Pre- and postoperative care of pediatric liver recipients Bulgarian experience

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Purpose: Many advances have been achieved in pediatric liver transplantation since the first attempted liver transplantation by Thomas E.Starzl in 1963. Orthotropic liver transplantation (OLT) is established as the standard care for end-stage liver disease in developed world. In the developing countries the appropriateness of such costly interventions has been questioned.
We undertook an analysis of liver transplanted Bulgarian children in order to establish the outcomes of transplantation service in the Pediatric University Hospital, Medical University in Sofia, Bulgaria.

Methods: This is a retrospective review of pre-operative and post-transplantation management of 30 Bulgarian children.

Results: In 1993 a Bulgarian child was liver transplanted in Belgium. Since then 29 Bulgarian children have been liver transplanted: 17 abroad, after 2004 – 13 children in Bulgaria. The first OLT in Bulgaria was done by Prof. M.Malago and Dr.L.Spasov, Lozenec University Hospital, Sofia, in November, 2004.

Etiology of underlying liver disease: Biliary atresia was the most common indication for transplantation in infants (63.3%). Metabolic diseases was the second leading indication (16.6%), followed by congenital hepatic fibrosis (14.3%), cryptogenic cirrhosis and tumors. We found that PFIC represents the main indication for OLT among the metabolic diseases at our center.
Three children were living-donor liver transplanted using parental liver grafts for inheritable metabolic disorders, i.e. GSD type IV – 1 child and PFIC type I and III – 2 children. One child diagnosed as PFIC III was transplanted with deceased donor liver. Both the children and their living donors have favorable outcomes.
Combined liver-kidney transplantation was performed in one child due to primary oxaluria.

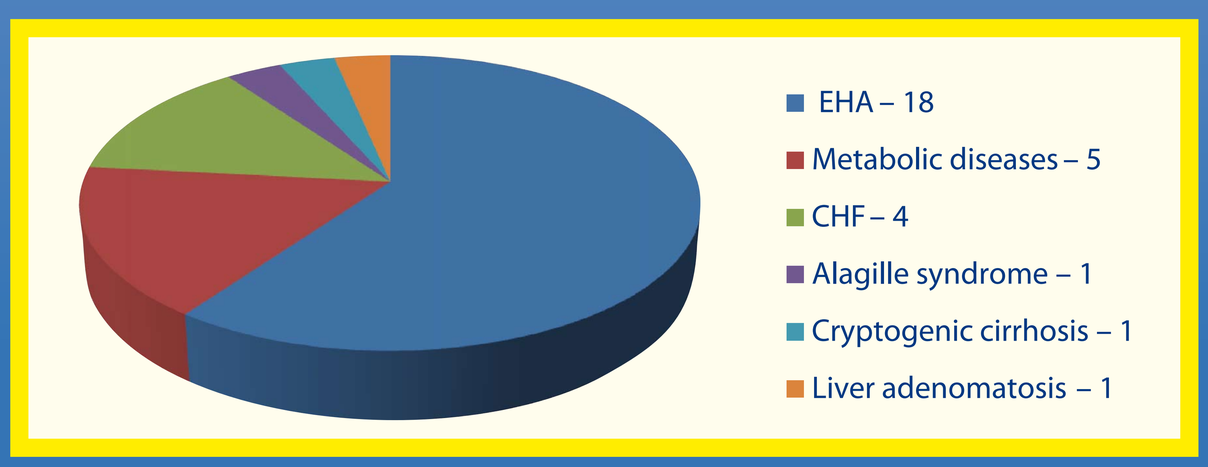

Fig. 1. Indications for OLT.

Age at transplantation: The children were transplanted at the age of 5 months – 3 years-63%, 3 years – 18 years-37%.

Gender: There was a slight predominance of the male patients: male – 17 female-13.

Eleven children received deceased donor livers, 19 received living donor organs. Early referral of potential recipients allows for the timely evaluation of potential living donors. All the living donors had favorable outcomes. They stated they had good quality of life.

Mortality: In our experience the main causes of early post-transplantation death were primary-non-function (PNF) in 2 children and central pontine myelinolysis (CPM) in 1 child. One child was re-transplanted due to PNF. One child died while on the waiting list. Patient survival post-OLT is 88,9% after 1 year.

