Readers' Forum

Current Antibiotic Choice for Enteric Fever

Q. *Several commercially available antibiotics in India are claimed to be effective for enteric fever and recommended as the first line drug for this disease. Currently, what should be the choice for prescribing antibiotics for enteric fever in children ?*

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A. Earlier, multiple antibiotics like chloramphenicol, co-trimoxazole, ampicillin, amoxycillin and now fluoroquinolones and third generation cephalosporins are effectively used in the treatment of enteric fever. Ideally the choice of therapy depends on the cost and the level of resistance to the conventionally used drugs in the community.

The recent data on antibiotic sensitivity of culture proven *Salmonella typhi* from our center has shown that more than 90% isolates are sensitive to chloramphenicol, amoxycillin and co-trimoxazole (unpublished data). Similar reports have come in from other centers(l,2). It appears that after the emergence of multi drug resistant strains to the conventional drugs over the last few years the isolates are once again sensitive to them.

Currently, it is recommended that chloramphenicol should be used as the first line of therapy in enteric fever. Amoxycillin given at the rate of 100 mg/kg body weight in four divided doses would be as efficacious and could be substituted for chlorampehnicol.

It would be reasonable to use fluoroquinolones as alternative therapy if there is no response within 5 days. Some may persuasively argue that since fluoroquinolones produce an earlier defervescence with shorter duration of therapy(3) as compared to the conventional drugs they should be used as the initial treatment in enteric fever. In addition, the cost of treatment in the present settings is comparable. The earlier reservation that fluoroquinolones are toxic to the cartilage and joints and may hamper growth in children may not be a major concern. Studies from Vietnam and India have demonstrated no effect on growth velocity after a 2 year period of having received ciprofloxacin (45-70 mg/kg) for 3-7 days or 15-25 mg/kg for 9-16 days, respectively. These studies suggest that fluoroquinolones can be given safely as a short course therapy in childhood typhoid(4,5). One may respect this argument but in our settings where fluoroquinolones are vital for other multiple difficult to eradicate infections, it would be prudent to preserve these drugs for more severe life threatening complications or where very high resistance rates of *Salmonella typhi* to conventional drugs have been documented.

In hospital settings, third generation cephalosporins like ceftriaxone may be a better choice for the treatment of resistant enteric fever reserving the fluoroquinolones for other microrganisms(6). Need for parenteral administration of ceftriaxone would limit its use in the out patients. Oral

cefixime may be another choice, however, it is very expensive and would not be practical.

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Defense Mechanism of Breast-milk

Q. *What is the protective role of IgA in breastmilk?*

A. The breastfed infant receives 3-5 g of secretory IgA (S IgA) in colostrum in the first 24 hours. Production of sIgA gradually declines to 1 g/day at the end of the first week. However, this production is finely tuned to the baby's requirements(l-3).

Secretory IgA is produced in mammary glands by plasma cells which originate from immunocompetent lymphocytes in maternal gut-associated lymphoid tissues (GALT) and bronchus-associated lymphoid tissues (BALT). Because of these 'entero-mammary' and 'bronchomammary' pathways, human milk is rich in sIgA antibodies against micro-organisms which the newborn baby is most likely to encounter(l,2).

Secretory IgA is relatively resistant to proteolytic degradation in neonatal intestine because of the presence of a dimeric structure and the secretory component. As a result, 75-90% of ingested sIgA gets excreted intact in the feces. A small proportion (approximately 10%) also gets absorbed into the circulation(l,2).

Secretory IgA interferes with bacterial adherence to cell surfaces and has direct antitoxic action. It also inhibits internalization and intracellular replication of certain viruses. It is also believed to decrease the occurrence of atopic diseases by 'immune exclusion'(l).

Q. *What is the role of IgM and IgG in breastmilk?*

A. The precise role of IgM and IgG in

breast-milk is not clear. The concentration of these immunoglobulins in breast-milk is 1/100th that of IgA. Moreover, unlike SIgA which continues to be produced even in the second year of lactation, IgM and IgG become undetectable in the second month of lactation(2).

IgM and IgG supplement the protective role of IgA as the immune repertoire of the latter immunoglobulin does not include complement fixation and specific bacterial activity. These immunoglobulins, moreover, may have an important role to play in the protection of neonates born to IgA deficient mothers. It has been shown that the concentration of secretory IgM is increased in individuals with selective IgA deficiency(1-3).

Though secretory IgM can also resist proteolytic degradation in the neonatal gut to some extent, it is not as stable as SIgA. the protection afforded by SIgM can, therefore, never be comparable to that provided by SIgA. IgG in breast-milk is not associated with a secretory component and this probably suggests a passive transfer rather than active secretion. IgM and IgG in breastmilk probably play only a minor role in mucosal immunity(l,2).

Q. *Does the breast-milk provide any protection against respiratory tract infections occurring in the infant?*

A. Several studies indicate that exclusively breastfed babies have a lower incidence of acute respiratory infections, including otitis media(2,4). Unlike the gastrointestinal tract, where the protective role of breast-milk is well defined, the precise mechanisms by which protection is afforded to the respiratory system are less well understood(l,2). It is known that approximately 10% of IgA in breast-milk gets absorbed into the neonatal circulation. However, this is unlikely to play a very significant role in the lower respiratory tract as IgG is the major antibody class at this site.

Human milk, however, is known to modulate development of the infant's own mucosal and systemic immune system. Hormones, growth factors and cytokines present in breast-milk play important regulatory roles. For instance, epidermal growth factors may make mucosal surfaces more resistant to injury. Further, it has been shown that breastfed infants produce higher blood levels of alpha-interferon in response to respiratory syncitial virus infections and have higher levels of fibronectin in blood as compared to top-fed infants(l-3).

These indirect effects of breastfeeding on the developing immune system may explain the lower incidence of acute respiratory infections in breastfed infants(2).

Q. *What is the role of white blood cells present in breast-milk?*

A. Colostrum contain $1\text{-}3 \times 10^6$ cells/ml. Approximately 60-70% of these cells are monocytes/macrophages, 15-25% are neutrophils and 5-15% are lymphocytes (both T and B)(2,5,6).

Macrophages possess phagocytic and direct bactericidal activity and can participate in antibody-dependent cell-mediated cytotoxicity against viruses. Milk macrophages also contain IgA in their cytoplasm and are believed to play a role in delivery of intact IgA to critical areas(2,2).

Breast-milk lymphocytes play an extremely important role in modulation of the infant's immune system(5,6). As some of these lymphocytes can enter the neonatal circulation, it is believed that they can transfer specific immune reactivity from the mother to the infant(2).

While humoral factors in breast-milk provide short-lived protection, the T-lym-

phocytes may be responsible for transfer of so-called 'immunological memory'. For instance tuberculin reactivity can be transferred from the mother to her breast-fed baby. It is also known that the beneficial effects of breast-milk on the infants immune system may persist long after breast feeding has ceased. Epidemiological studies suggest that breast-fed infants have a lower risk of Type I diabetes mellitus, lymphoma and Crohn's disease(l-3).

Q. *How does breastfeeding protect against malaria?*

A. While it is believed that breasfeeding confers some protection against malaria, the precise immunological mechanisms that are involved remain unclear. In hyperendemic areas, certain humoral factors in breastmilk may provide some protection against malaria. Human milk is relatively deficient in para-amino-benzoic-acid (PABA). As the latter is absolutely essential for the erythrocytic stages of malarial parasite, human milk indirectly provides protection against malaria. However, transfer of maternal immune reactivity through T-lymphocytes present in breast-milk play a more direct role in this context.

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