

RECENT ADVANCES IN MANAGEMENT OF NEONATAL SEPTICEMIA

Systemic bacterial infections during the neonatal period continue to take their toll despite the development of newer broad spectrum antimicrobials and advances in neonatal life support services. Cause-specific mortality for early onset neonatal septicemia has declined by nearly 60% over the past half century(1) but the mortality amongst the very low birth weight with septicemia has not exhibited a similar decline(2). Several immunologic handicaps in the preterm contribute to this gloomy scenario. Factors like low levels of immunoglobulins, opsonins (e.g. fibronectin) and complement factors possibly contribute to the increased risk of infection. However, it appears that the key factor determining risk and severity of infection is the polymorphonuclear leucocyte function. Poor chemotaxis, rapid depletion of the small neutrophil storage pool and the inability of maximal stem cell proliferation in meeting demands of cell removal resulting in neutropenia also contribute to a poor outcome in neonatal septicemia amongst preterm and low birth weight babies(3-7).

Laurenti *et al.*(8) suggested that if the neutrophil pool could be enhanced by provision of neutrophils from a human source, it may improve survival of infected neutropenic neonates. The augmentation in quantum of neutrophils in the recipient neonate was expected to be 60×10^6 cells

with a fresh blood transfusion, 336×10^6 cells with a double volume exchange transfusion and 735×10^6 cells with granulocyte transfusion (20 ml/kg).

Newer Treatment Modalities

1. Exchange Transfusion

The rationale of using exchange transfusion in neonatal septicemia is based on its ability to provide functional granulocytes to the depleted neutrophil pool, improve opsonic activity, removal of circulating endotoxins, improved perfusion and oxygenation, improved coagulation and provision of platelets. Several studies(9-12) have shown moderate to significant improvement in neonatal survival with the use of exchange transfusion as an adjunct immunotherapy in neonatal septicemia. However, most of these studies are non-blinded, uncontrolled and non-randomized making data interpretation difficult(13). Available evidence, however, suggests that exchange transfusion holds promise for the treatment of neutropenic septicemia infants with disseminated intravascular coagulation and/or septic shock.

2. Granulocyte Transfusions

Laurenti *et al.*(8) evaluated the response to granulocyte transfusions in 38 septicemic neonates and demonstrated a significant decline in mortality. However, the study results excluded neonates dying within 48 hours of onset of infection. Other workers have also observed improved survival after granulocyte

transfusion(4,14). Stork *et al.*(15) in a recent prospective randomized study failed to show any benefit of granulocyte transfusion amongst 25 neutropenic septicemic babies. In view of the risks of graft versus host disease, leucocyte alloantigen sensitization, and risk of transmission of infection like AIDS and the limited experiences of its use, granulocyte transfusion can currently be recommended only in severely neutropenic neonates unresponsive to conventional therapy and only in institutions with facilities for leucapheresis.

3. Intravenous Immunoglobulin (IVIG)

Severe immunodeficiency in preterm neonates (<32 weeks) prompted use of human serum globulin as a mode of adjunct therapy as early as 1963. The availability of intravenous immunoglobulin has prompted its use in prophylaxis and treatment of neonatal septicemia. IVIG in doses ranging from 120-500 mg/kg has shown promise in reducing sepsis related mortality when used prophylactically particularly amongst very low birth weight (<1500 g) neonates(16,17). When used as rescue therapy too, IVIG has shown improved outcome(18,19). Kim *et al.*(20) have, however, shown that the use of high doses of IVIG in animal models could lead to increased mortality due to non-specific reticuloendothelial blockade. It appears that levels of 700 mg/dl of IgG in sera offer best protection to neonates against nosocomial infection. Currently, because of the variable levels of functional specific antibodies against common neonatal pathogens, *e.g.*, Group B Streptococci, *Esch. coli*, *etc.* in each lot of IVIG and the potential risk of non-specific reticuloendothelial blockade with high doses of IVIG, this modality should be used with caution

as rescue therapy. The use of monoclonal immunoglobulins (IgM) directed against specific pathogens as an adjunct immunotherapy holds promise for rescue therapy of septicemic neonates. However, the prohibitive cost of IVIG preparation may preclude its use even as prophylactic therapy of very low birth weight infants in the developing world.

4. Future Research

The administration of purified fibronectin to improve opsonisation and rapid clearance of bacterial immune complexes and tissue debris by the reticuloendothelial cells has been advocated as another mode of adjunct immunotherapy(21). The recent purification of colony stimulating factors (CSFs) and their use to prime neonatal neutrophils for enhanced chemotaxis and bacterial killing(22) has opened new vistas of research in the management of neonatal septicemia.

No matter what the advances are, basic protocols of asepsis still remain the cornerstone in the control of sepsis in neonates.

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NOTES AND NEWS

NATIONAL WORKSHOP-CUM-SEMINAR ON DEVELOPMENTAL DISABILITIES

The XXIX National Conference of Indian Academy of Pediatrics to be held at Nagpur from 9-12 January 1992 will be preceded by a National Workshop-cum-Seminar on Developmental Disabilities on 9th January, 1992. The Workshop will highlight the *Multidisciplinary Approach to Diagnosis and Management of Developmental Disabilities both in the Clinical and Community Setting*. We propose to organize an exhibition of books/pamphlets/directory of services/teaching material/daily care material/Indian adaptation equipments side by side.

The tentative faculty includes members from all the National Institutes apart from Dr. Dubowitz (UK), Dr. M.S. Mahadeviah (Developmental Neurologist, Bangalore), Dr. N.B. Kumta (Bombay) and many other experts working in the field. Apart from lectures on various topics, there is a panel discussion on Cerebral Palsy, clinical demonstration of Developmental Diagnosis and Neuro-Kinesiologic evaluation. The Workshop is open to all concerned medical specialists, therapists, psychologists, special educators and medico-social workers. Registration is open to first 50 candidates on first come first served basis till 31st November, 1991.

Registration fee of Rs. 100/- by Demand Draft/Crossed Cheque (add Rs. 20/- as Bank collection charges for outstation cheques) drawn in favour of XXIX National Conference of Indian Academy of Pediatrics, payable at Nagpur, may be sent to the following:

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