Evaluation of the safety and tolerability of Neoral and Sandimmune: a meta-analysis

Shah M B, Martin J E, Schroeder T J, First M R

Authors' objectives
To compare the safety and tolerability of Neoral and Sandimmune.

Searching
A computer search was performed, no further details are given.

Study selection
Study designs of evaluations included in the review
Randomised and non-randomised trials, blinded or open label design. Articles were excluded which only examined Neoral from a pharmacokinetic standpoint, only examined Neoral without making a comparison to Sandimmune or discussed both Neoral and Sandimmune, but did not give any quantitative data to support their conclusions.

Specific interventions included in the review
Neoral versus Sandimmune (dose schedules not reported).

Participants included in the review
Transplant recipients (including renal and liver recipients), either stable or de novo transplant recipients. Both adults and children were included.

Outcomes assessed in the review
Number of adverse events, incidence of rejection, graft loss, serum creatinine levels.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
The authors do not state that they assessed validity.

Data extraction
Data were extracted regarding number of adverse events, incidence of rejection, graft loss, serum creatinine levels, type of organ transplant, status of study population, age, number of centres, blinding, randomisation and study design. The data were compiled into a Microsoft Excel database. No details are given of how many reviewers extracted data.

Methods of synthesis
How were the studies combined?
To determine levels of significance the Fisher's Exact Test for a chi-square analysis was used.

How were differences between studies investigated?
The authors do not state how differences between the studies were investigated.

Results of the review
Forty-nine studies were included (n=7157 stated in text, 5924 stated in table).
Numbers given are events per patient.

Rejection: all stable transplant recipients has a similar incidence of rejection comparing Neoral and Sandimmune (0.06 versus 0.07, p = not significant). Subgroup analysis showed no significant differences in rejection incidence comparing Neoral and Sandimmune in stable renal and liver patients. Rejection was higher in de novo transplant recipients in the Sandimmune group (0.51 versus 0.37, p<0.05). In de novo renal transplant recipients rejection was also higher in the Sandimmune group (0.46 versus 0.34, p<0.05) and the same was seen in de novo liver transplant recipients (0.59 versus 0.43, p<0.05).

Adverse events: All stable transplant recipients had similar numbers of adverse events comparing Neoral and Sandimmune (1.04 versus 1.04, p = not significant). Subgroup analysis of stable renal and liver recipients showed no significant differences. De novo transplant recipients had similar numbers of adverse events comparing Neoral and Sandimmune (4.58 versus 4.83, p = not significant). De novo renal transplant recipients had similar numbers of adverse events (1.37 versus 1.38). De novo liver recipients had twice as many adverse events on Sandimmune than on Neoral (14.2 versus 7.1, p<0.00001).

Graft loss: similar in the Sandimmune and Neoral de novo and stable patients in both kidney and liver recipients and did not reach statistical significance in any of the studies.

Serum creatinine levels: the majority of the studies did not record serum creatinine levels. In most cases the authors stated that no difference in renal function was observed when comparing Neoral and Sandimmune.

Cost information
The authors state that switching patients from Sandimmune to Neoral has economic benefits. There were no differences in rejection and adverse events in stable patients when switching from Sandimmune to Neoral. However since Neoral has greater bioavailability than Sandimmune a lower dose is utilised to achieve the same therapeutic drug levels as Sandimmune. Neoral has a lower price than Sandimmune on a milligram-to-milligram basis and therefore the cost of Neoral therapy can be significantly reduced over the course of a year.

Authors' conclusions
When comparing Neoral and Sandimmune the benefits of Neoral clearly outweigh any disadvantages. Therefore Neoral is preferred over Sandimmune for immunosuppressive therapy.

CRD commentary
There are many methodological details missing from this review. The literature search is poorly reported and it seems unlikely that an attempt was made to search for unpublished material. It also seems odd that the review authors searched for publications on Neoral but not on Sandimmune. However the review question is clear and some inclusion criteria are given. All study designs are included and pooled without taking into account differences in reliability between the studies. No assessment of validity was undertaken and there is no description of how decisions on the review were taken or on how data was pooled. Some study details are given and the results are clearly presented. The authors' conclusions do follow from the results but they should be viewed with great caution given the methodological limitations listed above.

Implications of the review for practice and research
The authors did not state any implications for further research and practice.

Bibliographic details
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.