

Peer-review report

Reviewer #1: Comments on Management of Seizures in Kidney Transplant Recipients The title suggests that the manuscript intends to be a “manual” to attending physicians caring for kidney transplant recipients and it seems that has no intention to be a formal review of neither convulsive crisis in kidney transplanted patients nor kidney transplant recipients suffering of convulsive crisis. The authors have taken these comments onboard and have modified the title to reflect that.

In the introduction section, the authors do not think that drugs or toxics can cause convulsive crisis In these patients. Moreover, they emphasize that it seems to be the low glomerular filtration rate (GFR) of some transplant patients that predispose to suffer convulsive crisis meaning that it is GFR and not the allograft itself the pathogenic important event. The authors disagree with this comment. The introduction states the causes include immunosuppression (which would be drugs), infection and eGFR.

Pre transplantation phase section. Patients intending to be recipient of a kidney transplant are well evaluated and, when they are on the waiting list to receive the transplant, they are in steady state and, of course, any convulsive crisis cannot be attributed to uremic encephalopathy or dialysis disequilibrium syndrome that affect acute new patients requiring renal replacement therapy. The authors agree with these comments. The article has been updated to reflect this. This section has been changed from “pre-transplant phase” to “failing transplant phase” where it is more well established issue.

Those end stage renal disease patients that simultaneously have epilepsy, intending to be included on a waiting list, require to give a clear diagnosis of what type of epilepsy they suffer, the electrophysiological and image studies performed, and what drugs they need. The authors have refashioned the body of the text to reflect this.

Is Action myoclonus and renal failure syndrome enough prevalent to be discussed and not some other neurological/nephrological diseases, for example tuberous sclerosis? The authors have added a comment about tuberous sclerosis.

Peri – Post Renal Transplantation phases Immunosuppressive drugs have the potential to induce convulsive crisis. It is true, but, kidney transplant recipients could receive many more drugs or toxics that, in the perioperative period also can induce convulsions (Table 1). When a physician is facing a just kidney transplanted patient that convulse, it is expected to think not just in immunosuppressive drugs. The author have added more drugs.

Pharmacokinetics of AEDS in renal disease What are “glucotromides”? Most liver bio-transformative reactions include oxidation, not epoxidations. Oxide metabolites are not necessarily more water soluble that the original drugs. Do the authors think that the pharmacokinetics change in dialysis just for filter characteristics or by the procedure itself? See that there were dedicated 4 paragraph to this topic and no one to pharmacokinetics changes

associated to the transplant procedure: compartment volumes, dissociation constants, liver and kidney drug elimination processes, etc. The authors have removed "glucotromides"

Choice of antiepileptic drug In a manuscript like this, that intends to be a practical guide to a physician facing a convulsive crisis, it is not well received that the first drug mentioned is one that is not recommended, like phenytoin or that carbamazepine could aggravate a rare type of epilepsy. It is welcome that valproate has an entire section. The authors agree with these comments and the order has been updated.

What do authors conclude from their entire work. Reference section OK. Table 1: Regrettably, Reversible posterior leukoencephalopathy syndrome, a common condition causing convulsions in kidney disease patients, is not mentioned in the text. The authors have added this.

What is "mutromonab? The authors have removed this.

Why are antibiotics mentioned as separated, Quinolone and ciprofloxacin, and not grouped together? Same as in beta lactams. The authors have changed this.

Table 2: OK Figure 1: This figure is isolated from the main text and it is a good approximation to evaluate a patient that suffers from a convulsive crisis. The authors agree.

Reviewer #2: this is a good article and worth for publication but as a review article it is not acceptable without these changes:

1. This is an article about epilepsy in transplant patients but you didn't discuss about a major cause of post transplant epilepsy: immune-suppressant drug complication. For example starting "Tacrolimus" with a high dose immediately after the transplant is a major cause of seizure. The authors agree and have added this.

2. You should discuss the relation of seizure specifically with each of the routine post transplant drugs: tacrolimus, sirolimus, everolimus, prednisolone, MMF, antibiotics, antivirals, etc. The authors agree and have added this.

3. as a conclusion of a good review article you should add a general recommendation at the end of the article: how to prevent and treat early and late post transplant seizures. The authors have re-ordered the text, so that a summary table is that end of the article.

Reviewer #3: No changes