

The use of antiviral prophylaxis following corneal grafts

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On behalf of the UK Transplant Ocular Tissue Advisory Group

Background

- Prophylactic antiviral medications are used in the management of Herpes Simplex Virus (HSV) related keratitis.
- However, there are very limited data available on their effect on corneal graft survival.
- Following the introduction of new national data collection forms in April 1999, there are now sufficient data to investigate this effect.

Data

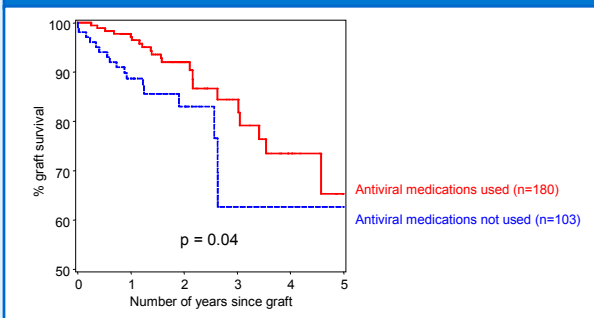
- There were 326 first Penetrating Keratoplasty (PKP) performed between April 1999 and October 2003 where the graft was required due to a viral infection.
- Of these 326 grafts, 283 (87%) had reported follow-up outcomes of graft survival.
- No data are available on the specifics of the type of viral infection. It is likely however, that a large proportion of patients within this category are HSV related.

Methods

- Kaplan-Meier survival curves were used to illustrate effects.
- Cox regression analysis considered the influence of:
 - Pre-operative factors
 - Post-operative antiviral prophylaxis
 - Time to first rejection episode
- This was modified to a Piecewise Cox Model to allow for non-proportional hazards.
- Time dependent covariates were used to model post-operative factors.

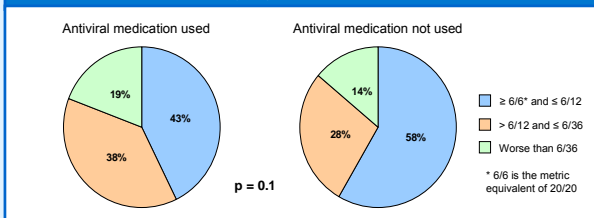
Results

Five year graft survival, by use of antiviral medication



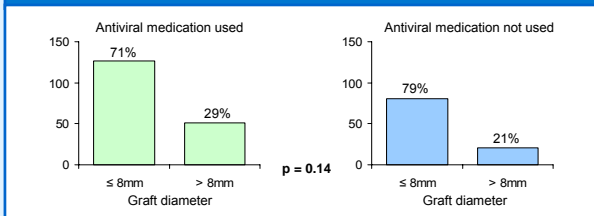
- Antiviral medication was used post-operatively in 180 (64%) of the 283 corneal grafts included in this study. Patients receiving antiviral medication had better graft survival than those who did not receive them.

Pre-operative visual acuity, by use of antiviral medication



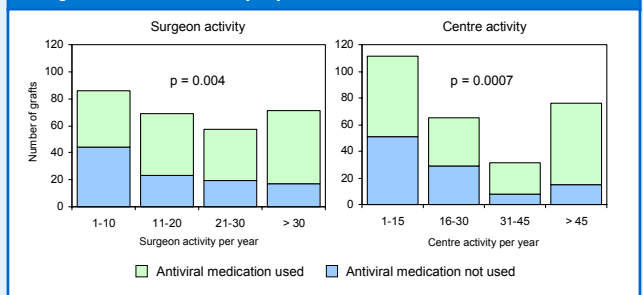
- Patients receiving post-operative antiviral medication generally had worse pre-operative visual acuity than patients who did not receive them.

Graft size, by use of antiviral medication



- There was a larger percentage of grafts that were greater than 8mm in diameter among patients who received antiviral medication.

Surgeon and centre activity, by use of antiviral medication



- Antiviral medications were more frequently used by surgeons who performed larger numbers of grafts per year. This effect was even stronger when considering centre activity.

Relative risk of graft failure at five years

Factor	Level	RR	95% CI	p
Superficial vascularisation	< 1 year	1.0	-	
	None	1.1	0.4 - 3.6	0.81
	1-2 years	1.0	-	
	None	5.5	1.3 - 22.6	0.02
	2-3 years	1.0	-	
> 3 years	None	29.6	5.1 - 172	0.0002
	1 or more	1.0	-	
	None	23.6	3.0 - 186	0.003
Inflammation at time of graft	No	1.0	-	
	Yes	3.0	1.5 - 6.1	0.003
Graft size	≤ 8mm	1.0	-	
	> 8mm	2.8	1.4 - 5.9	0.006
Antiviral medication	Yes	1.0	-	
	No	3.5	1.7 - 7.5	0.001
Rejection episodes	None	1.0	-	
	One or more	7.2	3.2 - 16.3	< 0.0001

- Of the pre-operative factors considered, superficial corneal vascularisation, graft size and whether or not the eye was inflamed at the time of the graft were all found to affect graft survival.

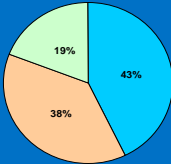
- There was also a statistically significant association between graft survival and the use of prophylactic antiviral medications (p=0.001). Grafts where patients did not receive antiviral medications post-operatively were 3.5 times more likely to have failed at 5 years, when compared with patients who did receive them.

- Patients who experienced one or more immunological rejection episode also had an increased risk of graft failure.

Summary

- The use of post-operative antiviral prophylaxis improved graft survival, even when taking account of other factors that may affect graft survival.
- Therefore, it would appear that the use of antiviral prophylaxis should be seriously considered in the post-operative period following corneal grafts for HSV.
- However, as there are no data on the specifics of the type of viral infection, perhaps a prospective study could be undertaken. This would also enable additional data to be collected on the type and duration of medication.

Antiviral medication used



- 6/12 or better
- > 6/12 and <= 6/36
- > 6/12 and <= 6/36

6/12 or better
Worse than 6/36
> 6/12 and <= 6/36