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Rhabdomyolysis due to interactions between CDK4/6 inhibitors and statins during breast cancer treatment: a case-based systematic review

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Introduction: Cyclin-dependent kinase 4 and 6 inhibitors (CDK4/6) are a significant advance in the treatment of hormone receptor-positive and human epidermal growth factor receptor-type 2-negative (HR+/HER2-) metastatic breast cancer, with improved survival rates. Nonetheless, their concurrent use with statins, a frequently prescribed class of drugs, may increase the risk of rhabdomyolysis as a consequence of pharmacokinetic and pharmacodynamic interactions.

Objective: This systematic review analyzed literature case reports to provide practical insights into clinical presentations, therapeutic strategies, and outcomes, aiming to guide safer real-world clinical practices. **Methods:** The databases PubMed, Embase, and Web of Science were searched for case reports and case series reporting rhabdomyolysis in individuals treated with CDK4/6, from inception to January 2025. Data on demographics, clinical features, laboratory findings, management strategies, and patient outcomes were extracted. Quality assessment of the included cases was performed based on the Joanna Briggs Institute critical appraisal checklists. The protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO), under CRD42025631033. **Results:** Six case reports were analyzed involving female patients aged 55–81 years. All patients were treated for metastatic breast cancer with CDK4/6 (ribociclib or palbociclib) alongside statins (simvastatin, atorvastatin, or rosuvastatin). The onset of rhabdomyolysis occurred between 3 days and 48 months after combination therapy. Clinical presentations included myalgia, muscle weakness, and dark urine, with creatine kinase levels ranging from 3,070 to 47,000 U/L. Acute kidney injury was identified in four cases. Management primarily involved cessation of the implicated drugs (CDK4/6 or statins) and hydration, with adjunctive treatments such as corticosteroids, plasma exchange, or intravenous immunoglobulin. Five patients recovered fully, while one fatality was reported. **Conclusion:** Rhabdomyolysis due to CDK4/6–statin interactions is a rare complication, albeit with a potentially life-threatening risk. Monitoring, prompt intervention, and individualized treatment strategies are paramount to preventing complications and improving patient outcomes.

Keywords: breast cancer; statins; rhabdomyolysis; myopathy.