Treatment of the MDR-TB

Monitoring the Response

W.H.O.
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Treatment of the MDR-TB

Monitoring the Response

- Objectives

1.- To evaluate the Clinical and Bacteriological response to the Treatment

2.- To monitor the Adverse Reaction to the Anti-Drugs
Diagnosis of TB disease

1. Clinical Evaluation
2. Microbiology
3. Radiology
4. Tuberculin Test
5. Anatomical pathology
6. Non-Conventional and New Methods
Diagnosis of TB disease

1. Clinical Evaluation
2. Microbiology
3. Radiology
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5. Anatomical pathology
6. Non-Conventional and New Methods
Clinical and X-ray film Manifestations of the TB

The Importance in the Follow-up and in the suspect of Failure
Limitations of the Clinical and X-ray film in the Dg of MDR-TB and in the suspect of Failure

- The not Improvement in the clinical and/or x-ray film manifestations during the treatment are very not specific data to diagnose MDR-TB

- Other Disease, frequently associated with TBC (Bronchiectasias, Resp. Infections, etc), can justify this not improvement

- These data must be evaluate only as a data more in the context of the patient

Never accept MDR-TB or a Failure only based in Clinical and/or X-ray film criteria
Radiological Manifestations of TB

- **In the diagnosis**
  - Very easy and of great value in suspected diagnosis
  - Unspecific: All X-ray patterns can be found in other diseases

- **In the prognosis** and in treatment response, it is not of decisive value either
  - % deterioration in 1-2 months of treatment
  - It is only indicated to take two chest X-rays for TB patients, at the start and end of treatment

**Not Differences with MDR-TB**
Radiological Manifestations of TB

MDR-TB at the beginning the Treatment

MDR-TB, 2 m Tr., good bacteriol. evolution
Conventional Microbiological Techniques in TB Diagnosis

1.- Bacilloscopy - Smear
2.- Culture
3.- Identification
4.- Antibiogram (DST)
Limitations of the Direct Smear in the Dg of MDR-TB and in the suspect of Failure

- Relative Importance in the Follow-up (Died Bacillus)
- Limitation to Classify the Failure (Bk- 4º Mes)
- Contamin./Apparition other Mycobacteria
- Necessary CULTURE to Ident. and DST

Anyway, Sm is very important in the Follow-up
Mycobacteria Culture

ADVANTAGES
- the only Diagnosis confirming TB
- more sensitive KB (detects 10 KB / ml)

DISADVANTAGES
- Very Slow Growth (3-8 Weeks)
- Less accessible than KB
- More expensive than KB

Pivotal in the Diagnosis and Follow-up of MDR-TB
2 Concept that can Complicate the Follow-up of the patients with TB sensible and MDR

Died Bacillus

Bacilary Escapes
Although all the MDR-TB must be confirmed by DST, these tests have important Limitations. This Limitations increase if we perform a DST during the MDR-TB Treatment.
What is the true value of the Drug Susceptibility Test?

First Line Drugs

- Very Good for H and R
- Less for S and E (More reliable the Susc. Result)
- Z needs BACTEC in many countries
What is the true value of the Drug Susceptibility Test?

Second Line Drugs

- Relatively good for Aminoglycosides and Quinolones
- Low Reliability in the others, above all:
  - Eth/Pth, Cs, PAS
Monitoring Response Treatment

1. To evaluate the Clinical and Bacteriological response to the Treatment

1. **INITIAL** Phase (usually Hospitalized). **MONTHLY**

   - Clinical evaluation → Above all to control the Side effects
   - Smear and Culture
   - X-ray film → Every 6 months

2. **CONTINUATION** Phase. Ambulatory. Every **2-3 Months**

   - Clinical evaluation → Above all to control the Side effects
   - Smear and Culture
   - X-ray film → Every 6 months

*DST* only should be requested when a new *Failure* was accepted → *Interpretation*?
Treatment of the MDR-TB

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2.- To monitor the Adverse Reaction to the Anti-Drugs
Most Common Adverse Anti-TB Drugs Reactions (AATDR)

Suspected Agents Involved and Suggested Management Strategies
Adverse ATDR. **Hepatitis**

Suspected Agents: **Z, H, R, Th, Of, L, Cx, Eth, PAS**

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**Suggested Management Strategies**

1) Stop therapy

2) Rule out other potential causes of hepatitis

3) Re-introduce drugs grouped serially while monitoring liver function, with most likely agent introduced last

* History of prior hepatitis should be carefully analysed to determine most likely causative agent(s); these should be avoided in future regimens

** Generally reversible upon discontinuation of suspected agent

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Suggested Management Strategies

1) Discontinue suspected agent

2) Consider using Cm if an aminoglycoside had been prior parenteral in regimen

* History of diabetes or renal disease is not a contraindication to the use of the agents listed here, although patients with these co-morbidities may be at increased risk for developing renal failure

