Siderophores – potential candidate in the therapy of neonatal meningitis

The mortality and morbidity associated with neonatal meningitis remain significant in spite of advances in antimicrobial chemotherapy (Kim, 2003). *Escherichia coli* k1 is a successful pathogen capable of invading the brain despite the protective effect of physiological barriers between the blood stream and the central nervous system. Inadequate knowledge regarding the pathophysiology of this organism along with poor drug delivery to the brain has resulted in a lack of success following therapy of this infection. Investigations regarding neonatal meningitis have focused on the determination of resistance to antibiotics, but alternate therapies exploiting the modulation of the environment for invading bacteria have not been explored (Nigrovic et al., 2004; Shah et al., 2004; Kumar, 2004).

Iron supply for many microbes plays a decisive role in the infection process. Acquiring iron from the environment has a significant effect on the establishment of infection in the host, and microbial pathogens have evolved different mechanisms to overcome iron restriction. The role of iron chelation in virulence has been evaluated for microbial organisms (Dale et al., 2004). Iron facilitates the progression of high-level *E. coli* bacteremia to meningitis. Indeed, it has been shown elsewhere that the ferric-siderophore interaction is critical in the therapy of neonatal meningitis. (Dale et al., 2003). Negre et al. (2004) showed that the iron chelation gene plays a key role in the virulence of *E. coli* and an iron-dependent siderophore receptor differs from the wild-type strain in its ability to cause bacteremia, suggesting that iron acquisition by a siderophore is the most likely mechanism of the iron-associated virulence. Thus, stress generation by the acquisition of iron by a siderophore will reduce invading *E. coli* burden. The role of different siderophores in reducing the *E. coli* burden, and therefore their role in therapy, remains to be determined and justifies further studies in this regard. An understanding of this process could result in a novel therapeutic strategy for management of neonatal meningitis.

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