Anti-Inflammatory and Immunomodulatory Effects of Macrolides: Biological Mechanisms and Clinical Use in the Management of Chronic Diseases

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Background and Objectives: Macrolides are well established antimicrobial agents; however, accumulating evidence suggests they also possess clinically meaningful anti-inflammatory and immunomodulatory properties. This review aimed to evaluate the biologic mechanisms underlying these effects and assess the clinical evidence supporting the use of macrolides as adjunctive therapy in the management of chronic diseases. Additionally, safety considerations and the potential impact of long-term macrolide therapy on antimicrobial resistance were examined.

Methods: A structured literature review was conducted using the PubMed electronic database. Search strategy development was guided by a PICO framework and included English-language studies published between 1987 and 2023. Adults (≥18 years) with chronic diseases treated with macrolide therapy were included, with randomized controlled trials prioritized. Chronic disease states reviewed included chronic obstructive pulmonary disease (COPD), cystic fibrosis (CF), asthma, chronic rhinosinusitis (CRS), non-cystic fibrosis bronchiectasis (NCFB), diffuse pan bronchiolitis, and rheumatoid arthritis (RA). Data were organized using a literature matrix and synthesized through thematic analysis focusing on clinical efficacy, mechanisms of action, dosing strategies, symptom effects, adverse events, and antimicrobial resistance.

Results: Macrolides demonstrated multiple immunomodulatory mechanisms, including promotion of anti-inflammatory macrophage polarization, modulation of T-cell responses, suppression of pro-inflammatory cytokines and chemokines, inhibition of NF-κB signalling, and disruption of bacterial biofilm formation and quorum sensing. The strongest clinical evidence was observed in COPD, CF, and NCFB, where long-term macrolide therapy consistently reduced exacerbation frequency, improved quality of life, and, in several studies, stabilized lung function. More limited and heterogeneous evidence was identified in asthma, CRS, and RA, where benefits appeared restricted to selected patient populations, including atypical bacterial infection, low-IgE CRS, post-operative CRS, and early active RA. Across all disease states, long-term therapy was consistently associated with increased antimicrobial resistance, while ototoxicity, gastrointestinal intolerance, and potential QT prolongation remained important safety considerations.

Discussion: The available evidence suggests that the clinical benefits of macrolides extend beyond antimicrobial activity and are likely mediated through multiple complementary anti-inflammatory, immunomodulatory, and anti-virulence mechanisms. Their therapeutic value appears greatest in chronic respiratory diseases characterized by recurrent exacerbations and persistent neutrophilic inflammation. Conversely, evidence supporting routine use in asthma, CRS, and rheumatologic disease remains insufficient. Careful patient selection and ongoing monitoring are essential to balance clinical benefit against adverse effects and antimicrobial stewardship concerns.

Conclusions: Macrolides represent promising disease-modifying adjunctive therapies for selected chronic inflammatory diseases, particularly COPD, CF, and NCFB. Future research should prioritize biomarker-guided patient selection, optimization of dosing strategies, and investigation of long-term effects on antimicrobial resistance and the airway microbiome to better define their role in chronic disease management.

Keywords: macrolides; immunomodulation; COPD; asthma; rhinosinusitis; cystic fibrosis

Estimating the Carbon-Footprint, Cost, and Healthcare Resource Use in the Last Week of Life for Patients who Died on Inpatient Wards: A Retrospective Cohort Study

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Background and Objectives: The clinical teaching unit (CTU) is a universal educational model for medical trainees in the setting of acute ward-based care. The presumption of the standard of care on a CTU is to cure acute illness, which may not reflect the patient's prognosis, goals of care or values. It is unknown how the CTU model affects care for inpatients with terminal illness with or without palliative care goals. We hypothesize that there may be under-recognition of end-of-life (EOL) presentations on the CTU and the value of shifting towards care plans that demedicalize death. To examine the timing of recognition of likely death and subsequent transition to comfort-focused goals of care (GoC); to quantify medicalization of expected death; and lastly, to quantify resource use and their associated carbon emission equivalents pre- and post-transition.

Methods: We conducted a retrospective cohort study of adult inpatients who died during admission to the 8.2 CTU at the Halifax Infirmary between January 1, 2023, and December 31, 2023 (N=103). Patients who died in other hospital settings were excluded. Electronic medical chart reviews were performed to collect demographic data and resource utilization data for the final 7 days of life. Resource data informed analyses of inappropriate medicalization, cost, and associated carbon emissions. The primary outcomes were i) the proportion of medicalized days; ii) total inpatient costs; and iii) total estimated healthcare-associated greenhouse gas emissions during the final week of life. Multivariable logistic regression was used to describe predictors of medicalized death. Total inpatient costs and carbon emissions were quantified via generalized linear models with gamma distribution and log link.

Results: In our study population, 86.7% of patients experienced a medicalized death. From the time of recognition of imminent death, patients experienced a median of 2 medicalized days (IQR 1-4) and a median proportion of 66.7% medicalized days (IQR 25-100%) before they died. A delay of ≥ 2 days to transition a patient to comfort care after imminent death was recognized