

ISSUES IN PEDIATRICS

Addressing the Special Needs of Children in Gastroenterologic Practice

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Pediatric Liver Transplantation

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G&H Could you describe the population of patients requiring pediatric liver transplant?

EA The population of patients that we serve at our hospital is characteristic of the population at large pediatric transplant centers throughout the country, where approximately one third of patients have a single disorder, biliary atresia, a fibro-inflammatory disorder of the extrahepatic biliary ducts. The cause of this inflammation is unknown, but onset occurs most commonly in infants, some time between birth and 8 weeks of age. This fibro-inflammatory process destroys the bile ducts, causes obstruction of bile flow, and injures the liver. We currently believe that biliary atresia is related to a genetic disposition activated by injury to the liver or possibly exposure to a virus.

Some of our patients are transplanted as infants and others as older children. Approximately 15% of the population that we transplant has acute liver failure. They are healthy children without any evidence of liver disease who suddenly take ill. In some of these cases, a specific diagnosis is found. In others, we never know what causes the liver failure. A variety of other disorders, including metabolic diseases, autoimmune diseases, and inherited diseases of the biliary system, also cause cirrhosis and ultimately require liver transplantation in children.

G&H How are pediatric patients usually referred to the transplant center?

EA Referral generally depends on the child's diagnosis. Many children with biliary atresia are referred by pediatric

surgeons or pediatric gastroenterologists in the surrounding area. Acute liver failure patients are for the most part referred by critical care attending physicians who have admitted them and are attempting to care for them in their hospital. Most other referrals, however, come from other subspecialists.

One concern related to referral is that, occasionally, community gastroenterologists will manage pediatric patients with acute liver failure beyond the point where it is easy to transfer care to a transplant center. Once acute liver failure or serious liver injury with the potential to progress to acute liver failure has been identified, those patients need to be transferred. Over the past 10 years, awareness of this need has risen among local critical care physicians and gastroenterologists, largely through postgraduate courses and continuing education sponsored by the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and other professional societies. As a result, referrals are coming appropriately, at earlier stages, with pediatric patients that are generally well managed.

G&H What specific concerns exist in terms of monitoring and providing supportive care to pediatric transplant candidates?

EA There is always a concern about the safety of medical therapies in pediatric patients because many drugs have not been tested for their indications in children. However, for example, use of beta-blockers in children with portal hypertension has been shown to be safe, as has the use of medications like octreotide for acute variceal bleeding. Many of the surgical procedures utilized in adults can safely be performed in children as well.

There have been several studies looking at the safety and use of percutaneous liver biopsy in young children and infants. The procedure seems to be very safe with few complications. When there are complications, they are generally related to the sedation, not the biopsy itself. Liver biopsy is an important part of monitoring progression of liver disease, even in young infants.

Another issue in pediatric liver disease is that the course of progression in children is generally more rapid than in adults. Many adults are transplanted due to complications from hepatitis C or alcoholic liver disease, which are relatively slow-progressing diseases. Children are more likely transplanted due to disease states that progress quickly to liver insufficiency. Further, children have developmental concerns that require immediate intervention, even in chronic diseases. Any liver disease will have a serious impact on children's nutritional status, growth, and overall development. In cases of delayed transplant, children become malnourished and developmentally delayed and are characterized by a general failure to thrive. The severity of these problems prior to transplant impacts long-term outcomes. Children that have slow linear growth and shorter height after transplant, even when the transplant is successful, are likely the children with growth failure prior to transplant. Delaying transplant for a long period of time can seriously impact outcomes, even years after a successful transplant.

Otherwise, pretransplant supportive care in children is similar to that administered to adults. Nutrition is generally emphasized to optimize growth. However, the reality is that pediatric patients with advanced liver disease do not grow until they have better liver function via transplantation. Other complications that need to be addressed—variceal bleeding, ascites, spontaneous bacterial peritonitis, gram-negative infection, pneumonia—are similar to those experienced by adult patients and are treated in the same manner.

G&H Are there specific concerns in pediatric patients during the transplant process?

EA With regard to the transplant process itself, children often receive a technical variant graft, which is a reduced-size, split, or living-donor graft rather than a whole live graft. Without the utilization of technical variant grafts, waiting-list mortality in pediatric patients would be huge. However, although this practice minimizes waiting-list mortality, it incurs the heightened risk of additional postoperative complications following the very complex surgical procedures required with this type of transplantation. Children are more likely to develop vascular thromboses, biliary complications, and bleeding after technical variant transplant. In fact, re-operation

after transplant in pediatric patients is common, with up to 50–60% of recipients requiring a second surgery to address some complication. The average hospital stay for children is about 20 days at most centers, whereas for adults, the median is lower and their required level of medical attention and supportive care posttransplantation is much less than it is for children.

G&H Is the donor pool for pediatric transplant candidates separate from that for adults?

EA The pool of organs for children is the same pool that is utilized for adults. Adults can donate a segment of their liver to a child via living-donor transplantation as described above. In adults, the right lobe is transplanted; in children, the left lateral segment or left lobe is utilized. Livers of any size from deceased donors can also be transplanted in children, though, when using the whole organ, there needs to be a weight-based match. Deceased adults can also donate a segment of their liver to a young infant. In many situations, the left lateral segment of a deceased donor is used for an infant and the right lobe from that same deceased donor is transplanted to an adult. This is known as split liver transplantation.

It works the other way as well, in that if a 7- or 8-year-old deceased donor is available, sometimes the graft, by priority, will be offered to an acutely ill adult with the hope that it will be large enough to function.

G&H Does a patient's age affect their prioritization within the donor pool?

EA Currently, organs are allocated according to the risk of death from remaining on the waiting list, not by where the transplant might be most successful or what the risk of complications following transplant might be. I believe that the next frontier in transplantation of both children and adults will be to balance the risk of pretransplant mortality with the risk of posttransplant morbidity.

It is clear that if pediatric organs were given only to children (up to the age of 18) and never used in adults, children would not have nearly as long a waiting time as they currently have, on average. Further, modeling suggests that this policy would not increase waiting-list mortality in adults because pediatric donors make up such a small percentage of the pool. However, it seems fundamentally wrong, on a case-by-case basis, to take a graft from a 16-year-old and cut it down for an infant who is at home, when there are adults dying in intensive care units. Conversely, a graft from a child donor is often taken by a critically ill adult recipient when there are children waiting at home for transplant. Those children

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have growth failure and advancing malnutrition that may be impacting their cognitive development and growth potential for years to come.

This is a hotly debated issue. At every level of mortality risk, children get first priority before the organ is offered to adults with similar likelihood of death. The United Network for Organ Sharing (UNOS) and various subcommittees within UNOS are currently trying to create a more balanced formula that factors in the concept of “net life benefit” and gain in quality-of-life years, in order to reprioritize pediatric versus adult patients both within and across levels of mortality risk.

Suggested Reading

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