## Macrolides: Are They Safe Bet in Management of Community Acquired Pneumonia (CAP) in Elderly Patients Admitted to an Intensive Care Unit (ICU)

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## **Abstract**

ICNARC data from UK ICU has demonstrated 125% increase in patients requiring ICU admission for advance ventilator support following a severe Community-Acquired Pneumonia (CAP). They constitute one of critically ill patient's cohorts in ICU. Cardiovascular (CVS) morbidity and mortality associated with CAP has been well-known for several decades. Macrolides form integral part of antibiotic bundle worldwide in management of severe CAP in the ICU setting. We attempt to suggest strategy to mitigate CVS morbidity and mitigate this risk. Daniel et al., recently reported patients with CAP were younger (78 vs. 80 years), significant respiratory symptoms including fever, cough, dyspnoea and pleuritic chest pain as compared to those patients with those patients coded as pneumonia on discharge. They had fewer constitutional symptoms and significantly higher mortality (17% vs. 14.3%, p=0.003). However, Sub-Saharan Africa has significantly higher mortality in relatively young patient due to Human Immunodeficiency Virus (HIV) prevalence in the region; and coinfection with tuberculosis and opportunistic infections is common. Feldman Anderson reported significant cardiac complications in severe pneumococcal pneumonia despite herd immunity following pneumococcal conjugated vaccine. Interestingly, in developed and developing countries, diabetes mellitus prevalence was significantly increased with CAP hospital admissions and was associated with longer hospital stay and increased mortality. Community-Acquired Pneumonia (CAP) is a common and potentially serious illness. An acute severe infection of lung parenchyma ultimately leads to grey hepatisation which impairs gas exchange across alveolar membrane. CAP is associated with considerable morbidity and mortality, particularly in elderly patients and those with significant comorbidities. Pneumonia Severity Index (PSI) and British thoracic society CURB65 criteria were less predictive at outcomes such as requirement for ICU admission and need for invasive ventilation. They are of limited use in the critical care environment In temperate

and subtropical climates; Murdoch et al, demonstrated an association between seasonal variation and the occurrence of CAP.At present, overall about 22-42% of CAP patients require hospital admission, of whom 5-10% will be admitted to an ICU. Hospital and ICU admission rates for CAP are increasing for all ages. In a Finnish study, the incidence of CAP rose dramatically with age, with a sixfold increase in incidence between ages 30-44 years and ≥75 years. In Portugal, case fatality rates were 4.5% for patients aged 18-50 years, 19.4% for those aged ≥50 years and 24.8% for those aged ≥75 years. A UK study reported case-fatality rates of 5.6% in those aged <65 years and 47.2% for those aged ≥85 years. This study also found a 12-fold higher OR for death within 30 days of hospital admission for adults aged ≥85 years than for those aged <65 years. With the projected increase of those aged  $\geq$ 65 years to 20% of the adult population in developed regions of the world by 2025, the burden of CAP will be felt even more acutely in the years to come. The physiological changes and cardiopulmonary interactions in mechanical ventilated patients are significantly different with respect to normal breathing conditions. Lung-protective ventilation, using lower tidal volumes, combining lower airway pressures with the open lung concept, aims to minimise barotrauma and atelectatic lung injury by Mechanical Ventilation (MV). Effects of MV on Right Ventricular (RV) loading have declined by lung-protective ventilation but remain unpredictable. Left Ventricle (LV) has a knockon effect as both ventricles pump in series. In addition, both lung and chest wall compliance significantly affect the amount of positive airway pressure transmitted to the

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intra-thoracic cavity during MV, with huge inter-patient and intra-patient variability. Declining lung compliance often demands increments in applied airway pressures, thus likely resulting in increase in RV afterload. Contrary to this, impaired chest wall compliance has the potential to increase intra-thoracic pressures at unchanged tidal volumes likely decreasing RV preload. Furthermore,

impaired baseline cardiac function or fluid status can aggravate the haemodynamic effects of mechanical ventilation. This can all lead to a vicious circle of hypotension and hypoxia with a decrease in coronary perfusion pressure and subsequent myocardial ischaemia, resulting in a further reduction in cardiac output. Antimicrobial cardiac safety is of particular concern during the treatment of community-acquired pneumonia (CAP) in elderly patients, due to the presence of comorbid conditions and the use of multiple medications that may individually or synergistically affect cardiac repolarization. As a part of routine ICU ward round check list care bundle, QT interval monitoring should be done. ICU physicians should be vigilant to these cardiac complications of macrolides and minimize duration of exposure to these agents to best possible extent.