Derakhshan, 1:9
http://dx.doi.org/10.4172/scientificreports.432

Open Access Scientific Reports

Letter Open Access

Tacrolimus May Improve Neurologic Function in Solid Organ Transplant Recipients

Nima Derakhshan*

Shiraz Nephro-Urology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

Tacrolimus(FK506) is a macrolide immunosuppressant, introduced in 90's and approved by FDA for prevention of allograft rejection in solid organ transplantations [1]. Tacrolimus and Cyclosporin A exert their immunosuppressive properties by binding to immunophillins. Immunophilins also called FK506 binding proteins (FKBPs) are prolyl-isomerases that participate in a wide variety of cellular functions including hormone signaling and protein folding [2]. Previous studies on Tacrolimus indicated broad functional roles for the immunophilins in the nervous system.

Unlike Cyclosporine A, Tacrolimus readily crosses the brain-blood-barrier and, thus together with its derivatives, may represent a novel approach to the treatment of neurological disorders [3].

Neuronal effect of Tacrolimus are explained via two different mechanisms; Neuroprotection via reduced NO formation (calcineurin-dependent mechanism) and a fast induction of heat shock proteins [3] and another process called neuroregeneration (via calcineurin-independent mechanisms).Thus, administration of non immunosuppressant ligands for FKBPs was hypothesized to represent important new drugs for the treatment of a variety of neurological disorders [1]. Animal study proved accelerated neuroregeneration after oral administration of a non immunosuppressant FKBP-12 ligand in rats [4].

The neuroregenerative property of Tacrolimus was believed to depend on the 12-kDa FK506-binding protein (FKBP-12). Another study suggested that the neuroregenerative properties of Tacrolimus and steroid hormones are mediated by disruption of steroid-receptor complexes. It remained unclear which component mediates neurite outgrowth, although the most likely candidates were FKBP-52, hsp-90, and p23 [5]. Gold BG et al. designed a study on human neuroblastoma SH-SY5Y cells, and proved that Immunophilin FKBP-52 (and not FKBP-12) mediates the neuroregenerative action of Tacrolimus. In these cells, the neuroregenerative action of Tacrolimus (10 pM to 10 nM) was completely prevented by the addition of a monoclonal antibody (50-100 nM) to the immunophilin FKBP-52 (also known as FKBP-59 or heat shock protein 56), a component of mature steroid receptor complexes [6].

This neuroregenerative aptitude of FK506 can be applied as a favorable pharmacologic potential, for selecting tacrolimus as the post-transplant immunosuppressant of choice for those who suffer from neurodegenerative disorders as well as end stage organ failure.

Further studies, especially double-blind, placebo-controlled clinical trials on human allograft recipients who suffer a neurodegenerative disorder should be designed to study the neuronal effects of tacrolimus on human subjects.

References

1. Gold BG (1997) FK506 and the role of immunophilins in nerve regeneration. Mol Neurobiol. 15: 285-306.
2. Sanokawa-Akakura R, Cao W, Allan K, Patel K, Ganesh A, et al. (2010) Control of Alzheimer's amyloid beta toxicity by the high molecular weight immunophilin FKBP52 and copper homeostasis in Drosophila. PLoS One 5: e8626.
3. Klettner A, Herdegen T (2003) FK506 and its analogs-therapeutic potential for neurological disorders. Curr Drug Targets CNS Neurol Disord 2: 153-162.
4. Gold BG, Zeleny-Pooley M, Chaturvedi P, Wang MS (1998) Oral administration of a nonimmunosuppressant FKBP-12 ligand speeds nerve regeneration. Neuroreport 9: 553-558.
5. Gold BG (1999) FK506 and the role of the immunophilin FKBP-52 in nerve regeneration. Drug Metab Rev. 31: 649-663.
6. Gold BG, Densmore V, Shou W, Matzuk MM, Gordon HS (1999) Immunophilin FK506-binding protein 52 (not FK506-binding protein 12) mediates the neurotrophic action of FK506. J Pharmacol Exp Ther. 289: 1202-1210.

***Corresponding author:** Nima Derakhshan, Shiraz Nephro-Urology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran, Pediatric office 71937, Namazi hospital, Shiraz, Iran, Tel: +98-9177161290; E-mail: Nima_med83@yahoo.com

Received September 13, 2012; **Published** November 03, 2012

Citation: Derakhshan N (2012) Tacrolimus May Improve Neurologic Function in Solid Organ Transplant Recipients. 1:432. doi:10.4172/scientificreports.432

Copyright: © 2012 Derakhshan N. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.