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BRIEF REPORT

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Treatment of IgA deficiency in liver transplant recipients with human breast milk

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Abstract IgA deficiency is associated with high mortality (42 % at 120 days) following liver transplantation (OLTx). Most of the mortality has been associated with enteric infections. Mother's milk, or human breast milk (HBM), is a rich source of IgA that is considered to have beneficial effects in terms of protection from microbial translocation and enteric infections. Two IgA-deficient OLTx recipients were given HBM orally for 10 days perioperatively. HBM was given in order to replenish intestinal IgA. Both patients had an excellent infection-free post-operative course. IgA levels in the serum rose from 5 to 10 mg/dl in one patient and from 7 to 30 mg/dl in the other. No complications from HBM administration were observed. We conclude that HBM can be used in IgA-deficient liver transplant recipients to reduce the risk of infectious complications in the post-operative period.

Key words Liver transplantation, IgA deficiency, breast milk · IgA deficiency, breast milk, liver transplantation · Breast milk, IgA deficiency, liver transplantation

Introduction

IgA deficiency has been identified as a major risk factor for perioperative mortality following liver transplantation [13]. Normally, IgA functions to provide an immunological barrier against the normal flora, particularly that of the intestine, preventing translocation of such organisms across mucous membranes into either the peritoneal cavity or the portal venous circulation. The reported mortality of IgA-deficient liver transplant (OLTx) recipients has been 62 % at 2 years, with most of this mortality occurring in the first 120 days post-transplantation. Most of the deaths of IgA-deficient OLTx recipients result from infections with enteric pathogens.

Human breast milk (HBM) is a rich source of IgA [5]. Its IgA content can be as great as 20 g/l in colostrum. As breast milk production increases, the concentration of IgA in breast milk declines [11]. The absolute amount of IgA available daily in breast milk, however, remains stable as a consequence of the increase in volume of milk produced. HBM can be used to provide a temporary source of IgA for patients with IgA deficiency. Herein, we report on two patients with IgA deficiency to whom HBM was administered orally in an attempt to correct IgA deficiency, at least intraluminally, following OLTx [3].

Methods and materials

HBM was obtained from nursing mothers in a maternity ward 1–7 days postpartum using sterile suction devices and was kept frozen at – 18 °C until usage. It was administered orally without additives. Each subject received approximately 100 cc HBM every 8 h beginning immediately prior to surgery and continuing for 10 days post-transplantation. This amount was chosen to correlate with an infant's average intake of breast milk [1]. Serum IgA levels were measured preoperatively, on days 3 and 7 postoperatively, and 1 week following cessation of treatment. IgA levels in breast milk were measured in four samples. IgA determination was done by immunoelectrophoresis.

Results

The preoperative IgA level in the serum of both patients was less than 7 mg/dl. Following the oral administration of mother's milk, the serum levels rose to values of 26 and 30 mg/dl in one of the two patients and to values of 8 and 10 mg/dl in the other. Upon cessation of the breast milk treatment, the serum levels of IgA declined to their preoperative values. IgA levels in human breast milk varied according to the samples chosen and ranged from 0.3 to 1.9 g/dl.

The postoperative course of both IgA-deficient patients was excellent: they were totally free of any infection. The patients were discharged and went home 10 and 14 days, respectively, after OLTx.

Discussion

IgA deficiency is a relatively common problem in the general population, occurring at a rate of up to 1 in 200 people [3, 7, 8]. In view of the reported increased mortality of IgA-deficient liver transplant recipients, HBM may be used to reduce the vulnerability of these patients to lethal bacterial or fungal translocation and sepsis.

In a large series of patients recently described by Van Thiel et al. [13], of a total of 1684 liver transplant recipients, 14 were found to be IgA-deficient (0.8 %). The 4-month postoperative mortality for these IgA-deficient subjects was 42 %, a value eight times greater than the 5 % value reported for non-IgA-deficient OLTx recipients. Due to the relative rarity of this problem in a single center, we can only compare our results to larger series reported by others.

Interestingly, patients with either an IgG or IgM deficiency had a mortality rate similar to that of transplant controls without any Ig deficiency. While IgG can be easily supplemented with commercially available intravenous Ig infusions, IgA cannot be given intravenously because no intravenous IgA preparation currently exists, and there is a substantial risk for an allergic reaction to IgA if IgA-deficient individuals are given the material intravenously. In addition, even if it was possible to give IgA intravenously to IgA-deficient subjects, the intravenous IgA would probably not provide mucosal protection against potential bacterial or fungal invasion from enteric sources.

The normal mechanical and immunological barriers to bacterial translocation from the bowel are seriously hampered in the early postoperative period following OLTx. The reasons for this include extensive intraoperative dissection, portal outflow obstruction (lasting for various lengths of time during the transplant operation), immunosuppressive treatment, hypoalbuminemia, edema, and antibiotic therapy that alters the normal gut flora. As a result, the risk for bacterial or fungal translocation from the gut into the peritoneal cavity or the portal venous system is quite high. These factors could account for the high mortality, due to infections, that occurs in liver recipients who are IgA-deficient.

HBM is an extremely rich source of IgA that is readily available. Moreover, it is the only known source of this particular immunoglobulin subclass. In the early neonatal period, breastfeeding imports passive immunity to newborn children because of its IgA immunoglobulin content [4–6, 9, 10]. The concentration of IgA in colostrum can be as high as 2 g/dl. After birth, the concentration of IgA in breast milk rapidly falls as the volume of lactation increases so that the amount available to a breastfeeding infant remains stable on a daily basis. Thus, HBM obtained from a maternity unit is a rich source of IgA that can be used to partially replenish the IgA-deficient patient undergoing major surgical procedures such as OLTx. The choice of a 300-cc daily dose was selected because it corresponds approximately to the daily intake of HBM by an infant.

The experience herein report suggests that HBM is well tolerated by OLTx recipients; no complications attributable to its administration occurred. The twofold increase in the serum level of IgA observed in one of the two patients treated probably reflects some intestinal absorption of the orally administered IgA. The increase in humoral IgA observed is probably not relevant to its alleged success, as the effect of orally administered IgA is probably limited solely to its role in the intestine. However, the increase in the serum IgA levels noted in both patients documents that reasonable amounts of IgA were given and present in the gut following the administration of mother's milk to the two patients reported.

Because IgA deficiency is relatively common, one can reasonably expect that a certain percentage of liver recipients will be IgA-deficient. This is especially true for patients with autoimmune-associated liver diseases (i.e., autoimmune hepatitis PBC, sclerosing cholangitis), which are known to be associated with IgA deficiency [2, 12]. In view of the previously reported increased mortality in IgA-deficient OLTx recipients, the use of HBM to replace insufficient IgA may provide IgA-deficient patients with sufficient protection from infectious complications secondary to translocation following OLTx.

Though the results presented here are encouraging, firm conclusions cannot be drawn because of the small sample size. Multicenter randomized trials need to be performed to verify the efficiency of this treatment.

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