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There are no clear benefits of acid blockers in neonates, particularly in preterm neonates but they continue to be used as prophylaxis or therapy of stress ulcers and gastroesophageal reflux disease (GERD) because of their perceived safety and potential benefit among many subspecialists caring for neonates. Multiple studies show that these drugs facilitate the onset of infections in adults and children. Similar observational studies have reported an association between the use of H2-blockers and neonatal sepsis and/or NEC. This makes sense as gastric acid is a major non-immunologic defense against ingested pathogens, and inhibition of gastric acid can allow pathogenic bacteria to proliferate in the gastrointestinal tract leading to bacteremia and infection. Terrin et al conducted a prospective cohort study to determine whether there was an increased risk of infectious diseases, NEC, and mortality in preterm newborns exposed to ranitidine treatment. Unique to most cohort studies, a prospective sample size calculation was done, lending additional credibility to this study. The primary outcome was the rate of infectious diseases. Secondary outcomes included NEC, death, and length of hospital stay. The study included 274 VLBW infants with birth weight between 401 and 1500 g or gestational age between 24 and 32 weeks. In this population, 91 infants were given ranitidine and 183 did not receive it. The patient characteristics between the group exposed to ranitidine and the unexposed group are similar with regards to important risk factors for infection and NEC, including birth weight, gestational age, sex, Apgar scores, CRIB scores, persistent ductus arteriosus, duration of endotracheal intubation, and central vascular access duration. Many of these potentially confounding risk factors have not been accounted for in previous studies. Thirty-four (37.4%) of the 91 children exposed to ranitidine and 18 (9.8%) of the 183 not exposed to ranitidine had contracted infections (OR = 5.5, 95% CI, 2.9–10.4, $P < .001$). The risk of NEC was 6.6-fold higher in ranitidine-treated VLBW infants (95% CI, 1.7–25.0, $P = .003$) than in control subjects. Mortality rate was significantly higher in newborns receiving ranitidine (9.9% vs 1.6%, $P = .003$). The authors concluded that ranitidine therapy was associated with an increased risk of infections, NEC, and fatal outcome in VLBW infants. The results from this prospective study provides the most useful and current information regarding the potential risks of H2-blocker use in preterm neonates, and they should be used with care in this population.

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