New Theoretical Background for Tuberculosis Treatment

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Tuberculosis

Tuberculosis (TB), a highly contagious chronic bacterial infection, is still a leading killer of young adults worldwide. TB has recently emerged as a major health concern. Each year, approximately 2 million persons worldwide die and 9 million become infected. TB has returned to concentration at the target site. In recent years, one of the best ways to achieve higher drug levels in the lungs has been the development of new particulate sustained release formulations that are directly delivered to the lungs via pulmonary route. Current literatures available on pulmonary delivery of anti-tubercular agents are focusing only on development of extended release particulate systems using variety of biopolymers. Presently in addition to extended release drug delivery approach an attempt is also being made to include the beta-cyclodextrin as solubility and permeation enhancer in alveolar epithelium-lining fluids to make the TB treatment more effective.

Etiology of Tuberculosis

Mycobacteria are aerobic, rod shaped, non-spore forming, and non-motile bacilli with a waxy coat that causes them to retain the red dye when treated with acid in the acid-fast stains. Mycobacteria typically have a unique cell wall structure crucial to their survival. The well-developed cell wall contains a considerable amount of fatty acid, mycolic acid, covalently attached to the underlying peptidoglycan-bound polysaccharide arabinogalatan, providing an extraordinary lipid barrier. This barrier is responsible for many of the medically challenging physiological characteristics of TB, including resistance to antibiotics and host defense mechanisms. The composition and quantity of the cell wall components affect the bacteria’s virulence and growth rate. The cell wall and its compositions are the key to the survival of mycobacteria, and a more complete understanding of the biosynthetic pathways and gene functions and the development of antibiotics to prevent formation of the cell wall areas of great interest [4].

Tuberculosis Chemotherapy

The treatment of TB has witnessed many important changes over the years. With the advent of effective antitubercular chemotherapeutic agents in the early 1950s, the two main biological obstacles to successful treatment of TB were the high rate of failure during treatment and the high risk relapse after treatment. The former was due to the selection of drug resistant mutants of M tuberculosis during the initial stages of treatment when the bacterial populations in the lesions were large. Relapse was due to the re-growth of viable organisms that had persisted in the latent state. To overcome these obstacles it was necessary to give the patients a three-drug combination initially and secondly to continue the treatment for 18 to 24 months with two drugs, and so, long-term treatment with a combination of drugs is required [5]. Treatment of active TB with a single drug should never be attempted, and a single drug should never be added to failing regimen, the result being development of multi drug resistance TB [6]. With the introduction of Rifampcin the outlook for treatment of TB changed dramatically. It was no longer necessary to give streptomycin daily for three months initially to prevent failure. The relapse rate also came down steadily even though the duration of treatment was considerably shorter. This was possible because complete or almost complete sterilization of the lesions became feasible with the introduction of rifampcin and pyrazinamide [7].

New theoretical background

The current treatment of TB involves systemic therapy with multiple drugs. However, pulmonary infections do not always respond well to such systemic therapy, due to insufficient drug diffusion into pulmonary tissue and lume [8]. Bacteria that have persisted over treatment may develop resistance, but higher drug doses to compensate for poor diffusion may lead to systemic toxicity. Additionally, most patients find it difficult in adhering to treatments that necessitate to several administrations a day to maintain efficient antibiotics concentration. Therefore it is imperative to develop new ways to deliver and use antibiotics to avoid spread of resistance and to improve patient’s compliance by decreasing dosing frequency. Antibiotic delivery systems administered through pulmonary route aim to deliver high drug concentrations directly at the site of infection while minimizing systemic biodistribution and toxicity. Rifampicin is a so-called concentration-dependent antibiotic [9]. The rate and extent of bacterial kill is related to the attainment of sufficiently high maximum concentration. Its bacterial activity is directly proportional to concentration at the target site. In recent years, one of the best ways to achieve higher drug levels in the lungs has been the development of new particulate sustained release formulations that are directly delivered to the lungs via pulmonary route. Current literatures available on pulmonary delivery of anti-tubercular agents are focusing only on development of extended release particulate systems using variety of biopolymers. Presently in addition to extended release drug delivery approach an attempt is also being made to include the beta-cyclodextrin as solubility and permeation enhancer in alveolar epithelium-lining fluids to make the TB treatment more effective.

References