** Renal impairment may be permanent

**Adverse ATDR. Arthralgias**

Suspected Agents: Z, Of, L, Cx

**Suggested Management Strategies**

1) Therapy with non-steroidal anti-inflammatory drugs
2) Initiate exercise regimen
3) Lower dose of suspected agent, if this can be done without compromising regimen
4) Discontinue suspected agent if this can be done without compromising regimen

* Symptoms of arthralgia generally diminish over time, even without intervention
** Uric acid levels may be elevated in some patients but are of little therapeutic relevance and anti-gout therapy (e.g. allopurinol, colchicine) is of no proven benefit in these patients

Adverse ATDR. **Gastritis**

Suspected Agents: **PAS, Th, H, Eth, Cfz, Z**

**Suggested Management Strategies**

1) Antacids (e.g. Calcium carbonate, H2-blockers, proton-pump isoniazidibitors)

2) Hold suspected agent(s) for short periods of time (e.g. one to seven days)

3) Lower dose of suspected agent, if this can be done without compromising regimen

4) Discontinue suspected agent if this can be done without compromising regimen

*WHO/HTM/TB/2005.361. Guidelines for the programmatic management of drug-resistant TB*
Adverse ATDR. Nausea and vomiting
Suspected Agents: PAS, Th, H, Eth, Cfz, Z

Suggested Management Strategies

1) Rehydration
2) Initiate anti-emetic therapy
3) Lower dose of suspected agent, if this can be done without compromising regimen
4) Discontinue suspected agent if this can be done without compromising regimen

**Adverse Anti-TB Drugs Reactions. SEIZURES**

Suspected agent(s): **Cs, H, Of, L, Cx**

**Suggested Management Strategies**

1) Initiate anti-convulsant therapy (e.g. phenytoin, valproic acid)

2) Increase pyridoxine to 300mg daily

3) Lower dose of suspected agent, if this can be done without compromising regimen

4) Discontinue suspected agent if this can be done without compromising regimen

**Peripheral Neuropathy**

Suspected Agents: **S, Km, Am, Cm, Th, Cs, Eth, Of, L, Cx**

**Suggested Management Strategies**

1) Increase pyridoxine to 300mg daily
2) Change parenteral to Cm if patient has documented susceptibility Cm
3) Begin exercise regimen, focusing on affected regions
4) Initiate therapy with tricyclic anti-depressant drugs
5) Lower dose of suspected agent, if this can be done without compromising regimen
6) Discontinue suspected agent if this can be done without compromising regimen
7) Initiate therapy with neurontin

*WHO/HTM/TB/2005.361. Guidelines for the programmatic management of drug-resistant TB*
**Adverse ATDR. Hearing loss**

Suspected Agents: **S, Km, Am, Cm, Clr**

**Suggested Management Strategies**

1) Change parenteral to Cm if patient has documented susceptibility Cm

2) Lower dose of suspected agent, if this can be done without compromising regimen

3) Discontinue suspected agent if this can be done without compromising regimen

* If patients have received prior treatment with aminoglycosides, they may start therapy with hearing loss  ** Hearing loss is generally not reversible

Adverse ATDR. **Psychotic symptoms**

Suspected Agents: **Cs, Of, L, Cx, H, Th**

**Suggested Management Strategies**

1) Initiate anti-psychotic drugs

2) Hold suspected agent for short period of time (one to four weeks) while psychotic symptoms brought under control

3) Lower dose of suspected agent, if this can be done without compromising regimen

4) Discontinue suspected agent if this can be done without compromising regimen

Adverse ATDR. **Depression**

**Suspected Agents:** Socio-economic circumstances, Cs, Of, L, Cx, H, Th

**Suggested Management Strategies**

1) Improve socio-economic conditions
2) Group or individual supportive counselling
3) Initiate anti-depressant drugs
4) Lower dose of suspected agent, if this can be done without compromising regimen
5) Discontinue suspected agent if this can be done without compromising regimen

Adverse ATDR. Hypothyroidism

Suspected Agents: PAS, Th, especially when given in combination

Suggested Management Strategies

1) Initiate thyroxine therapy

2) Substitute equally efficacious agent for Tha or PAS

Comments

- Completely reversible upon discontinuation of PAS or Tha

Monitoring Response Treatment

2. To monitor the **Adverse** Reaction to the Anti-Drugs

**1. INITIAL Phase** (usually Hospitalized). **MONTHLY**

- Clinical evaluation → Above all to control the Side effects
- Serum creatinine, potassium, Liver enzymes, Hemogram
- Thyroid stimulating hormone → Every 6 m. if Eth/PAS

**2. CONTINUACION Phase. Ambulatory. Every 2-3 Months**

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