Prolonged Antibiotics Risky for VLBW Infants

BY MITCHEL L. ZOLER

FROM THE EASTERN SOCIETY FOR PEDIATRIC RESEARCH ANNUAL MEETING

PHILADELPHIA – A week-long course of empiric antibiotic treatment in neonates may result in a higher subsequent rate of chronic lung disease, compared with infants treated for just 2 days, based on an association seen in a review of more than 900 very low birth weight newborns.

But this finding is not yet ready to definitively guide practice, as it came from a nonrandomized, retrospective study that may have failed to control for all possible confounding variables, Dr. Alexandra Novitsky said at the meeting.

In her adjusted analysis, which controlled for several baseline variables, the 159 very low birth weight (VLBW) neonates who received a "long" course of empiric antibiotic treatment, usually for 7 days, had a statistically significant, twofold higher rate of also having chronic lung disease during follow-up, compared with the 747 neonates who received a "short" antibiotic course, usually for 2 days, said Dr. Novitsky, a neonatologist at Christiana Hospital in Newark, Del.

"It's too early to draw conclusions about changing therapy," based on this finding, said Dr. David A. Paul, associate director of neonatology at Christiana Hospital, who collaborated on the analysis. "We did our best to control for possible confounders, and it still suggested that longer antibiotic treatment altered outcomes, but there may have been things [for which] we did not control," he said in an interview. The next step is to design a prospective study and determine if changing the duration of empiric antibiotic therapy changes outcomes. "But the current findings raise concern that we should

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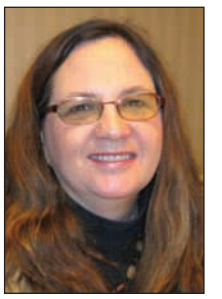
VIEW ON THE NEWS

Don't Overuse Antibiotics

The findings of this analysis suggest that physicians should not treat neonates with antibiotics when not necessary. If they do, they risk making the babies worse.

A neonatologist may be tempted to prescribe a more prolonged course of antibiotics out of fear that the infant may have an infection. To be cautious, she overtreats. These new data suggest that this practice can actually do harm. This is another reason not to overtreat.



It is reasonable to infer that the treating physician had seen something in some of these children to prompt the longer duration of treatment. The infant must have somehow seemed sicker. The physician may have been concerned that if antibiotic treatment stopped sooner, the neonate's condition would have worsened. The optimal duration of treatment is always something to think about.

It is plausible that just a few extra days of antibiotic treatment can make an important difference. A 2-day duration of treatment probably does not change the background flora in the esophagus as much as a 7-day course. Longer exposure to antibiotics can result in a higher rate of fungal infection, which can trigger increased inflammation.

RITA M. RYAN, M.D., *is chief of neonatology at the Women & Children's Hospital of Buffalo (N.Y.). She made these comments in an interview. She said that she had no relevant financial disclosures.*

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be cautious about the duration of treatment," said Dr. Paul.

In the cases reviewed, each physician delivering care determined the duration of antibiotic treatment. Some may have opted for a longer course of treatment because they were concerned that "not all babies have culture-proven sepsis," Dr. Paul said in an interview. The physicians "may have feared that the babies had infections that were missed in their blood cultures. They treated presumed sepsis," he said.

Dr. Novitsky reviewed all the VLBW infants seen in the neonatal ICU at Christiana Hospital between July 2004 and June 2009. The regimen used on all neonates who received empiric antibiotic treatment consisted of ampicillin and gentamicin. The infants who received a longer antibiotic course had

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DR. NOVITSKY

a significantly higher prevalence of several markers of a worse clinical profile, including lower birth weight, younger gestational age, a higher score for neonatal acute physiology (SNAP), and a lower 5-minute Apgar score. They also had higher rates of clinical chorioamnionitis, mechanical ventilation, and endotracheal tube colonization (endotracheal tubes underwent routine, weekly colonization assessments).

The infants who received a longer course of antibiotics also had a higher prevalence of antibiotic-resistant, gram-negative organisms colonizing their endotracheal tubes, a 6% rate compared with a 2% rate among the infants who received a short course of treatment – a significant difference. The two groups of infants had roughly identical prevalence rates of colonization with antibiotic-resistant gram-positive strains.

Dr. Novitsky defined the primary outcome evaluated in the analysis, chronic lung disease, as the need for supplemental oxygen by the infant at 36 weeks postmenstrual age. This outcome occurred in 185 of the 906 (20%) neonates in the study: 17% of the infants who received a short antibiotic course, and 36% of those who received a long course.

The multivariable analysis adjusted for differences in gestational age, SNAP score, Apgar score, maternal antibiotic treatment, chorioamnionitis, preeclampsia, cesarean delivery, prolonged rupture of membranes, and need for mechanical ventilation. After adjustment, the two patient groups failed to show a significant difference in their rates of necrotizing enterocolitis or sepsis.

To further examine the relationship between duration of antibiotic treatment and chronic lung disease, Dr. Novitsky also presented the results of a subgroup analysis that focused on the 418 high-risk neonates in her study group, because of their delivery at 28 weeks' gestation or younger and their SNAP score of 8 or greater.

Within this subgroup, the adjusted rate for developing chronic lung disease ran 70% higher in the 108 infants who received a long course of antibiotics, compared with the 310 who received a short course, also a significant difference.

Dr. Novitsky and Dr. Paul said they had no relevant financial disclosures. ■

VERBATIM

'My advice to the young couple … (and to anyone else who asks!) was not to spend their money on baby DVDs. Interaction with a real person, reading books together, and letting children touch and explore the three-dimensional world around them is a much more effective way to stimulate their learning and development.'

Dr. Lee Savio Beers, p. 24