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AN INTRODUCTION TO DRUG RESISTANT TB

Orthopaedics

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KEYWORDS

Drug Resistant TB (DR TB)

Multidrug-resistant TB (MDR TB) is caused by an organism that is resistant to at least isoniazid and rifampin, the two most potent TB drugs. These drugs are used to treat all persons with TB disease. Extensively drug resistant TB (XDR TB) is a rare type of MDR TB that is resistant to isoniazid and rifampin, plus any fluoroquinolone and at least one of three injectable second-line drugs (i.e., amikacin, kanamycin, or capreomycin).Because DR TB is resistant to the most potent TB drugs, patients are left with treatment options that are much less effective. DR TB is of special concern for persons with HIV infection or other conditions that can weaken the immune system. These persons are more likely to develop TB disease once they are infected, and also have a higher risk of death once they develop TB.

Drug-susceptible TB and drug-resistant TB are spread the same way. TB bacteria are put into the air when a person with TB disease of the lungs or throat coughs, sneezes, speaks, or sings. These bacteria can float in the air for several hours, depending on the environment. Persons who breathe in the air containing these TB bacteria can become infected.

Resistance to anti-TB drugs can occur when these drugs are misused or mismanaged. Examples include when patients do not complete their full course of treatment; when health-care providers prescribe the wrong treatment, the wrong dose, or length of time for taking the drugs; when the supply of drugs is not always available; or when the drugs are of poor quality.

Drug resistance is more common in people who:

- Do not take their TB medicine regularly
- Do not take all of their TB medicine as told by their doctor or nurse
- Develop TB disease again, after having taken TB medicine in the past
- Come from areas of the world where drug-resistant TB is common
- Have spent time with someone known to have drug-resistant TB disease

The most important thing a person can do to prevent the spread of MDR TB is to take all of their medications exactly as prescribed by their health care provider. No doses should be missed and treatment should not be stopped early. Patients should tell their health care provider if they are having trouble taking the medications. If patients plan to travel, they should talk to their health care providers and make sure they have enough medicine to last while away.

Health care providers can help prevent MDR TB by quickly diagnosing cases, following recommended treatment guidelines, monitoring patients' response to treatment, and making sure therapy is completed.

Another way to prevent getting MDR TB is to avoid exposure to known MDR TB patients in closed or crowded places such as hospitals, prisons, or homeless shelters.

Suspecting who is at risk of MDR TB prior to the return of susceptibility test results is the first step in early detection of drug resistance.

The most important predictors of drug-resistant TB are

1. A previous episode of TB treatment
2. Progressive clinical and/or radiographic findings while on TB therapy
3. Origin from, history of residence in, or frequent travel to a region/country with high rates of drug resistance
4. Exposure to an individual with infectious drug-resistant TB, including in facilities where drug resistance has occurred; e.g., correctional institutions, homeless shelters, or other congregate settings

Risk Factors of MDR TB in Persons with a History of TB

Suspicion for drug-resistant TB should be high if the patient has 1 or more of the following characteristics on current or prior treatment

1. Large bacillary load with extensive (bilateral or cavitary) disease
2. Lack of conversion of cultures to negative during therapy
3. Lack of improvement or only partial improvement in TB symptoms
4. Worsening of TB symptoms or radiograph findings
5. Nonadherence or intermittent or erratic ingestion of prescribed anti-TB regimen
6. Lack of directly observed therapy (DOT)or poorly supervised therapy
7. History of an inappropriate treatment regimen, including
8. Administration of single-drug therapy
9. Too few effective drugs
10. Inadequate drug doses

Risk Factors of MDR TB in Persons without Prior TB History

Clinical suspicion of drug resistance should occur when a patient with TB symptoms and signs has a history of 1 or more of the following

1. Exposure to a person with documented drug-resistant TB
2. Residence in or travel to a region with high rates of drug-resistant TB
3. Residence or work in an instiMion or setting in which drug-resistant TB is documented
4. Treatment of pulmonary problems with a prolonged course of multiple medicines or an injectable agent for more than a few weeks in a foreign country (the patient may not realize that he/she was treated for TB)
5. Treatment of a pulmonary problem with a fluoroquinolone
6. Previous treatment for latent TB infection (LTBI) when signs of TB disease were not recognized

Principles of Management

Investigations-

- Xray, MRI, routine blood tests
- Culture LJ media -6to 10 weeks incubation period
- Bactec 460 – costly
- MGIT – from all specimens expect blood
- Biopsy and CBNAAT/Gene Xpert test -A more efficient and cost-effective alternative is the achievement of culture isolation by the means of biopsy (computed tomography or fluoroscopy guided) for more complete detection of the new cases of drug-resistant tuberculosis and the testing of all initial culture isolates for susceptibility to at least the primary antitubercutous drugs-ideally all of them.

Rapid identification of drug resistance in a patient with TB is critical in order to

1. Treat the patient with the most appropriate empiric regimen
2. Minimize transmission
3. Minimize potential drug side effects
4. Provide the best chance of cure
5. Prevent further drug resistance
6. appropriate care to contacts

Principles of Treatment-

- Treatment regimens for MDR-TB spine have to be tailor made according to the drug sensitivity profile of each patient. It can be started empirically if the drug sensitivity prevalent in the community is known or individualized according to the drug sensitivity testing of the patient.
- Diabetes and HFV are more frequently associated with drug resistance making treatment even more difficult.
- Refer/Consultation of all cases to chest physicians with experience in managing pulmonary MDR-TB.
- Drug sensitivity testing, available from a reliable laboratory, should be used to guide therapy.
- Regimens should consist of minimum four new drugs not used previously. Patients with overall five or more drugs do better.
- An injectable aminoglycoside should be should be used for a minimum period of 2 months.
- Never add a single drug to a failing regimen-"addition syndrome" must be avoided.
- Treatment should be for a minimum duration of 24 months.
- Patients on second-line drugs need to be monitored carefully for side effects.
- Check for baseline complete blood count (CBC), renal, liver profile, audiogram and visual assessment.
- Serum creatinine should be repeated twice monthly. CBC, liver enzymes and audiological and visual assessment monthly and thyroid status assessment 6 months after the initiation of treatment (if ethionamide/paraaminosalicylic acid (PAS) used.
- Gastrointestinal side effects are the most common and can require hospitalization. Hepatotoxic drugs need to be stopped if the liver enzymes are five times their normal value. Drug-induced neuropathies form a considerable group to the extent that pyridoxine should be an integral part of the regimen from the outset.
- Due to the above considerations, the importance of regular and long-term follow-up to ensure compliance, to assess side effects and development of further resistance should be emphasized to the patient.

Positive predictors of a successful outcome in MDR-TB

1. Progressive clinical improvement over 6 months and radiological improvement during treatment (3 months and 6 months from the start of treatment)
2. Disease strains exhibiting resistance to less up to three anti tubercular drugs
3. Use of less than up to three second-line drug classes in treatment
4. Absence of coexistent HIV infection/diabetes
5. Continuation of same regimen during treatment