Use of Fresh Frozen Plasma in the Treatment of Hemolytic Uremic Syndrome in Children

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Introduction

Hemolytic Uremic Syndrome (HUS) is an acute disease characterized by thrombocytopenia, microangiopathic hemolytic anaemia and renal involvement, ranging from a mild microhaematuria and proteinuria to renal failure with or without oligoanuria. In many cases other organs are involved as well: bowel, liver and central nervous system. HUS is a typical disease of the first years of life; it is the most frequent cause of ARF in infants. The most typical characteristic of HUS is heterogeneity of possible etiologic agents, type and the way it is shown, prodroms, histological aspect of lesions and evolution. There is an epidemic form, affecting young children during summer time, after a diarrhoea episode, characterised frequently by a good prognosis, and a sporadic form, typical for the older children and adults, with no season variability, no clear prodromic signs or showing only mild respiratory signs and having generally a poor prognosis.

Platelets interferes in the normal mechanisms of the repair of the vascular damage, contact with the sub-endothelial structures, causes the platelets activation, which adheres to the damaged part, aggregate and degranulate, releasing mediators which amplify aggregation and stabilise the existing thrombotic thrombi. The intensity and stability of aggregation and the possibility of coagulation is controlled by a fine homeostatic mechanism, regulated by two metabolites of arachidonic acid, thromboxane A2 (TXA2) and prostacycline (PGI2). TXA2, released by activated platelets is a strong vasoconstrictor and anti agregator. PGI2 produced by the endothelium is a strong vasodilator and the most efficient endogenous inhibitor of aggregation. Equilibrium exists in physiological condition between the pre aggregation action of TXA2 and anti aggregation action of PG12, which limits aggregation, but allows, at the same time, the e adhesion and interference of the platelets in the mechanism of repair of the endothelial lesion. This lesion plays an important role in the genesis of HUS. The importance of endothelial damage is confirmed by the frequent association of the disease with infections caused by endothelial-toxic agents, as Shigella and E.Coli, or by bacteria or viruses which produce neuraminidasis, an enzyme which can expose the antigen Thomsen-Friedenreich (TF), which is present at the glomeruli, red blood cell and platelet level; the reaction with antibodies anti-TF which are present at the serum occurs following by a direct endothelial damage or a damage mediated by red blood cells and platelets. After the endothelial lesion the formation of thrombus in microcirculation occurs, as well as the haemolytic anaemia related to the mechanical damage of the red blood cells, which passes through the damaged vessels. Multiple studies done on HUS showed a variety of factors, which interferes in its fizpathology.

Aim

In this introduction we bring the experience of our clinic during the years 1996-2001 in the use of Fresh Frozen Plasma (FFP) during the treatment of the hospitalised children with HUS.

Materials and Methods

10 children diagnosed with SHU, admitted at our clinic during 1996-2001 are taken in study.

Their age varied from 1 month to 12 years old. All children fulfilled three major criteria of the syndrome definition: microangiopathic haemolytic anaemia, thrombocytopenia, ARF.

Based on a study done in 1995 in Paediatric Hospital "Bambin Gesu" in Rome, (Italy), and in lack of special treatment as Haemodialysis, we have used FFP in the patients with HUS, apart from the supportive therapy. Its use is justified in the background of deficiency of "plasmatic factor", which will regulate the production of prostacycline.

Results

Below are described the main clinical signs presented by our patients. Six of them presented the typical form of HUS, preceded by an episode of diarrhoea.

Four children developed progressive decrease of diuresis to complete anuria, five children developed high blood pressure. The immediate initiation of supportive therapy, (Dopamine, Diuretics, Antihypertensive drugs, Antibiotics etc, and application of FFP improved significantly the clinical signs and the lab tests in the majority of patients.

- In five patients the kidneys regained their normal function
- In four children the disease evolved towards CRF.
- A twelve years old child, who showed an atypical form of HUS, died after 7 weeks, although was treated with dialysis in a hospital abroad.

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Discussion

It is impossible to think about an etiological treatment of HUS for the moment. Significant clinical variability makes randomised therapeutic trials difficult, which remains, however, the only logical way to face this difficult problem. Different authors propose various therapies, in different periods of time. Today's therapeutic orientation consists on a fast treatment of ARF and the its related disorders. It means a precocious dialysis treatment: Haemodialysis in older children and peritoneal dialysis in smaller children. Introduction of dialysis treatment has significantly decreased the mortality of children with HUS.

In the conditions of lack of haemodialysis, as ours, we have used FFP, with the intention to replace "the plasmatic factor" of prostacycline stimulation. The lack of this factor is noticed in some adults, and the use of FFP in these group ages seems to have improved the disease prognosis. A study done in children showed more endothelial lesions in electronic microscopy in children that aren't treated with FFP. Our results are similar to that described in the literature; smaller age children and those having the gastrointestinal prodrome had a better prognosis.

However, the results of this modest study that doesn't pretend to reach to conclusion are in favour of the use of FFP, especially in clinics that doesn't afford to have such treatment as haemodialysis.

We are recently creating conditions in our clinic, to initiate the haemodialysis, which is not done till now due to some different administrative constraints. We hope to initiate this treatment soon, which will significantly improve the service's quality.

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