OFF-SIDES: Management of complex Non-Tuberculosis mycobacterial infections in an 'Aminoglycoside free' hospital

Miatke D[1], Mann T[1], Chellaram V[1].
[1]Pharmacy Department, Northern Health, Epping, Victoria, Australia.

CLINICAL FEATURES:

The simultaneous management of two patients requiring complex, multi-drug antimicrobial regimes to treat severe Non-Tuberculosis mycobacterial infections. Admitted in May 2023 both patients required long term aminoglycoside therapy, complicated by factors such as age, frailty and renal failure

At Northern Health, use of aminoglycoside antimicrobials has long been discouraged; this is largely due to the high risk of toxicity associated with aminoglycoside use and the availability of newer, safer agents.

PATIENT ONE

72M with disseminated Mycobacterium chelonae infection secondary to extensive medicine induced immuno-suppression

May 2023:

- Painful lesions covering arms, legs, hands and face
- Biopsies grew Mycobacterium chelonae
- Complex Rheumatolological and Cardiac history

Sensitivities:

(S) Clarithromycin, Tobramycin, Tigecycline
(I) Ciprofloxacin, Moxifloxacin, Imipenem, Linezolid
(R) Cotrimoxazole, Doxycycline, Cefoxitin

Tobramycin: 5mg/kg IV daily
Clarithromycin: 500mg PO BD
Tigecycline: 50mg IV BD

PATIENT TWO

45M with Mycobacterium abscessus Tenckhoff-related intra-abdominal soft tissue infection

May 2023:

- Abscess at PD site complicated by complex, enhancing collection
- Swabs grew heavy growth of Mycobacterium abscessus
- Tenckhoff removed, changed to Haemodialysis

Sensitivities:

(S) Amikacin, Tigecycline, Linezolid
(I) Cefoxitin, Imipenem
(R) Macrolides, Ciprofloxacin, Doxycycline

Amikacin: 10mg/kg stat when pre-dialysis levels are <10
Linezolid: 600mg PO daily
Tigecycline: 50mg IV BD

CHALLENGES

Toxicity: Mycobacterial infections usually require months of therapy to achieve cure, as a result likelihood of aminoglycoside toxicity was an unavoidable risk.

Lack of infrastructure: No approved procedures detailing aminoglycoside management with limited access to in-house therapeutic drug monitoring software and laboratory assays for rarely-prescribed antimicrobials.

Clinician experience/knowledge: Organisational avoidance of their use has resulted in limited experience in prescribing, administering and monitoring of aminoglycosides.

Supporting evidence: Due to the rarity of the infections, there was a dearth of supporting evidence for treatment regimens. This was further compounded by the complex co-morbid states of both patients, as well as the resistance profiles of infecting organisms.

TAKING THE LEAD

Management was led by the Antimicrobial stewardship (AMS) pharmacy service. The AMS pharmacy team:

- Directed dosing, monitoring and modelling of the antimicrobials.
- Provided extensive education to the physician, pharmacy and nursing teams looking after the patients.
- Helped co-ordinate the offsite processing of aminoglycoside levels.
- Ensured potential medication interactions and concomitant co-morbid states were identified and managed throughout the patient journeys.

Comparison of Tobramycin dose modelling between online therapeutic drug monitoring program TDMx (Figure 1) and DoseMe Rx (Figure 2).

- DoseMe Rx was used to validate the results of TDMx to ensure safe administration and monitoring.

