EDITORIAL VIEWS

Anesthesiology
82:807-808, 1995
© 1995 American Society of Anesthesiologists, Inc.
J. B. Lippincott Company, Philadelphia

When Is the Ex-Premature Infant No Longer at Risk for Apnea?

In 1982, Steward! alerted anesthesiologists to the occurrence of postoperative apnea in ex-premature infants recovering from minor surgical procedures after general anesthesia. In subsequent years, several investigators further defined this problem, examining such issues as the role of anemia,! the potential for caffeine (a long-acting analog of theophylline, the medication typically used to treat apnea in neonates) to reduce the incidence of apnea,2 and possible benefits of regional versus general anesthesia.3 Although each study examined particular issues, two questions recurred: Did apnea occur in ex-premature infants undergoing general anesthesia for minor surgical procedures? At what gestational or postconceptual age did apnea no longer occur? Consistently, the answer to the first question was that apnea did occur in these patients. Because the latter question—the age at which no risk remained—was more difficult to answer, several markedly different findings emerged. Kurth and Lebard! reported that the risk of apnea persisted until as late as 60 postconceptual weeks. In contrast, Liu et al.6 and Malviya et al.7 suggested that the likelihood of apnea was nearly absent by 46 and 44 postconceptual weeks, respectively. Consequently, establishing a consistent policy for postoperative management of these patients, many of whom require repair of inguinal hernia, remained problematic.

One problem intrinsic to each of these studies was that any single institution is unlikely to care for enough of these infants to permit a sufficient sample size. One solution is to pool the results of all published studies, a technique known as meta-analysis. Coté and Zaslavsky initially considered this approach but chose instead to cooperate with other investigators to access original data from published studies. This resulted in a new type of pooled study—termed a “combined analysis” by the investigators—published in this issue of ANESTHESIOLOGY.

Compiling the original data from several studies, Coté et al.8 generate a model of the risk of apnea at different gestational and postconceptual ages and determine whether this risk is influenced by such factors (covariates) as preoperative anemia, the use of muscle relaxants or opioids intraoperatively, or a complicated perinatal course. Coté et al.8 analyze the data using logistic regression, a type of nonlinear regression in which the dependent variable is dichotomous (e.g., apnea being present or absent) and independent variables are either continuous (e.g., gestational or postconceptual age) or dichotomous (e.g., anemia being present or absent). Although possible unfamiliar to many anesthesiologists, logistic regression has been used to determine MAC of inhaled anesthetics9 and to determine the lowest end-tidal anesthetic concentration at which learning occurs.10 With this model, Coté et al.8 “predict” the likelihood of apnea occurring at any combination of gestational and postconceptual ages and with or without covariates, such as anemia. In turn, they estimate the breakpoints in conceptual and gestational age beyond which the risk of apnea becomes negligible.

The combined analysis by Coté et al.8 provides important new insights into the risk of apnea in ex-premature infants. By combining data from several studies, Coté et al. gained statistical power lacking in previous studies. In addition, they were able to examine issues omitted from specific studies such as the contribution of anemia to the incidence of apnea. Coté et al. also observed that the incidence of apnea varied as a function of the level of monitoring, i.e., that investigators who used impedance pneumography and nursing observation were less likely to detect apnea than those investigators who used continuous recording devices incorporating computer-assisted technology. Assuming that the difference in the incidence of apnea can be explained by differences in monitoring technique rather than undetermined differences in institutional clinical practices, Coté et al.9 raise the interesting question as to whether apnea detectable only by sophisticated techniques is clinically important.

Can the clinician accept Coté et al.’s recommendations without reservation? Possibly not. The validity of their model depends on the data used in its development and, even with a combined analysis, Coté et al.’s sample size was limited: Of their 255 patients, only...
68 were 46–50 weeks' postconceptual age (and only 41 exceeded 50 weeks' postconceptual age). Extrapolating from their logistic regression, Coté et al. claim that the incidence of apnea decreases to less than 1% at postconceptual age of 54–56 weeks. Yet, using another statistical approach recommended by Hanley and Lippman-Hand, Coté et al.'s entire sample size is smaller than the 300 patients necessary to ensure 95% probability that the incidence of apnea does not exceed 1% in a particular age group.11

Establishing policy regarding the postoperative management of ex-premature infants undergoing inguinal hernia repair requires a decision regarding acceptable risk. Malviya et al.7 suggest that a 5% incidence of postoperative apnea may be sufficiently low to avoid the need for postoperative monitoring and permit early hospital discharge. Others might argue that 5% is grossly excessive and that only a 1% or 0.1% risk of apnea is acceptable. Although Coté et al.'s analysis has more statistical power than previous studies of apnea in ex-premature neonates, I still question whether a consistent policy regarding postoperative disposition of these patients can be determined based on the current information.

Dennis M. Fisher, M.D.
Department of Anesthesia
University of California, San Francisco
521 Parnassus Avenue
San Francisco, California 94143-0648
Electronic mail: fisher@zachary.ucsf.edu

References

1. Stewart DJ. Preterm infants are more prone to complications following minor surgery than are term infants. Anesthesiology 56: 304–306, 1982
10. Choroff BS, Bennett HL, Eger EI II. Subanesthetic concentrations of isoflurane suppress learning as defined by the category-example task. Anesthesiology 79: 16–22, 1993

Anesthesiology, V 82, No 4, Apr 1995