Caffeine therapy for apnea of prematurity does not have long-term harmful effects on sleep

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Caffeine therapy for apnea of prematurity has no long-term harmful effects on sleep or control of breathing, according to a new study of 201 preterm children assessed at ages 5-12, the first study in humans to examine the long-term effects of neonatal caffeine treatment on sleep regulation and ventilatory control.

"Animal studies have suggested that administration of neonatal caffeine to premature infants, while improving survival and other outcomes, may have long-term detrimental effects on sleep and control of breathing during sleep," said lead author Carole L. Marcus, MBBCh, of Children's Hospital of Philadelphia. "In our prospective follow-up study of 201 premature infants who participated as infants in the randomized, double-blind, placebo-controlled Caffeine for Apnea of Prematurity study, we found no evidence of long-term detrimental effects of caffeine treatment on sleep duration or sleep apnea during childhood."

The findings were published online ahead of print publication in the American Thoracic Society's *American Journal of Respiratory and Critical Care Medicine*.

At follow-up, the 201 study participants, 98 of whom received caffeine as infants, underwent two weeks of actigraphy, which measures sleep versus wakefulness based on movement, along with one night of home polysomnography to detect sleep-related medical conditions. Caregivers

completed sleep diaries and questionnaires.

There were no significant differences between children who received caffeine or placebo as infants in actigraphic total sleep time or in the apnea hypopnea index, which indicates sleep apnea severity based on the number of apneas (complete cessation of airflow) and hypopneas (partial cessation of airflow) per hour of sleep. Polysomnographic sleep efficiency did not significantly differ between the caffeine and placebo groups at follow-up; nor did the percentage of children with obstructive sleep apnea or elevated periodic limb movements of sleep.

Interestingly, the study also showed that the prevalence of children with obstructive sleep apnea syndrome (9.6 percent) and/or elevated periodic limb movements of sleep in the pathologic range (14.2 percent) in the study population overall, regardless of whether or not they received caffeine treatment, was much higher than population estimates for school-age children, which range from 1 to 4 percent for sleep apnea and 5 to 8 percent for elevated periodic limb movements of sleep.

"Administration of therapeutic caffeine to premature infants had no long-term negative effects on sleep or sleep disorders in our study," said Dr. Marcus. "Ex-preterm infants, whether treated with caffeine or not, have a higher than expected prevalence at school age of obstructive sleep apnea syndrome and periodic limb movements during sleep."

"This data should help ease concerns about the long-term effects of caffeine treatment in premature infants."

Provided by American Thoracic Society