Treatment of TB – a pharmacy perspective

Colm McDonald,
Antimicrobial Stewardship Pharmacist (Acting)
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Overview of presentation

- Role of the pharmacist in the TB service
- Case study No. 1; Treatment of pansensitive TB
- Case study No. 2; Treatment of MDR TB
- Treatment regimens for Latent TB Infection
- Access to TB medication nationally
- Questions

References provided at appropriate points throughout the presentation.
Not included in this presentation; TB and HIV as this is an area covered by specialist HIV pharmacists at St. James’s Hospital
Role of the pharmacist in the management of TB

*It is recommended that a pharmacist is a member of the clinical team and attends the clinics, where they have an important role to play in:
1) dispensing of TB medications to patients and maintaining dispensing records
2) providing appropriate written and verbal information to patients to enable them to understand and comply with their medication
3) promoting and monitoring patient compliance with their medication regime

* Reference; Guidelines on the Prevention and Control of TB in Ireland, National TB Advisory Committee, April 2010
Role of the pharmacist in the management of TB

4) screening for potential drug interactions, monitoring adverse drug reactions and advising on their management, particularly for patients with MDR-TB and HIV-TB co-infection

5) maintaining links with community and hospital pharmacy services where appropriate and

6) Participating in clinical audit
Case Study 1; treatment of pansensitive TB (1st Clinic visit)

- Patient AB, symptomatic household contact of pansensitive case attends TB clinic
- AFB visible on sputum microscopy (sent for C&S)
- Weight = 80kg, baseline FBC, U&E, LFTs (all normal)

Prescribed:

**Rifater®** 6 tablets once daily PO
(rifampicin, isoniazid and pyrazinamide) and

**Ethambutol** 1.2grams (15mg/kg) once daily PO, and

**Pyridoxine** 20mg once daily PO
Case Study 1; treatment of pansensitive TB – main references

4. BTS Chemotherapy and management of TB in the UK, 1998. (now officially superceded by NICE CG117, but has some useful additional information)
Case Study 1; treatment of pansensitive TB (1st Clinic visit)

- TB medication best given as combination tablets where possible to ensure compliance, and avoid inadvertent monotherapy
- Pyridoxine to prevent isoniazid induced neuropathy
- Small risk of ocular toxicity with ethambutol – check baseline renal function, and baseline and regular visual acuity and colour discrimination
- Interactions; many with rifampicin – check for any other medications, and advise patient not to commence other medicines without advice.
- Avoid alcohol, paracetamol
Case Study 1; treatment of pansensitive TB (1st Clinic visit)

- Patient education points;
  Take tablets once daily as a single dose on an empty stomach
  Expect urine to turn orange-red; may stain contact lenses
  Contact clinic immediately (or attend A&E) if rash, fever, malaise, vomiting, jaundice, sight problems
- Provide patient information leaflets, (language barrier is sometimes a problem here)
- Provide clinic contact phone numbers (incl. nurse and pharmacist bleep numbers)
- Dispense exact supply of medicines as prescribed until next clinic appointment
Case Study 1: treatment of pansensitive TB (2nd and subsequent visits)

- Next clinic visit; C&S showed *M. tb* sensitive to all first-line medicines – ethambutol stopped
- Check bloods again, particularly LFTs
- Monitor patients weight and ensure doses are amended if necessary
- Check compliance?
- Any adverse events?
- Reinforce previous education points
- Dispense again until next appointment
Case Study 1; treatment of pansensitive TB – duration of therapy*

- Isoniazid, rifampicin and pyrazinamide (with ethambutol until sensitivity is known) for the initial two months (intensive phase)
- Followed by isoniazid and rifampicin (as Rifinah® combination tablet) for at least a further four months (continuation phase)
- Duration should be extended to nine months (or longer) for certain patients – check references

Case Study 1;
adverse event – elevated LFTs

- Rifampicin, isoniazid and pyrazinamide are all potentially hepatotoxic.
- Baseline, and regular LFTs (particularly ALT) in patients who are at risk of hepatotoxicity
- Warn patients to report s/e such as malaise, vomiting, jaundice immediately
- Modest increases in transaminases not uncommon when starting therapy
Case Study 1;
adverse event – elevated LFTs

- **BUT** if AST or ALT rise to 5 x Upper Limit of Normal (ULN), or bilirubin rises above ULN; rifampicin, isoniazid and pyrazinamide should be held.
- Bridging therapy?
- Sequential escalating rechallenge when LFTs normalise (isoniazid or rifampicin first and second, followed by pyrazinamide)
Isoniazid and Rifampicin are the most important 1st line anti-TB drugs