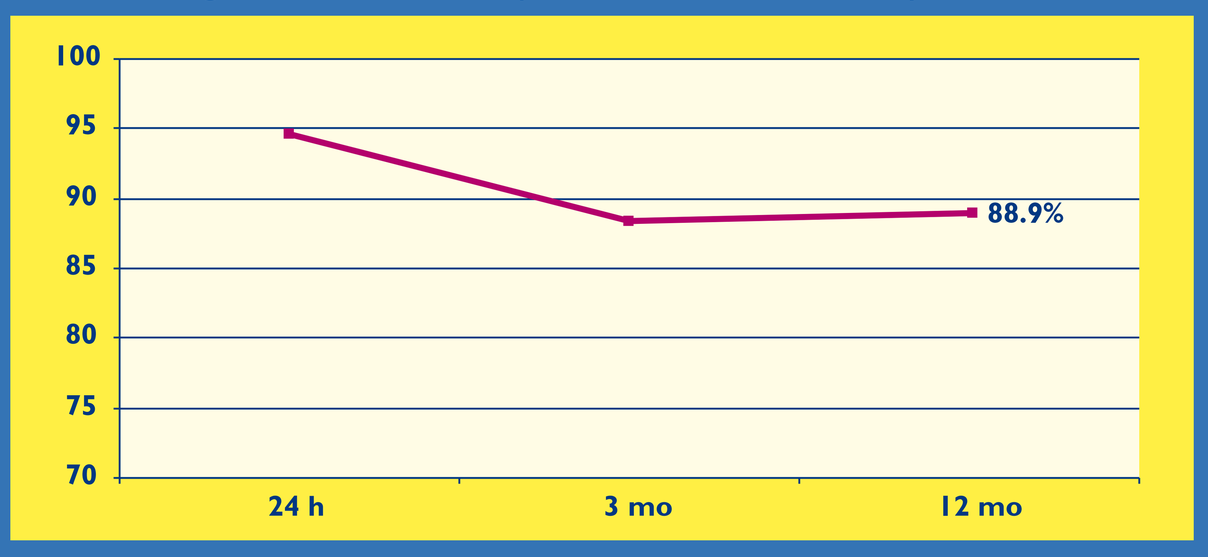

Fig.2. Patient survival post-OLT after 1 year.

Our immunosuppressive protocol is based on an early withdrawal of steroides – 6 months to 1 year after OLT as well as on keeping relatively low levels of CsA (70-90 ng/ml) and Tacrolimus (4-6 ng/ml) 2 years after OLT. We have not seen any serious side effects of immunosuppression with the exception of 1 boy who suffered bilateral necrosis of the femoral head. He had a history of pre-transplantation chronic renal failure. He was successfully treated with biphosphonates and oxygen camera.

The main complications following OLT were (Tabl. 1).
early onset :
Biliary complications, defined as obstruction, strictures and leakage, occurred in 6 patients. The biliary obstruction and strictures were diagnosed 2 to 3 years post-OLT. The clinical presentation was that of a moderate to severe cholangitis. All the cases were surgically treated.
There were 2 cases of primary non-function, one of them was re-transplanted, the other one died.
The 2 cases of hepatic artery stenosis did not demand surgery.
Portal vein thrombosis was observed in 2 patients. There was no need of any treatment due to the sufficient collaterals.
Central pontine myelinolysis occurred in 1 patient who had an unfavorable outcome. The patient demonstrated a dominant neurologic impairment and marked CAT findings.
Small for size dysfunction occurred in 1 patient who suffered a lot of problems related to the graft synthetic malfunction. The patient was checked for re-evaluation.

Complications	Number of patients	Percentage
Biliary complications	6	20
Acute rejection	5	16
Infections with CMV and EBV	3	10
Primary non-function	2	6.6
Portal vein thrombosis	2	6.6
Hepatic artery stenosis	2	6.6
Small for size dysfunction	1	3.3
Central pontine myelinolysis	1	3.3
B cell lymphoma	1	3.3

Tabl. 1. Main complications following OLT.

The experience of our center once more underlines that biliary complications remain a troubling complication after pediatric OLT.

Acute rejection diagnosed in 5 patients was treated with i.v.methylprednisolone successfully.

The major causes of **late onset complications are infections with CMV and EBV**. Our strategy to CMV infection is pre-emptive treatment. Two children were treated with Ganciclovir until negative CMV DNA.

Two children suffered mononucleosis-like syndrome and were diagnosed as EBV-infection. They were treated with reduction of immunosuppression and Ganciclovir. One of them who was diagnosed as late EBV, 6 months later developed B cell lymphoma. It was succesfully treated with Rituximab. Possible factors related to PTLD could be the 2 episodes of acute rejection, treated with steroid-bolus and ATG.

We believe that the low incidence of CMV and EBV complications is due to the low level of immunosuppression we try to keep, frequent viral monitoring as well as the pre-emptive treatment of CMV.

Follow up: Apart from the 3 children who died, all the children show normal physical and mental development, they have a good quality of life.
Three children diagnosed as PFIC showed remarkable improvement of their physical development. The velocity range was 13 cm per year for the first 2 years after OLT. All the children developed neither steatohepatitis nor severe diarrhea as some centers reported. The one-year patient survival rate in PFIC was 100% in our center.

Conclusion: We find several factors dependant on the pediatrician that predict the successful outcome of OLT in children: early diagnosis, close monitoring and treatment of the complications of the end-stage liver disease, management of nutrients and vitamines deficiency. Our experience supports the benefits of early withdrawal of steroides and keeping a low level of immunosuppression. An improvement in growth in PFIC children after OLT has been well demonstrated. Living donor transplants are a good option for Bulgarian children.

We thank sincerely Prof. Dr. med Martin Burdelski (Universitätsklinikum Schleswig-Holstein Campus Kiel), Prof. Massimo Malago (Consultant General, Hepato-Biliary-Pancreatic and Transplant Surgeon, The London Clinic Liver Centre, London) and Prof. Dr. X. Rogiers (University Hospital and Medical School Dept. of Surgery and Transplantation Gent, Belgium) for their support to our team, for sharing experience with us. We hope to keep our good professional relations.

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