

Caffeine use to regulate breathing of very preterm babies, long-term benefits

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Very premature babies who were given caffeine to regulate their breathing have a significantly lower incidence of disabilities at the age of two years, according to an international study led by researchers at McMaster University.

Researchers studied more than 2000 premature babies who were either treated with caffeine or given a placebo. The latest results of this large clinical trial will appear in the Nov. 8 issue of the *New England Journal of Medicine*. Babies receiving the caffeine were less likely to develop cerebral palsy and cognitive delay.

Caffeine and similar drugs have been used for more than 30 years to make the breathing of very preterm babies more regular, but without sufficient knowledge of the possible benefits and risks.

The study involved infants who weighed between 500 and 1250 grams at birth, and who were at risk of apnea – interrupted or irregular breathing due to immaturity. The ongoing study, with colleagues in Canada, Australia, the US, Europe and Israel, will continue to follow the children until they reach the age of five. The project is funded by the Canadian Institutes of Health Research and the National Health and Medical Research Council of Australia.

According to Dr. Barbara Schmidt, the principal investigator of the research project, the latest results of the study showed that 46 percent of the infants receiving the placebo died or survived with a

neurodevelopmental disability. Among the babies receiving caffeine therapy, only 40 percent had an unfavourable outcome by the time they reached the end of their second year of life.

“It definitely gives hope to parents,” Dr. Schmidt concluded. “Of all the drugs we use in the neonatal intensive care unit, caffeine is the first to have been shown conclusively to reduce long-term disability in very preterm babies.” Caffeine reduced the rates of cerebral palsy and cognitive delay but had no significant effect on the rates of death, bilateral blindness and severe hearing loss.

"This international study provides important follow-up to the earlier results reported by Dr. Schmidt and her colleagues and should have a major impact on the treatment and prevention of apnea in preterm infants," said Dr. Michael Kramer, Scientific Director of the CIHR Institute of Human Development, Child and Youth Health.

The Caffeine for Apnea of Prematurity (CAP) project enrolled 2006 premature infants who were born between October 1999 and October 2004 in nine countries. The research project was designed to address long-standing concerns about possible adverse effects of caffeine therapy in pre-term infants. All children will be re-assessed at five years to obtain more precise information on their development as they approach school age.

Apnea occurs in about 85 per cent of infants who are born at less than 34 weeks gestation. For more than 30 years, therapies known as methylxanthines, including caffeine, have been used to reduce the frequency of apnea and the need for mechanical ventilation. However, it has remained uncertain whether the use of methylxanthines has any additional benefits or risks in premature infants.

Earlier findings released last year by the same research team revealed

that babies who received caffeine had a lower incidence of abnormal lung development than infants who were given a placebo.

Dr. Schmidt said that half of the beneficial treatment effect at two years of age was explained by the fact that babies receiving caffeine therapy came off ventilators sooner. “Ventilation is a double-edged sword,” she said. “While it is life-saving, at the same time, it causes injury – scarring the immature lung which is very susceptible to damage.”

Source: McMaster University

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