum screening for foetal aneuploidy at 11–12 weeks’ gestation, were given hygiene information and prospectively tested for CMV until delivery. Suggested hygiene measures included frequent hand washing after exposure to children’s bodily fluids, frequent washing of surfaces touched by the child (toys, high chair, stroller, etc.), avoid kissing the child on the mouth/cheeks, and sharing utensils, washcloths, food or drink, as well as putting in the mouth whatever may have been in the child’s mouth. The control arm consisted of women enrolled at delivery who were neither tested for, nor informed about CMV during pregnancy, and who had a serum sample stored at the time screening for foetal aneuploidy. The primary outcome was CMV seroconversion.

Four out of 331 (1.2%) women seroconverted in the intervention group compared to 24 out of 315 (7.6%) in the control group ($\Delta = 6.4\%; 95\% \text{CI} 3.2–9.6; P < 0.001$) (Figure 1). There were three newborns with congenital infection in the intervention group and 8 in the control group (one with cerebral ultrasound abnormalities at birth). Of the four seroconverting mothers in the intervention group, one was most likely already infected at the time of enrolment, one reported sleeping in the same bed with her sick child, one reportedly followed recommendations, while the last one reported scepticism about hygiene measures since enrolment. Apparently, her scepticism was shared by her obstetrician as well. Apart from the latter case, the study was generally well accepted by the obstetricians caring for the participants.

As for acceptance of, and compliance to recommendations, 93% of women felt hygiene recommendations were worth suggesting to all pregnant women at risk for infection, and 80% reported substantial or complete adherence to hygiene recommendations.

In conclusion, we hope that in view of the strikingly positive results obtained in our study, the view point of some that ‘Currently, there

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**Figure 1.** Seroconversion rate in the intervention and in the control group. Seroconversion rate among women who did not receive cytomegalovirus (CMV) information rises to 9% when nine women diagnosed with a recent primary CMV infection at first testing at 12 weeks gestation are included.
are inadequate data to show that education actually changes behaviour and that this behaviour change translates into decreasing maternal infection and subsequent congenital infection \(^{11}\) will be revised in the near future. Clearly, there are still many obstacles ahead, such as poor training of health professionals in behavioural counselling, and some scepticism among obstetricians about the effectiveness of behavioural intervention. Unfortunately, the latter is sometimes shared by patients too. Indeed, both categories (i.e. physicians and patients) are keener to consider solving health problems by means of a medical act (drug, surgery) rather than through a modification of behaviour which is certainly more time-consuming and demanding (on a personal level) to achieve. Additionally, an updated cost-benefit analysis of a behavioural intervention needs to be performed which, in turn, raises the thorny and complex issue of prenatal CMV screening.

Nevertheless, we believe that the reported feasibility and effectiveness of a primary prevention intervention will help, in the first instance, by providing evidence-based data. Strong experimental data together with the identification of the best channels to reach health professionals and pregnant (childbearing) women and to deliver the most appropriate health messages will eventually lower barriers to the implementation of behavioural prevention strategies.

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References


Biographies

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