Methylmalonic acidaemia (MMA) is an autosomal recessive inborn error of metabolism that presents in infancy with episodes of metabolic acidosis (i.e., buildup of methylmalonic acid and other harmful substances in the blood) that can lead to intellectual disability, chronic kidney disease, and, in some cases without treatment, coma and death. Long-term symptom management requires a protein-restrictive diet, but patients can still suffer from recurrent metabolic crises, chronic renal disease, and neurologic disorders [1]. Despite advances in research and improved understanding of the disease process, long-term management remains a burden for patients and families, and at significant cost [2].

Recently, liver transplantation has become an alternative treatment for MMA. For example, liver transplantation (LT) and combined liver–kidney transplantation (LKT) have been demonstrated to improve patients’ quality of life, with benefits including increased energy, decreased hospitalizations, and the ability to attend school [3]. While LT or LKT decreases levels of methylmalonic acid in the blood, it is still unclear whether early LT improves long-term neurologic outcomes for patients [3]. It is hypothesized that, in MMA, methymalonic acid is produced \textit{de novo} in the central nervous system, contributing to poor outcomes in spite of dietary restrictions and transplantation [4].

Determining the relative benefits of dietary management and transplantation for MMA is a complex judgment that requires weighing at least four well-known principles of medical ethics: autonomy, beneficence, nonmaleficence, and justice. Expressing beneficence for an MMA patient requires both dietary management and consideration of the potential benefits of transplantation. Nonmaleficence in the context of MMA care requires minimizing risks of harm to the patient, so discussion of long-term neurological outcomes following transplantation and risks associated with the procedure and long-term immunosuppression is critical. Expressing respect for an MMA patient’s autonomy means preserving that patient’s right to make health care decisions and also clarifying that a request for transplantation might not be honored. This is because, given organ scarcity, the principle of autonomy must be weighed against the principle of justice; clinicians and health care organizations must consider the interests of communities, not
just the interests of individual patients, when assessing criteria for organ allocation. One concept that can help us think more deeply about justice is utility.

For diseases other than MMA, such as alcoholic liver disease and hepatocellular carcinoma, there are clinical scenarios in which no viable alternative treatment beyond liver transplantation exists [5]. An ethical question related to justice in these cases is whether quality of life should be part of our definition of utility. If we assume that increased longevity has more ethical value than increased quality of life, a utilitarian perspective would not prioritize transplants for patients with MMA. An additional point to consider in this analysis is that the number of patients diagnosed with MMA could increase in the future. If newborn screening becomes more widespread, additional patients will likely be diagnosed with MMA, and if they are all eligible for liver transplants, this would place additional demands upon the scarce resource of deceased donor organs. So, the burden of providing transplants for all patients with MMA in the future is a factor the transplant community must consider in crafting new allocation policy.

Since it is up to individual clinicians to decide whether to list a particular patient for an organ, it is imperative that the transplant community engages clinicians, patients, and the public to develop clear policies regarding the use of deceased donor organs for transplantation. Furthermore, a robust public discussion is required to determine which values inform our conception of utility and whether patients with MMA should be prioritized lower or higher on the deceased donor organ waitlist than those patients for whom there is no therapeutic alternative to transplantation.

Transplantation considerations for patients with MMA should incorporate utility and also values such as clinical efficacy, equity, and respect for patient autonomy. Further research is needed to determine long-term benefits, risks, and rates of success of transplantation in patients with MMA. As the future of treatment for patients with MMA continues to evolve, the transplant community must continue to deliberate upon the ethical principles, including utility, which drive allocation policy for patients with MMA.

References


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