MDR-TB Treatment Regimens, Outcomes, and Cost in Haiti

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Two MDR-TB sites in Haiti

Working in close collaboration with PLNT, LNSP, MSPP
Overview of MDR-TB Treatment

- Need at least 4 drugs that are likely to be effective in the intensive phase.
- Do not count PZA or ethambutol, even if sensitive by DST, because DST is not perfect and nearly all patients have already received these medications.
- Always include an injectable agent (kanamycin or capreomycin) and a quinolone.
- Supervision of treatment: Twice-daily DOT is required.
- Monitoring therapy – requires culture capacity.
Empiric MDR-TB Regimen

1. **Injectable agent** – kanamycin or capreomycin
   * Capreomycin preferred for patients with risk factors for renal failure (diabetes), and for those living with HIV
   * If patient develops otoxicity or nephrotoxicity on kanamycin, switch to capreomycin

2. **Fluoroquinolone** – moxifloxacin or levofloxacin
   * Moxifloxacin is preferred for HIV-infected patients and those who present with very severe MDR-TB
   * For patients weighing >50 kg, higher dose levofloxacin (1000mg per day) is preferred

3. **Ethionamide** for all patients

4. **Cycloserine** – avoid if history of seizure disorder or psychiatric disease

5. **PAS** – if contraindication to cycloserine, for severe MDR-TB, or for HIV-infected

6. **Pyrazinamide** for all patients that did not have side effects in first-line regimen

7. **High dose isoniazid** (because about 20% of patients will be resistant to ethionamide when DST results available)
Individualized MDR-TB Regimen

- Stop high dose isoniazid when second-line DST results available
  - If resistant to ethionamide (due to cross-resistance with isoniazid; nearly 20% of patients) then add PAS
  - If sensitive to ethionamide then continue ethionamide
- If sensitive to ethambutol, add it but do not count it
- If patient is resistant to any of the other second-line medications, their regimen will be developed on an individualized basis.
HIV and MDR-TB Co-infection

- ART for all patients with HIV and MDR-TB, irrespective of CD4 cell count, as early as possible following initiation of MDR-TB treatment.
- Preferably treat with capreomycin, moxifloxacin, ethiomanide, cycloserine, PAS, and pyrazinamide
Duration of treatment and monitoring of therapy

- Intensive phase – continue injectable until 6 consecutive negative cultures (at least 8 months).

- Total treatment duration is 24 months

- Monthly AFB smear and culture (may decrease this frequency for clinically stable patients)
Laboratory Monitoring for Toxicity

- Baseline - potassium, creatinine, SGOT/SGPT/bilirubin, complete blood count, HIV test, pregnancy test for women of reproductive age
- SGOT/SGPT monthly X 3 months; if HIV+ then monthly throughout treatment
- Potassium and creatinine weekly for first month, then monthly while on injectable agent (2 weeks for diabetics, age>50, and HIV+); for HIV+ also monthly while on maintenance
- Complete blood count every 3 months; for HIV+ monthly throughout treatment
- TSH every 3-6 months
### Side effects at PIH (n=111 patients)

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Number/111 pts</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastric problem</td>
<td>19</td>
<td>17%</td>
</tr>
<tr>
<td>Psychosis/nervous breakdown</td>
<td>23</td>
<td>21%</td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
<td>24</td>
<td>22%</td>
</tr>
<tr>
<td>Ototoxicity</td>
<td>21</td>
<td>19%</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>9</td>
<td>8%</td>
</tr>
<tr>
<td>Vestibulo/cochlear problem</td>
<td>5</td>
<td>5%</td>
</tr>
<tr>
<td>Hyperactivity</td>
<td>5</td>
<td>5%</td>
</tr>
</tbody>
</table>
PIH MDR-TB outcomes

- 158 patients started on treatment since 2008
  - 78 (49%) women; 25 (16%) HIV+
- 12 (8%) died
- 13 (8%) lost to follow up
- 133 (84%) in care or completed treatment
  - 31 (23%) inpatient
  - 26 (20%) outpatient
  - 76 (57%) completed treatment
Side Effects at GHESKIO (n=76)

- Ototoxicity 22%
- Psychiatric toxicity (depression or psychosis) 20%
- Peripheral neuropathy 17%
- Severe nausea, vomiting, or diarrhea 17%
- Arthritis 12%
- Anemia 12%
- Hypokalemia 9%
- Hypothyroidism (TSH> 10) 8% (*TSH was not routinely checked*)
- Renal toxicity 4%
- Hepatitis 1%
GHESKIO MDR-TB outcomes

- 141 patients started on treatment since program started in 2008 (most since earthquake)
  - 72 (51%) women; 30 (21%) HIV+
- 17 (12%) died
- 6 (4%) lost to follow up
- **118 (84%) in care or completed treatment**
  - 32 (27%) inpatient
  - 46 (39%) outpatient
  - 40 (34%) completed treatment
- Outcomes are poorer in HIV+ patients (17 [57%] on treatment, 4 [13%] cured, 7 [23%] died, 2 [7%] abandoned)
Community-based MDR-TB care

- Inpatient care: ~3 months (if patient is clinically stable and adherent to medications)
- Outpatient: 21 months
  - DOTS
    - Close supervision of fieldworkers (GPS, daily phone calls, surprise visits)
  - Close monitoring for clinical response and toxicity
  - Strong partnership with patient and family members
  - Social support (transportation, phone cards, meetings, food rations, and a monetary prize upon completion of treatment)
Cost of Outpatient Medical Care (21 Months) w/out MDR-TB drugs

- Ancillary Drugs: $11/month; $231 total for 21 months
- Lab Testing and Radiology:
  - TB diagnostics (smear, GeneXpert, ID, culture and DST: $194
  - Monitoring for toxicity: ~$450
  - CXR every 6 months: $100
  - AFB/culture every month: $1134
  - Total laboratory: ~$1878
- Outpatient Medical Care
  - Transportation to clinic: $5/visit for about 36 visits - $180
  - Clinic-based labor with overhead (MD, nurse, social worker, etc): $40/month; $840 total
  - Total outpatient medical care: $1020
- Supervision of Medications
  - Auxiliary nurse ($100/month X ~5 months outpatient) or CHW ($50/month X 16 months outpatient) for DOT (2X daily DOT): $50/month = $1300 total
  - Transport for CHW: $130/month; $2730 total
  - Total medication supervision: $4,030
- Social Support
  - Phone cards: $11 per month; $231 total
  - Nutrition supplement: $50/month; $1050 total for 21 months
  - Total: $1281
  - End-of-treatment prize: $200
- TOTAL FOR 21 MONTHS OF TREATMENT: $8640
Needs for Scale-up of MDRTB Treatment

- Training:
  - Laboratory personnel
  - Health care workers (MDs, RNs, RN aides, fieldworkers)

- Legal/logistical aspects of care

- Scale-up MDR-TB treatment with guidance of PNLT

- Funding for drugs, medical care, and social support