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Efficacy And Safety Of Using Inhaled Amikacin For Treatment Of Pulmonary Non-tuberculous Mycobacteria

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INTRODUCTION

- Pulmonary non-tuberculous mycobacterium (NTM) infections are often multidrug resistant and require combination antibiotic therapy.
- Intravenous (IV) amikacin is commonly used but limited by nephrotoxicity and ototoxicity. Inhaled amikacin may be a viable alternative but there is limited data on efficacy and safety.
- **Aims:** Study the efficacy and safety of inhaled amikacin for pulmonary NTM.

METHODS

- Retrospective analysis of patients treated with inhaled amikacin as part of combination therapy for pulmonary NTM at Singapore General Hospital from January 2021 to December 2024.
- All patients were pre-treated with inhaled salbutamol 15 mins prior. IV amikacin solution was diluted with 3ml of 0.9% sodium chloride solution and administered via a commercially available jet nebulizer.
- A total of 18 patients were included in the study.

RESULTS

Patient characteristics are shown in Table 1

Patient characteristics, median (interquartile range) or number (%)	
Age	70.5 (57.5 – 74.0)
Male/ Female	6 (33.3), 12 (66.7)
BMI	18.2 (15.9 – 20.5)
History of smoking	3 (16.7)
Underlying pulmonary condition	
Bronchiectasis	17 (94.4)
Asthma	1 (5.6)
Post pulmonary tuberculosis	2 (11.1)
Allergic bronchopulmonary aspergillosis (ABPA)	1 (5.6)
Immunocompromised	
Endometrial cancer	1 (5.6)
Renal cell carcinoma	1 (5.6)
Rheumatoid arthritis	1 (5.6)
Ankylosing spondylitis	1 (5.6)
Steroid use for ABPA	1 (5.6)
Previous NTM infection	12 (66.7)
NTM Species	
Mycobacterium abscessus	12 (66.7)
Mycobacterium fortuitum	1 (5.6)
Mycobacterium avium complex	2 (11.1)
Mixed (M. abscessus, M. fortuitum, M. avium complex, M. Kansasii)	3 (16.7)
AFB Smear positive	6 (33.3)
Macrolide sensitivity	7 (38.9)

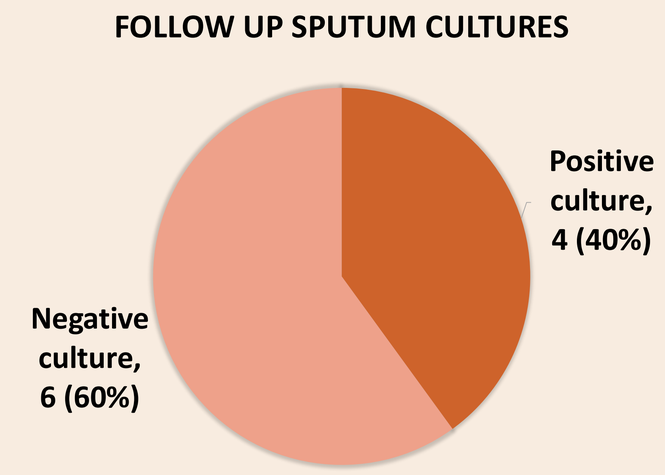
Median treatment duration of inhaled amikacin: 11.5 months (IQR 6-12)
Median dose: 500 mg once daily
16/18 (88.9%) were treated with combination antibiotics prior to starting inhaled amikacin for a median of 6 weeks

