Effect of FK506 Administration on Functional Outcomes of Peripheral Nerve Surgery: A Systematic Review and Meta-Analysis

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Background

In the repair of peripheral nerves, the extent of nerve regeneration directly affects functional recovery. There are many possible ways to repair injured peripheral nerves. End-to-end repair is preferred for short nerve gap distances. Nerve grafting and conduit repair is generally reserved for larger nerve gap distances.1 Autologous nerve grafting is the “gold standard” but has several limitations, including donor site morbidity and availability. When autograft repair is not indicated, living-related and cadaveric nerve allograft repair is a viable reconstructive alternative. The use of pharmaceuticals in peripheral nerve injury results in faster, more robust recovery. The immunosuppressant FK506 has been shown to promote nerve regeneration when administered using burst kinetic release.2-5 The purpose of this study was to determine the effect of FK506 administration on functional outcomes of peripheral nerve surgery in humans.

Methods

A systematic review of the PubMed database was conducted in February 2019 to identify all published literature on clinical outcomes of peripheral nerve repair and vascularized composite allograft transplantation of the upper extremities. Articles were split into groups: 1) peripheral nerve surgery with FK506 (FK506+) and peripheral nerve surgery without FK506 (FK506-). Statistical analysis was performed using a random-effects model with pooled estimate of \( \tau^2 \). The primary outcomes assessed were mean motor and sensory recovery.

Figure 1: Summary of Findings and Forest Plot of All Records Assessing Motor Recovery

In the FK506+ group, 54.5% of patients experienced motor recovery compared to 12.2% in the FK506- group. This resulted in a 42.2% increase in motor recovery in the setting of FK506 administration (P = 0.01).

Figure 2: Summary of Findings and Forest Plot of All Records Assessing Sensory Recovery

In the FK506+ group, 68.6% of patients experienced sensory recovery compared to 31.9% in the FK506- group. This resulted in a 36.7% increase in sensory recovery in the setting of FK506 administration (P = 0.04).

Results & Discussion

Conclusion

Administration of FK506 in the setting of allograft-based peripheral nerve surgery has significant potential to result in clinically favorable outcomes and enhanced nerve regeneration, although further clinical studies are needed to accurately establish this. A better understanding of the side effect profile and optimal immunosuppression regimen of FK506 can ultimately help identify candidate patients that would benefit from its use in peripheral nerve surgery. Future clinical trials are warranted to establish the use of FK506 in peripheral nerve allograft repair as a clinical practice guideline.

References