Cochrane Nursing Care Field: Steroid avoidance or withdrawal for kidney transplant recipients
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Key Words
steroid sparing, steroid withdrawal, steroid avoidance, kidney transplant, graft loss, mortality

Submitted May 2010 Accepted June 2010

Review Question:
What is the best available evidence on safety and efficacy of steroid withdrawal or avoidance in adult and paediatric kidney transplant recipients, including first and re-transplantation?

Relevance for Clinical Practice:
Kidney transplantation is the treatment of choice for people with end-stage kidney disease. However, despite short-term results continuing to improve, long-term results have only shown marginal improvement and death with a functioning graft and chronic graft failure are the most common causes of graft loss. More than 95% of transplant recipients receive corticosteroids as part of their immunosuppressive regimens to reduce the incidence of acute rejection. While short-term results have been favourable in terms of preventing acute rejection, long-term corticosteroid therapy is a cause of increased, long-term morbidity (weight gain, diabetes and bone health) and possibly mortality. Clinicians have attempted to reduce the steroid dosages used after kidney transplantation with “steroid-sparing strategies”.

This review was performed to determine the impact of these strategies on short and long-term outcomes particularly on safety and efficacy for kidney transplant recipients. The reviewers defined “steroid avoidance” as the use of steroids for two weeks or less and “steroid withdrawal” as the stopping of steroids after more than two weeks of treatment. All time periods after transplantation during which steroid withdrawal was performed were covered by this review, from immediately post-transplant to late maintenance phases. The results are potentially relevant to decision-making regarding the use and duration of steroid therapy in routine clinical practice, particularly for transplant nurses who administer immunosuppression, and are involved in the management of post-transplant patients.

Characteristics of the Evidence:
The evidence included in this summary is from a Cochrane systematic review containing 29 randomised controlled trials (RCTs) involving 5675 adult participants, ages ranged from 18-65 years. Fifteen out of the 29 RCTs investigated steroid withdrawal (2743 participants), 12 investigated steroid avoidance (2506 participants) and two studies compared steroid avoidance with steroid withdrawal (426 participants).

Only one RCT investigating steroid withdrawal was identified for children which was stopped after recruitment of 274 patients by the Data Safety Monitoring Committee due to an increased risk in post-transplant lymphoproliferative disease in both treatment groups.

Multi-organ (kidney-pancreas, kidney-liver, kidney-heart) transplant recipients were excluded. The methodological quality of the included studies varied. The quality items assessed (allocation concealment, blinding (participants, investigators, outcome assessors and data analysis), intention-to-treat analysis (ITT) and completeness of follow-up) were incompletely reported for most studies. Sixteen RCTs reported adequate methods of allocation concealment, two RCTs used inadequate methods and the remaining 11 RCTs were randomised but gave no clear indication of the

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allocation method used. Five RCTs reported blinding of both investigators and participants. ITT analysis was confirmed for 24 studies and it was unclear for the remaining five RCTs. Completeness of follow-up was not reported in eight RCTs.

Meta-analysis was undertaken where possible. The findings indicated:

- Steroid sparing strategies were not associated with increased mortality or graft loss (including and excluding death) compared to maintenance steroids especially in those not receiving Mycophenolate mofetil (MMF/Myf) or everolimus (RR 1.70, 95% CI 1.00 to 2.90).

- Acute rejection was more frequent in steroid sparing regimens when cyclosporine (CsA) was used.“ (RR 1.27, 95% CI 1.14 to 1.40).

- While steroid withdrawal strategies showed benefits in reducing antihypertensive drug need, serum cholesterol, antihyperlipidaemic drug need, new-onset diabetes after transplantation (NODAT) requiring any treatment and cataracts, steroid avoidance strategies did not alter serum cholesterol, but was associated with less frequent NODAT requiring any treatment. Cardiovascular events were also reduced with steroid avoidance.

- Reduced antihypertensive drug need and serum cholesterol were similar with CsA or with the new immunosuppressants tacrolimus (TAC). Reduced antihyperlipidaemic drug need was only evident with TAC, whereas the reduction in NODAT requiring any treatment was only evident with CsA. Infection was lower in steroid-sparing patients using CsA (RR 0.88, 95% CI 0.78 to 1.00).

**Implications for Clinical Practice:**

- All the steroid withdrawal studies included in the review were designed without any antibody induction treatment, so the safety of steroid withdrawal observed in this review was obtained without the need of antibody induction cover. Most of the steroid avoidance studies were designed with antibody induction in the steroid avoidance arm, so the results obtained cannot be confidently extrapolated for steroid avoidance protocols without adequate induction treatment.

- The review findings suggest that these immunosuppressive treatments may allow safe steroid avoidance a few days after kidney transplantation if antibody induction treatment is prescribed or safe withdrawal after three to six months if such induction is not used.

**Implications for Research:**

- Evidence regarding the beneficial effects of steroid avoidance or withdrawal in adult kidney transplant recipients is required. Further to this there is not enough information in paediatric recipients. Only one randomised study was identified in children. Studies in children need to be undertaken to determine if these results are applicable.

- Outcomes were only measured in the short-term and longer follow-up is needed.

**Reference:**