Studies Link Preeclampsia, Cardiovascular Disease

The two disorders are thought to have a common pathogenesis that is rooted in shared risk markers.

W omen who have had preeclampsia are at increased risk of cardiovascular disease later in life, suggesting that they should be targeted for primary prevention, according to a British review published online in the British Medical Journal.

Meanwhile, an accompanying population-based prospective study in Norway suggests that cardiovascular risk factors are associated with a higher risk of preeclampsia.

“The underlying link between pre eclampsia and cardiovascular disease is unclear. Although preeclampsia may initiate endothelial damage, it is thought to be more likely that preeclampsia and cardiovascular disease have a common pathogenesis rooted in shared risk markers,” wrote Dr. Laura Magee and Dr. Peter von Dadelszen of the University of British Columbia, Vancouver, in a commentary accompanying the two studies (BMJ 2007 Nov 2 [Epub doi:10.1136/bmj.39366.416817.BE]).

The overall risk of mortality was elevated following preeclampsia, with a relative risk of 1.49 after 14.5 years.

“We must recognise that these women are still young, their absolute risk of cardiovascular disease is low over the short term, and their risk will evolve over subsequent decades,” wrote Dr. Magee and Dr. von Dadelszen in their commentary.

“As such, we have an opportunity for primary prevention, especially as cardiovascular disease is largely preventable.”

They added, however, that the findings so far do not help physicians guide their primary prevention strategy.

“Evidence supports how to screen younger women for risk factors, and while recommending lifestyle change is good for such a recommendation is ‘not through an increased change their behavior,’ the authors wrote. “However, women might be more receptive if they have had a complicat ed pregnancy. Perhaps we could tailor the advice to women with newborns and young children,” they wrote.

The Norwegian study tracked 3,494 women who gave birth after participat ing in the Nordic Neonatal health study to link cardiovascular risk fac tors and preeclampsia. The women were linked to diagnoses for preeclampsia through the Norwegian birth registry to 2007 Nov 2 [Epub doi:10.1136/bmj.39366.416817.BE].

After adjustment, the odds ratio for preeclampsia in women with a baseline systolic blood pressure greater than 130 mm Hg (highest fifth) was 7.3, compared with those with a systolic blood pressure less than 111 mm Hg (lowest fifth). Simil arly, the odds ratio for women with a diastolic blood pressure greater than 78 mm Hg was 6.3, compared with those whose diastolic blood pressure was less than 64 mm Hg.

Women who were overweight or obese had a higher risk of preeclampsia than did women of normal weight, and the risk for preeclampsia rose with increasing waist circumference.

In addition, there was a weak association between preeclampsia and gestational diabetes, and a stronger association with lipid levels above the normal range.

“We found that cardiovascular risk factors that were present years before pregnancy are associated with a risk of preeclampsia,” wrote Elisabeth Balstad Magnussen, a research fellow at the Norwegian University of Science and Technology, Trondheim, and as sociates. “This finding suggests that unfavourable cardiovascular and metabolic profiles may represent primary causes of preeclampsia and that these factors predispose both to preeclampsia and to subsequent cardiovascular disease. This does not, however, rule out the possibility that the pre-eclamptic process in itself may also contribute to cardiovascular risk.”

Outcomes ‘Reassuring’ After Repeated Prenatal Steroids

R epeated courses of prenatal corticosteroids in pregnant women at high risk of preterm delivery do not appear to have adverse effects on neurocognitive or physical development of the child at 2 years of age, compared with a single course, investigators in two large randomized clinical trials reported.

Both research groups termed these findings “reassuring,” given that repeated doses have already become commonplace in the United States, the United Kingdom, and Australia.

U.S. clinicians have widely adopted weekly intramuscular injections of corticosteroids in high-risk pregnancies, even though there is insufficient data to support this practice.

Moreover, animal and observational human studies have suggested that repeated steroid injections may inhibit the offspring’s growth, impair brain development, predispose to neurosensory disability, increase aggression and hyperactivity, and raise blood pressure, investigators noted.

Current guidelines recommend repeated corticosteroid courses only in subjects participating in large randomized, controlled clinical trials to assess both short-term and long-term safety and efficacy of the treatment. Two such clinical trials are the Australasian Collaborative Trial of Repeat Doses of Steroids (ACTORDS) and a National Institute of Child Health and Human Development Maternal-Fetal Medicine Units (MFMU) Network trial.

Investigators in both studies previously reported their findings, which were then exposed to either a single dose or weekly repeated doses of steroids. Both studies showed better neonatal outcomes after repeated doses, with less need for mechanical respiratory support and survival rates free of major disability similar in children whose mothers received repeated steroid injections and those whose mothers received placebo.

Survival rates free of major disability were similar in children whose mothers received repeated steroid injections and those whose mothers received placebo.

Further follow-up is crucial, because other important cognitive outcomes, such as executive function, cannot be determined until the children reach school age.

Still, the investigators noted that “clinicians may wish to consider the use of a single injection of Celestone Chronodose, or equivalent, repeated weekly, if the woman remains at risk for very preterm delivery” 7 days after receiving an initial course (N. Engl. J. Med. 2007;357:1179-89).

In the MFMU study, Dr. Ronald J. Wagner of Columbia University, New York, and his associates assessed 248 children aged approximately 30 months who had been exposed to repeated corticosteroid courses in utero (12 mg given intramuscularly and at 24 hours) and 238 who had been exposed to a single steroid course initially and repeated placebo courses later.

As in the ACTORDS trial, the MFMU researchers found no significant differences between the two groups in anthropomorphic measures; scores on mental and psychomotor tests; blood pressure; or other health outcomes such as seizures, pneumonia, and the need for hospitalization during infancy.

They did find an increased frequency of cerebral palsy in children who had been exposed to repeated courses of corticosteroids, compared with a single course (2.9% vs. 0.4%). Although this difference was not statistically significant, it is still cause for concern, Dr. Wagner and his associates said (N. Engl. J. Med. 2007;357:1190-9).

Like the ACTORDS investigators, the MFMU researchers emphasized that further follow-up of these subjects through later childhood is warranted.

And although they characterized these findings as “reassuring,” Dr. Wagner and his associates concluded that their results argue against giving repeated prenatal corticosteroids until more data are collected.

“This approach may improve the condition of the neonate, but it does not convey long-term benefit and may cause possible harm in later life, they said.”

BY JONATHAN GARDNER London Bureau

BY MARY ANN MOON Contributing Writer

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