

Effects of FK-506 on Nerve Regeneration after side-to-end Neurorrhaphy. Study in rats.

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Background:

The side-to-end neurorrhaphy (SEN) represented an important advancement in the microsurgical peripheral nerves procedures. The distal end of the receptor nerve is sutured to the lateral side of the donor one, without harming it. Since 1994, FK506, an immunosupressive drug, has been used to prevent allograft rejection in organ transplants and presented, in some studies, as a secondary action, positive effects on peripheral nerve regeneration.

Objective

The aim of this work is to investigate whether the administration of FK506 would benefit nerve regeneration after side-to-end neurorrhaphy.

Methods:

Eigthy Wistar rats, weighing approximately 200 g, were divided into 4 groups. Each rat had its left fibular nerve sectioned and the distal stump sutured to the lateral of the tibial nerve. The animals of group I, II and III were subjected to the administration of FK-506 in an amount of 1.0 (GI), 0.5 (GII) to 0.25mg/K/day (GIII), respectively, for two months, while the aminals of the control group (GC) received no drug. Two months after surgery the rats were submitted to the walking test, eletrophysiological study and analysis of muscle and nerve fibers.

Results:

The group II (GII) showed cranial tibial muscle (MTC) with lower mass (p < 0.05) and higher amplitude (p = 0.019). The results by the total number of nerve fibers was higher for GII (p < 0.001). There was no significant difference between groups for functional indices.





Different letters indicate statistical differences.



Average functional indices in% (IFI De Medinaceli, IFI Bain, IFF Bain)

 $\label{eq:Kruskal-Wallis test - GC = GI = GII = GII \\ \mbox{IFIs De Medinaceli - } p = 0.102, \mbox{IFI Bain - } p = 0.144, \mbox{IFF Bain - } p = 0.313. \\ \mbox{Different letters indicate statistical differences.} \\$

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MLCL: GC = GI = GII = GIII / MLE: GII < GC = GI = GIII (p < 0.001).Differents letters indicates statistical differences.







 $\begin{array}{l} {\mbox{Kruskal-Wallis test followed by T test $-$ GC = $GI = $GII = GII} \\ {\mbox{Área (μm2$) - $p > 0,01$); Max. Diam. (μm$) - $p < 0,01$); Min. Diam. (μm$) - $p > 0,01$. Letras Differents letters indicates statistical differences.} \end{array}$



Common fibular nerve (N1). Sections stained with blue tuluidina 0.25% - 400x (MO).

Conclusion:

Based on our experimental model, we could conclude that the administration of 0.5 mg/Kg/dia of FK-506 decreased body mass gain and mass of MTC and increased regeneration of nerves fibers, although not able to change the functional response.

References:

- 1) Viterbo F, Trindade JC, Hoshino K, Mazzoni Neto A. Latero-terminal neurorraphy without removal of the epineural sheath: Experimental study in rats. *Revista Paulista de Medicin*a. 1992; 110: 267-275.
- 2) Chen B, Song Y, Liu Z. Promotion of nerve regeneration in peripheral nerve by short-course FK506 after end-toside neurorrhaphy. J Surg Res. 2009;152:303-10.

Muscle fibers of the MLEs. Sections stained with HE - 200X (MO).

Area (μ m2) - Kruskal-Wallis test followed by T test - GII> GI> CG (p> 0.01). Max. Diam (μ m) - Kruskal-Wallis test followed by T test – GII> GC = GI = GII (p < 0,05) Mín. Diam. (μ m) - Kruskal-Wallis test – GC = GI = GII = GIII (p > 0,01)