CURRENT TRENDS IN THE MANAGEMENT OF CHILDHOOD TUBERCULOSIS

***O. O. Oluwabiyi**

*Department of Paediatrics, University of Benin Teaching Hospital, Benin City, Nigeria

Correspondence:
Dr Opeyemi O Oluwabiyi
Department of Paediatrics
University of Benin Teaching Hospital
P.M.B. 1111Ugbowo
Benin City, Nigeria
Email: opefunmif@yahoo.com

INTRODUCTION

Tuberculosis (TB) is an ancient disease that was recognized even in prehistoric time. It is presently important worldwide in terms of morbidity, mortality and economic impact. It was declared a global health emergency in 1991(WHO).

EPIDEMIOLOGY

About 30% of the world's population is infected by the organism that causes tuberculosis. 8 to 10 million people develop the disease annually = 1000 new cases every hour. Of these, 11% occur in children <15yrs. Of the childhood cases, 75% occur annually in 22 high burden country that together account for 80% of the world's incidence.

About 2 million deaths occur annually which is equivalent to 52000 deaths weekly. Nigeria has the 5th largest TB burden worldwide. The FMOH declared TB a national emergency in April 2006. The world is presently witnessing resurgence in the incidence of TB. This may be attributable to worsening economic situation, multidrug resistance, the HIV pandemic, decline of national tuberculosis control programmes and large number of displaced persons living in poor conditions as a result of conflicts and wars.

TB occurs at any age with the highest burden of disease found amongst children less than 4 years of age. Mode of spread is mainly by 1) **inhalation**- commonest; 2) **ingestion**- through infected dairy products (this is rare) and 3) **penetration of skin and mucous membranes** (very rare). Children are infected from adult index cases with smear positive adults being 10 times more infective than smear negative cases.

Manifestation of TB in children can be predicted based on the Walgreen Timetable highlighted below:
Pulmonary tuberculosis – within a few months of primary infection.
Miliary and meningeal tuberculosis – 2-6 months.
TB adenitis - 3-9 months.
Bones and joints – several years.

Renal and genital tuberculosis – may take over a decade.

Pulmonary lesions occurring as a result of reactivation of a dormant focus previously established in the body takes a number of years after primary infection.

PULMONARY TUBERCULOSIS

This is the commonest form of TB in children. It occurs alone or in

combination with other forms in 70% of cases. Pulmonary TB in children consists mainly of the primary complex and direct progression of its components.

The early symptoms are usually vague and could include:

Chronic cough > 3wks
Fever
Anorexia
Weight loss/Failure to gain weight
Haemoptysis
History of contact

Relevant signs include:

Tachypnoea
Localized wheezing
Decreased breath sounds
Widespread crepitations
Bronchial breath sounds

Chest examination may actually reveal no abnormality.

Clinical features of reactivation TB in older children are similar to those of the primary infection but cough is usually productive and there may be chest pain.

The diagnosis of TB in children is difficult and a high index of suspicion is very important. Investigations which could be helpful include:

Tuberculin skin test: may be reactive

Chest radiograph: may reveal no abnormality. However, suggestive lesions include

-Hilar adenopathy

-Parenchymal lesions like patchy infiltrates, consolidations especially in the upper lobe, atelectasis, pleural effusion and rarely cavities.

-ESR usually markedly elevated

-Bacteriological investigations

Sputum) staining

-Gastric washings) and culture

TREATMENT

Mainstay of treatment is combination chemotherapy. Treatment is divided into 2 phases:

Intensive phase – 1st 2 months
Continuation phase – 6 months

To improve compliance, directly observed therapy (DOTS) is desirable at least during the intensive phase.

WHO declared in March 2000 that "the window of opportunity to prevent spread of drug resistant strain will be missed unless countries employ DOTS".

DOTS is a strategy designed for TB control that aims to ensure that TB patients take their drugs appropriately in the correct doses, frequency and duration to ensure complete treatment of the disease within a short time. This is done under the supervision of trained personnel. DOTS is not the final solution to TB crises but is a most effective way of treating TB.

