



A Systematic Review of Efficacy and Safety of Chemical Thromboprophylaxis in Renal **Transplantation**

Ruchika Kohli¹, Lise Estcourt², Abbas Zaidi³, Raj Thuraisingham⁴, Suzanne Forbes⁴, Peter MacCallum^{1, 5}, Joachim Tan⁶, Laura Green^{5, 7}

¹Haematology, Wolfson Institute of Preventive Medicine, Queen Mary University of London, London, ²Radcliffe Department of Medicine, University of Oxford, Oxford, ³Haematology, Barking, Havering and Redbridge University Hospital NHS Trust, ⁴Renal Medicine, ⁵Haematology, Barts Health NHS Trust, ¹ ⁶Statistics, St Georges University of London, ⁷Haematology, NHS Blood and Transplant, London, United Kingdom

Introduction

Individuals undergoing renal transplantation are at increased risks of thrombosis and bleeding. It is unclear what the risk benefit ratio is of administering chemical thromboprophylaxis (TP) in these patients as there have been no

previous systematic reviews to address this important question, which is reflected in the variations in national guidelines.

Objectives

To assess the efficacy (symptomatic, asymptomatic venous thrombosis and renal allograft thrombosis) and safety (major bleeding and mortality) of a form of chemical thromboprophylaxis intervention compared with another form, no intervention or placebo for up to 12 months post-transplant.





13 studies were included in the analysis (n= 1600 patients), of which 5 were randomised trials (RCTs), Figure 1. Each study used a different form of chemical TP, different timing of onset and TP duration. All RCT's were judged to be at high risk of bias (Figure 2). Symptomatic and asymptomatic VTE were very poorly reported, with only one retrospective study reporting on this outcome.

Figure 1: PRISMA diagram



Rates of renal allograft thrombosis were more likely to be reported and proportions were higher in the no intervention arm (up to 18.8%) compared to intervention arm (up to 6.3%). Only six studies reported on major bleeding, the definition of which was poorly defined between studies. Comparisons of different chemical TP showed huge variations in bleeding rates between studies.

Methods

Pubmed, MEDLINE, Embase, Cochrane, CINAHL, World Health Organisation (WHO) International Clinical Trials Registry Platform and ClinicalTrials.gov databases were searched from 1946 to present for randomised controlled trials (RCTs), controlled clinical trials, single and multiple intervention studies. Inclusion criteria included (1) participants undergoing renal transplantation only with no

Figure 2: Risk of Bias Assessment Using **Cochrane Methods for RCTs**

	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other sources of bias	Overall
Barnes (1974)	•	•	×	-	•	×	•	X
Horvath (1975)	-	•	•	+	-	×	•	X
Mathew (1975)	X	×	×	×	-	×	•	X
Ubhi (1989)	X	X	×	×	-	×	×	X
Osman (2007)	•	+	×	×	•	×	×	X

RCTs did not demonstrate a significant difference between chemical TP and no intervention. However, studies were small with very wide confidence intervals. A single metaanalysis for minor bleeding (for RCTs with follow-up to 3 months) showed no evidence of a difference between the unfractionated heparin (UFH) and no intervention arms (RR 1.65, 95% CI 0.89-3.07), Figure 3.

Figure 3: Clinically relevant non-major bleeding

	Thromboprophylaxis		No treatment		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
1.3.1 Follow-up up to	o 30 days						
Osman 2007	12	25	8	25	77.5%	1.50 [0.74, 3.03]	
Ubhi 1989	6	32	3	37	22.5%	2 31 10 63 8 511	

contraindication to TP and (2) no history/clinical suspicion of acute organ rejection.



0.001 1000 10 0.1 Favours UFH Favours no treatment

Conclusion

There is lack of good quality evidence to demonstrate the benefits of chemical TP during renal transplantation. There are signals that chemical TP (compared to no TP) may reduce the rate of renal allograft thrombosis but increase the risk of bleeding. However, large-scale randomised controlled trials are needed to determine the risk benefit ratio of TP in renal transplantation surgery.

> Wolfson Institute of Preventive Medicine r.kohli@qmul.ac.uk