Figure 1: Tobramycin modelling from May 29 2023 – June 10 2023 using TDMx

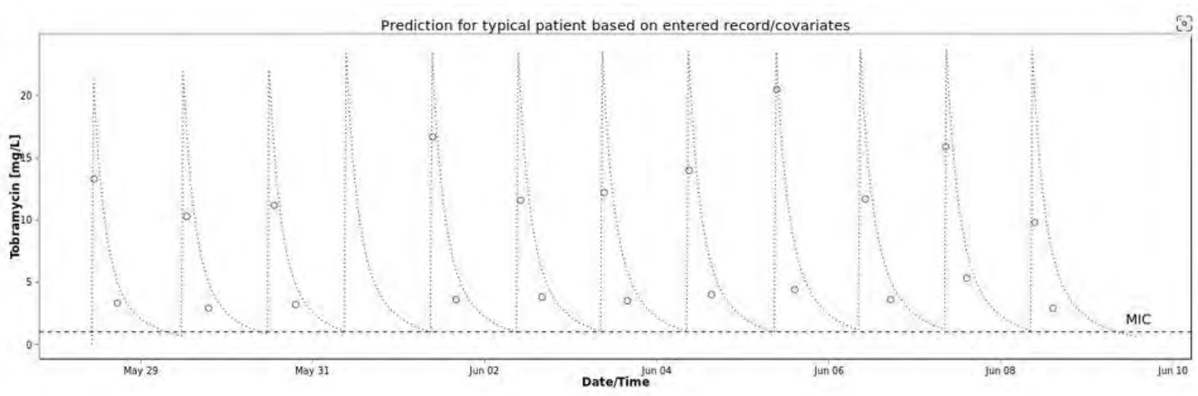
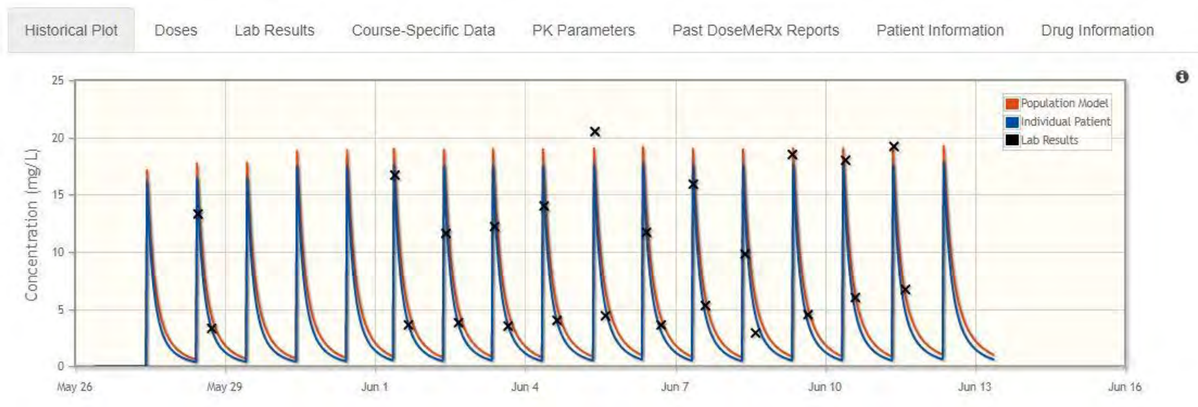


Figure 2: Tobramycin modelling from May 28 2023 – June 13 2023 using DoseMe Rx



LEARNINGS

Use your ingenuity

Lacking access to a proprietary product for TDM and urgently requiring an alternative. A literature search, provided an evidence supported, online aminoglycoside modelling program. Accuracy was validated using DoseMe Rx to ensure safe administration and monitoring.

In the absence of evidence-based guidelines, treatment plans were established through a combination of clinician experience, literature review and pharmacological expertise.

Patient knows best

To best mitigate risk of aminoglycoside toxicity extensive education was provided at time of initiation and repeated regularly throughout therapy.

Although both patients did eventually present with signs of aminoglycoside toxicity, symptoms were escalated early and acted upon. As a result both patients have had almost full resolution of toxicity related symptoms.

Ask and you shall receive

Help from other centres was integral to the success in these cases:

- Protocols from multiple networks guided practice in the absence of in-house documents
- Barwon Health assisted with therapeutic drug monitoring (TDM) through DoseMe Rx
- Royal Melbourne Hospital renal team provided specialist clinical advice
- Alfred pathology service facilitated TDM via urgent processing of aminoglycoside levels

Gracious thanks is extended to all who provided assistance

www.nh.org.au

safekindtogether

Northern Health