The currently used regimen

- INTENSIVE PHASE: 2 MONTHS
  STREPTOMYCIN OR
  ETHAMBUTOL
  PYRAZINAMIDE
  ISONIAZID
  RIFAMPICIN
- CONTINUATION PHASE: 6 MONTHS
  RIFAMPICIN OR
  ETHAMBUTOL
  ISONIAZID
  ISONIAZID

Occasionally, corticosteroids are required as adjuncts in the presence of a large pleural effusion, endobronchial TB, pericardial effusion or tuberculous meningitis. Other important supportive therapy includes improved nutrition, contact tracing and surgical intervention where necessary.

SPECIAL CASES NEWBORN INFANT OF A MOTHER WITH TUBERCULOSIS

- Mother's treatment should be commenced or continued if already started.

- Baby should start INH soon after delivery and continued till mother's sputum has been negative thrice.
- After this, the infant should have mantoux test:
  - If mantoux is negative, INH should be discontinued and child vaccinated with BCG
  - If mantoux is positive, infant should have CXR. If CXR is normal, continue INH for 12 months. If CXR is abnormal, treat as TB with combination chemotherapy.

MULTI-DRUG RESISTANT TUBERCULOSIS

Mycobacterium resistant to a number of first line antituberculous drugs including INH and rifampicin. An inverse relationship exists between use of DOTS and prevalence of resistant strains. Only 23% of all cases were managed under DOTS in 1999. Treatment requires the use of reserve antituberculous drugs. Examples of these drugs are:

Aminoglycosides (amikacin, kanamycin) Capreomycin
Fluoroquinolones (ciprofloxacin, ofloxacin)
Thioamides (prothioanamide, ethionamide)
Para-aminosalicylic acid
Cycloserine (and terizidone)

Treatment regimen consists of at least 4 drugs including an injectable and a fluoroquinolone in the initial phase and at least 3 of the most active and best tolerated drugs in the continuation phase.

Initial phase lasts for at least 6 months while the continuation phase lasts for 12-18months.

DOTS PLUS is a veritable tool employed by WHO in combating MDR TB.

TB AND HIV/AIDS

Children who acquire HIV by MTCT are also likely to be exposed to TB.

HIV Infection increase the severity of TB in children, morbidity is more prolonged, mortality is higher and treatment may take longer to be effective.

In UCH, 61% of HIV infected children are co infected with TB. They had more rapid disease progression and a higher rate of drug resistance. HIV/TB co infection is the leading cause of AIDS related deaths worldwide.

Managing a child with HIV/TB co infection can be perplexing. This is because history and examination findings are usually alike. The laboratory investigations are mostly non specific and unhelpful. Currently recommended drug therapy for both TB and HIV need modification in patients who are co infected.

-Stavudine /INH- risk of peripheral neuropathy
-Rifampicin/nevirapine/efavirenz used in children >3years
-Thiacetazone avoided because of fatal steven Johnson syndrome
-use of 3 NRTI occasionally, especially in children <3years.

Challenges of therapy include immune reconstitution inflammatory syndrome (IRIS), pill burden, poor adherence, treatment failure, drug toxicity, interaction and resistance.

NOVEL THERAPEUTIC APPROACHES/ADJUNCTS

Heat killed M. Vaccae

-given up to 12 doses at 2mth interval
-added to MDRTB regimen
-cured 18 of 22 patients involved in a clinical trial
-a single treatment is said to halve the incidence of treatment failure
-marked reduction in mortality

-hasten return to normal of most clinical parameters

Others:

- **IL 2**
- **Interferon alpha**
- **Granulocyte macrophage colony stimulating factor**-may ultimately prove to be useful
- **Antipsychotic agents** - Chlorpromazine>thioridazine>promethazine>promazine.

  However most of the above are still undergoing clinical trial and are yet to be licensed for use.

CONCLUSION

Tuberculosis is presently a common infectious disease. It is of major public health significance.

It is presently a global health emergency. Tuberculosis is completely treatable even in the presence of HIV infection.

DOTS when properly implemented represents the best and most effective strategy to curb this deadly disease.

Novel drugs and immunomodulation stategies may be important adjuncts to treatment in the future.

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