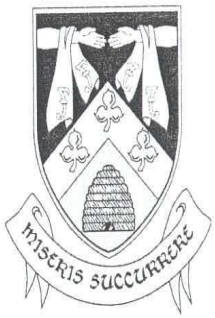
Withdrawal of Immunosuppression Treatment in the Failed/Failing Kidney Transplant Patient

Nephrology, Dialysis and Transplantation Directorate



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Document Number: 25	Reason for Change: New Guideline
Original Date of Approval: N/A	Originally Approved By: N/A 30th Nov 2010
Date Developed: May 2010-	Developed By: Dr S. Khilji
Recent Date of Approval:	Approved By:
Date Effective From	Superseded Documents: New Document
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CONTENTS

SECTION 1

Rationale

A significant proportion of Renal transplant recipients eventually require reinstitution of renal replacement therapy due to allograft failure once the eGFR is <15mls/min and patient is symptomatic for uraemia. The long term survival of these patients resuming renal replacement therapy remains low due to multiple co morbidities. There is always a consideration of withdrawal of immunosuppression in an optimal way and the scope of these guidelines is to address the issue.

Scope of Policy

This policy has been developed for medical staff working within the department of Nephrology caring for patients who have a failed/failing kidney transplant. It is the responsibility of the each medical practitioner caring for patients with failed/failing kidney transplant to be familiar with these up to date guidelines on the withdrawal of immunosuppression. Any immunosuppression withdrawal or amendment in the regimen must be discussed with the consultant in charge of the patient.
It is also the medical responsibility to ensure tapering doses of immunosuppression is clearly prescribed and that the patient is fully aware of the reasons for tapering the treatment and the likely complications associated with this decision.

Principles of the Policy

To make a uniformed strategy to withdraw immunosuppression in the failed /failing renal transplant patient and minimize complications

SECTION 2

Review Section

Date	Review no	Change	Ref Section
Sept 2010	1	New Guideline	N/A

SECTION 3
THE PROCEDURE

3.1 Reasons for withdrawal

- Increased risk of infections.
- Long term effects of corticosteroids.
- Neurotoxic effects of Calcineurin Inhibitors (CNI) in ESKD (may compound effects of Uraemia)
- Bone marrow suppression:Effects of MMF and Azathioprin.
- Susceptibility to infections.

3.2 Complications of withdrawal.

Precipitation of rejection, possibly requiring transplant nephrectomy

Secondary adrenal insufficiency

Loss of residual renal function

Potentially adverse immunologic effects among those pursuing another transplant.

3.3 Implications on residual renal functions.

The renal function deteriorates rapidly after withdrawal of immunosuppression in both haemodialysis and peritoneal dialysis patients. Thus a slow & longer taper of immunosuppression may permit the maintenance of some renal function while on dialysis. The residual renal function remains critical for the delivery of adequate dose of peritoneal dialysis.

3.4 Methods of withdrawal.

No controlled, prospective studies have been performed to determine the best method for tapering/withdrawing immunosuppression following renal allograft failure. The Recommendations vary for patients with and without residual renal functions.(i.e, good urine out put)

Tapering of Immunosuppression after graft failure and return to dialysis

1- Immediate withdrawal of anti-proliferative drugs (Azathioprine,

Mycophenolate Mofetil, Sirolimus)

2- Tapering and withdrawal of Calcineurin Inhibitors (CNI) over a longer period. (8-12 wks) if the graft failure followed acute immunologic events. (target Tacrolimus levels 2-4 ng/ml, CYA levels 50-75). Tapering and withdrawal of CNI over a period (4 wks) if the graft failure followed a slow and chronic Progression.

3- Slow tapering of Steroids with possible withdrawal (in a few months)

a- Maintain the same dose of steroids when dialysis is initiated for 1 month.

b- Then halve the dose of steroids every month until complete withdrawal however considering to avoid adrenal insufficiency or crisis.

c- In the case of disturbing symptoms requiring relatively higher dose of steroids, a graft nephrectomy should be considered .

Check for symptoms (fever, pain, graft swelling,haematuria)/Check for signs (CRP,WBC, CT scan)

This approach allows the patient with residual urine output to obtain the benefits of the additional solute and water clearance and recover nutritionally; without risking immediate rejection

4-The patients with failed renal allograft graft who are possibly candidate for living related/unrelated renal transplant,should be maintained on low dose immunosuppression to prevent aggravation of sensitization.Each individual case must be discussed with consultant Nephrologist incharge.

3.5. Indications for Transplant Nephrectomy after graft failure.

1-Forced Nephrectomy.

Peritransplant graft failure (Primary non function, technical failure, acute vascular events, hyper-acute rejection, etc.)

2-Strongly indicated Nephrectomy.

Signs and symptoms of severe/refractory acute rejection and /or severe inflammation/ graft failure within 1st year post transplantation.

3- Relatively indicated Nephrectomy.

HCV+ve patients where Interferon has been planned after return to dialysis and before a retransplantation (risk of acute rejection episode in the failed graft.)

4-Elective Nephrectomy.(Need for trials.)

No major symptoms/Surgical reasons.

SECTION 4

DEVELOPMENT AND CONSULTATION PROCESS – Consisting of:

CONSULTANT SUMMARY	
Date PPPG issued for consultation	6h September 2010
Number of versions produced for consultation	1
Committees/meetings where PPPG was formally discussed	Dates:11/5/10 8/6/10 14th September 2010

Where Received	Summary of Feedback	Actions/Response
Policy and Procedure committee	More in depth research to be looked at	No controlled, prospective studies have been performed to determine the best method for tapering/withdrawing immunosuppression following renal allograft failure

Policy Distribution.

It is the responsibility of the Policy Lead to ensure this policy is distributed

to each Head of Department.

It will be the responsibility of each Head of Department to appropriately

Distribute and maintain the policy within their Department. It is the responsibility of each manager and staff member to ensure that the Policy is utilised is the current version.

All old Policies should be destroyed as soon as a new version is received

this is the responsibility of each Head of Department.
The original document will be held in the Nurse Directorates office and an electronic copy will be available on the renal intranet system under guidelines.

SECTION 5

REFERENCE DOCUMENTS

1-Langon,AJ,Chuang,P.The management of failed renal allograft:An enigma with potential consequences.Semin Dial 2005;18:185
2-Kaplan,B,Meier-Kriessche,HU.Death after graft loss:An important late study end point in kidney transplantation.Am J Transplant 2002;2:970.
3-Smak Gregoor, PJ Zieste, R van Saase,JL et al.Immunosuppression should be stopped in patients with renal allograft failure.Clin Transpalnt 2001;15:397.