BUT; no new 1st line drugs in the past 40 years

Sporadic ingestion, monotherapy, inadequate doses, malabsorption of medication, can lead to susceptible strains of *M. tb* becoming resistant to drugs (perhaps within one month)
Case Study 2 – Treatment of MDR TB

Patient CC. Diagnosis of MDR TB;
(resistance to at least isoniazid and rifampicin)

DOT essential for these patients (usually BD)

Drug regimen;
- Pyrazinamide 2grams once daily PO
- Ethambutol 1gram once daily PO
- Amikacin 15mg/kg once daily IV
- Moxifloxacin 400mg once daily PO
- Protonamide 500mg BD PO
- Cycloserine 250mg mane/500mg tarde PO
References – MDR TB

Largely based on expert opinion, cohort and case series analysis

- **World Health Organization.** Guidelines for the programmatic management of drug-resistant TB; update 2008
- The **Curry International Tuberculosis Center (CITC)** University of California, San Francisco; “Drug resistant TB; A survival guide for clinicians (2008)” [available at www.nationaltbcenter.edu]
Case Study 2 – MDR TB Treatment Regimen

**STEP 1** Begin with any *first-line* agents to which the isolate is susceptible. Add a *fluoroquinolone* and an *injectable* drug based on susceptibilities

**STEP 2** Add *second-line* drugs until you have 4–6 drugs to which the isolate is susceptible (and preferably which have not been used to treat the patient previously). Oral second-line drugs; Cycloserine, Protonamide, PAS (all *bacteriostatic*)

**STEP 3** If there are not 4–6 drugs available in the above categories, consider *third-line* drugs in consultation with an MDR-TB expert. Third-line drugs include Clofazimine, Linezolid, Amoxicillin/Clavulanate, Imipenem, Macrolides, High-dose isoniazid
Case Study 2 – MDR TB Treatment Regimen - duration

- Intensive phase (incl. injectable) at least 4 to 6 months, guided by time to culture conversion

- Continuation phase (without injectable) a further 12-18 months
Case Study 2 – MDR TB Treatment Regimen – common adverse reactions

- Amikacin; hearing loss, vestibular toxicity, electrolyte imbalances, renal toxicity (need to monitor amikacin levels)
- Protonamide; hypothyroidism (CC commenced levothyroxine 25 micrograms once daily PO), nausea (CC prescribed antiemetics e.g. metoclopramide or prochlorperazine, and dose divided BD to reduce nausea)
Case Study 2 – MDR TB Treatment Regimen – other adverse reactions

- Cycloserine; risk of depression, seizures (monitor peak cycloserine levels), risk of peripheral neuropathy (CC prescribed high-dose pyridoxine)
- Moxifloxacin; risk of QT prolongation, and hepatic toxicity
- Risk of hepatotoxicity with both pyrazinamide and protonamide
- Regular eye tests required while on ethambutol
Latent TB Infection (LTBI)

3 Major groups treated for LTBI at SJH;
1. Contacts of active TB cases
2. Health Care Workers
3. Patients for TNF-alpha inhibitors

The recommended treatment regimens* for LTBI in adults are:
(i) isoniazid 5mg/kg daily (max 300mg daily) for a minimum of six months with an optimum duration of nine months, or
(ii) rifampicin for four months, or
(iii) a combination of rifampicin and isoniazid for a duration of at least three months and an optimum of four months

*Guidelines on the Prevention and Control of TB in Ireland, National TB advisory Committee, April 2010
2. TNF-alpha antagonists and TB, Kavanagh and Gilmartin, HPSC 2007
3. NICE Clinical Guideline CG117 on clinical diagnosis and management of TB, March 2011
4. BTS recommendations for assessing risk and managing \textit{M. Tb} infection and disease in patients due to start anti-TNF-alpha treatment, Thorax 2005; 60: 800-805
Access to TB medications

- 1947 Health Act – all aspects of management of TB, incl. medications, are free to patient.
- Traditionally via Health Board Centres or Health Board Pharmacies (e.g. “Central Pharmacy”)
- Certain regions – dispensing via Community Pharmacies with reimbursement via HSE
Access to TB medications

- Licensed vs. unlicensed status of medicines
- St. James’s Hospital – medicines supplied on-site at TB clinic, but paid for by HSE.
- HSE Dublin/Mid-Leinster area; current HSE advice is to liaise with the HSE Community Care Pharmacist if any queries re. access to and reimbursement of TB medicines which are to be supplied via community pharmacies
- The future nationally?
Thank you for your attention

Questions?