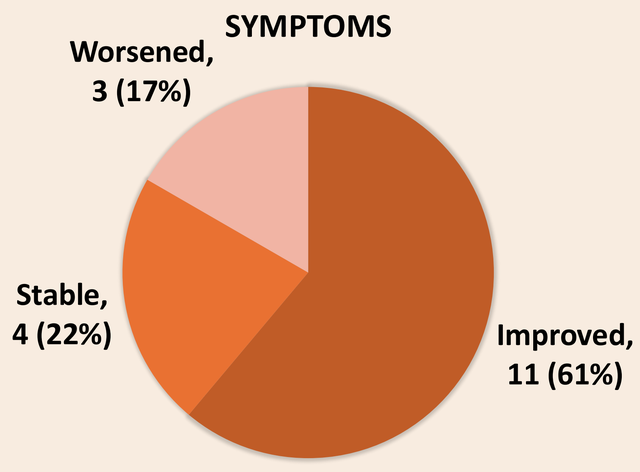
Adverse effects are shown in Table 2

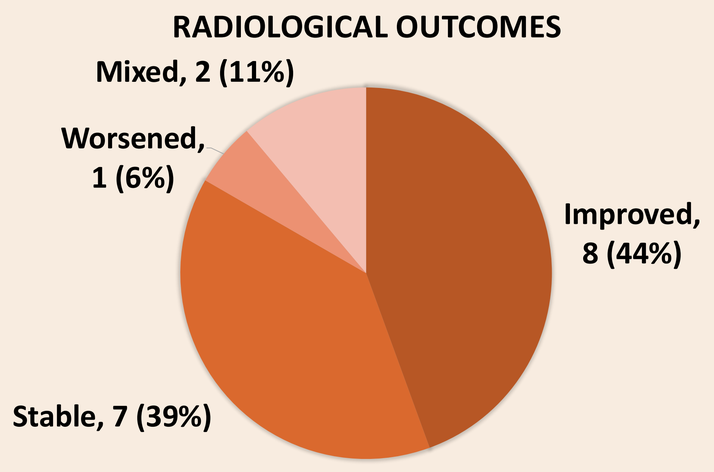
Adverse effects (AE), n (%)	
Nephrotoxicity	0/18 (0.0)
Audiological effects	
Baseline hearing loss prior to start of inhaled amikacin	15/18 (83.3)
Vertigo	1/18 (5.6)
Hearing loss (meeting audiometry threshold)	4/11 (36.4)
Prior use of IV Amikacin in patients with hearing loss	3/4 (75.0)
Other symptoms	
Palpitations	1/18 (5.6)
Itch	1/18 (5.6)
Chest tightness	1/18 (5.6)
Oral thrush	1/18 (5.6)
AE resulting in discontinuation of drug	5/18 (27.8)
Oral thrush	1 (5.6)
Vertigo	1 (5.6)
Hearing loss	2 (11.1)
Itch	1 (5.6)

- 16 patients had random amikacin levels done while on inhaled amikacin, all achieved levels <1.0

Clinical Outcomes







DISCUSSION

- Clinical outcomes comparable to other studies using inhaled amikacin. Previous studies reported 34-65.2%[1-2] had at least one negative sputum compared to 55% in our study. 61% of our patients reported symptomatic improvement and 44% had radiological improvement compared to 49% and 42% respectively in a large cohort by Jhun et al.
- No severe adverse effects reported. Most common adverse effects was hearing loss in 36.4%, but likely confounded by prior use of IV amikacin which can have delayed hearing loss[3], and other concomitant ototoxic drugs like azithromycin.
- Other common adverse effects reported in other studies[1, 4] like hoarseness of voice and dysphonia, were not reported in this study.
- Amikacin liposome inhalation suspension has been studied for pulmonary NTM (in particular, refractory MAC)[4], however it is expensive and not readily available. Our paper demonstrate safety and reasonable clinical outcomes with injectable formulation of amikacin.
- **Limitations:** Retrospective nature, no standardized protocols for monitoring of clinical outcomes like sputum collection, follow up radiology scans and symptom assessment. Ototoxicity only routinely monitored from May 2024 onwards.

CONCLUSION

Inhaled amikacin is a viable treatment option for pulmonary NTM, particularly in patients with limited alternatives. It was generally well tolerated, though monitoring for ototoxicity remains important.

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