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Sugar and spice and everything nice: Health differences in newborn girls and boys

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For generations, girls have whimsically been said to be made of "sugar and spice and everything nice," and boys from "snakes and snails and puppy dog tails." Inherent in these loving references is the fact that females and males are different, both when they are healthy and when they are ill.

Two studies using animal models may lead to a better understanding of sex-based health discrepancies among some newborns. One study found that gender differences in the heart may help explain why infant girls are more likely to die following heart surgery. The other study has determined that the rapid accumulation of acid in newborn female livers may shed light on why pediatric liver transplants are less successful when the livers are donated from infant girls.

The studies were conducted by Danny Quaglietta, Department of Physiology, Michael P. Belanger, Department of Surgery, and Carin Wittnich, Departments of Physiology and Surgery, at the University of Toronto, Toronto, Ontario, CN. Their studies are entitled, "Ability to Buffer Changes in pH During Ischemia -- Are There Sex Differences in the Newborn Heart?" and "Orthotopic Liver Transplantation in Newborns -- Lower Success Rates From Female Donors and Why Ischemic Metabolism May Play A Role," respectively. Their research is among the 100 presentations being offered at the upcoming conference, Sex and Gender in Cardiovascular-Renal Physiology and Pathophysiology. The meeting, sponsored by The American Physiological Society, is being held August 9-12, 2007 at the Hyatt

Regency Austin on Town Lake, Austin, TX.

Study 1: Sex Differences in the Newborn Heart

Clinical studies in children have shown that girls are at higher risk for death than boys following cardiac surgery. A recent nationwide study in the US has found that females under 20 years of age are at a 31 percent greater risk of in-hospital death following heart surgery. As studies have ruled out gender-differences based on access to and utilization of services, the Canadian team has explored a biological basis for the differences. In this study they considered whether a more rapid development of tissue acidity (acidosis) in the heart during a lack of blood flow (ischemia) might play a role.

The researchers used 20 young (3-5 days) male (n=7) and female (n=13) Yorkshire piglets to examine their theory. They took a full thickness left ventricular biopsy to compare the baseline levels of metabolites in both sexes prior to isolating the hearts. The hearts were then subjected to 60 minutes of normothermic ischemia and left ventricular biopsies were collected at the end of the period. All tissues were analyzed for adenosine adenosine triphosphate (ATP; the main energy source of the heart), creatine phosphate (CP; a readily available stored form of energy), lactate, and hydrogen ion (H+) concentration. Histidine concentration, which protects against acidosis, was also determined in baseline tissue alone.

The researchers found that the newborn female hearts had accumulated a significant 47 percent greater H+ level within 60 minutes of ischemia. This was associated with a significant 13 percent greater accumulation of lactate. They also found the CP reserve was 22 percent lower than baseline compared to males.

Based on these and other findings the investigators concluded that, for

this study:

-- male and female newborn hearts are not metabolically identical and have different metabolic responses to ischemia; and

-- newborn female hearts can develop greater acidosis during ischemia, which may place them at greater metabolic risk

According to the research team, the results suggest that the response of the newborn female heart (i.e., myocardium) to ischemia may increase its susceptibility to injury during ischemia and offer a potential explanation for the poorer clinical outcomes found in infant females following cardiac surgery.

Study 2: Lower Success Rates When Using Female Newborn Liver Donors

As many as 500 children undergo liver transplantation in the US each year. Data on pediatric liver transplantation shows that the outcomes are worse for children who receive organs from female donors. Clinical studies have shown that, compared to males receiving male livers, males receiving female livers experience a higher incidence of early complications and almost twice the amount of graft losses.

During liver transplantation, the organ undergoes a period of no-flow ischemia, or complete lack of blood flow, and therefore must rely in part on internal nutrient stores to produce energy anaerobically (without oxygen). The end-products of this process (anaerobic metabolism) are lactate and hydrogen ions (H+) which can accumulate in the liver cells during ischemia leading to detrimental affects.

Thus, to better understand the gender effects of infant liver

transplantation, the researchers examined anaerobic end-product accumulation in newborn male and female livers during no-flow ischemia. Baseline liver biopsies were harvested from anesthetized three-day-old male (n=4) and female (n=6) piglets and immediately afterward the liver was excised and placed in a normothermic bath for 45 minutes. Biopsies were then taken at 15, 30, and 45 minutes of ischemia. All biopsies were analyzed for anaerobic end-products lactate and hydrogen ion (H+) content.

The research team found that both male and female livers showed similar low levels of both lactate and H+ at baseline. But during ischemia, newborn female livers accumulated a greater amount of H+ compared to males. This difference persisted throughout the entire ischemic period. The results were paralleled by a similar greater and more rapid accumulation of lactate in newborn female livers, a difference that was sustained throughout the ischemic period.

Based on these findings and other considerations, the researchers concluded that:

-- the newborn female liver developed a greater and more rapid tissue acidosis compared to males during normothermic ischemia, which may be due in part to greater anaerobic glycolysis in females; and

-- more rapid lactic acidosis in newborn female livers may result in greater metabolic damage during ischemia.

Source: American Physiological Society

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