Optimizing the management of central retinal artery occlusion

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SUMMARY

The aim underpinning this thesis is to define the best management of acute central retinal artery occlusion (CRAO). Currently, there are no effective treatments for this condition and patients often suffer profound, permanent vision loss.

In this thesis, I review the literature on the current management of acute CRAO and evaluate subsequent visual outcomes. The management of CRAO involves three aspects: early reperfusion, treatment of secondary vascular risk factors and potential treatment of local ocular complications.

Early reperfusion strategies can be broadly divided as non-thrombolytic and thrombolytic. Non-thormbolytic treatments include measures such as ocular massage to dislodge the embolus and paracentesis to change the perfusion pressure across the optic nerve head. The management of acute management of CRAO is at the discretion of individual ophthalmologist and can vary significantly. I review the current practice in two teaching hospitals and show that despite differences in management of CRAO between two institutions in different countries, visual outcomes are similar. This suggests a lack of efficacy of current standard treatment in acute CRAO.

Thrombolytics have emerged as potential therapeutic options and I evaluated the feasibility of the novel treatment option of thrombolytic in the treatment of acute CRAO. This showed that thrombolysis is a biologically feasible treatment option in acute CRAO and patients receiving thrombolysis had a better visual outcome than those treated with standard therapy alone. A clinical trial protocol designed to

evaluate the effect of acute intravenous tissue plasminogen activator in CRAO was developed and I report on the outcomes of this randomized controlled trial.

In the management of secondary vascular risk factors, a high proportion of patients presenting with CRAO often have an undiagnosed vascular risk factor. In this study, 64% of patients had at least one undiagnosed vascular risk factor and a significant proportion required either the addition or escalation of existing macrovascular preventative medications and 18% required surgical intervention for carotid recanalization. As this population is at high risk of secondary ischaemic events, risk factor modification is prudent to prevent further ischemic events.

Neovascularisation is a local ocular complication following CRAO and in our study, the overall rate of neovascularisation was 18.2%. There was a clear empirical correlation between thromboembolic CRAO and neovascularisation. Given the association between neovascularisation and CRAO, prudent clinical practice would be to review all patients with acute CRAO at regular intervals as early as 2 weeks and up to 4 months post CRAO.

The results from this thesis showed that for now, the use of intravenous thrombolysis cannot be recommended in routine clinical practice in acute CRAO. Further studies are required to determine the optimal time window for treatment and the adjuvant therapies for thrombolysis. I discuss the optimal management to limit the ocular neovascular complications and investigations to optimize the systemic atherosclerotic risk factors to reduce secondary ischemic events after CRAO.

DECLARATION

I certify that this thesis does not incorporate without acknowledgment any material previously submitted for a degree or diploma in any university; and that to the best of my knowledge and belief it does not contain any material previously published or written by another person except where due reference is made in the text.

Signed …….. Date ……..

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CONTEXTUAL STATEMENT

None of the work submitted in this thesis has previously been submitted for any degree in the University or any other institution.

All the works are original. My contributions for each manuscript will be stated clearly in the Contribution Statement at the end of each chapter.

Publications that are directly related to this thesis are listed in Page 10. My other publications related to retinovascular disease and ischemic disorders of the eye are listed in Page 11-12.

PUBLICATIONS

The following is List of publications directly related to this thesis :

1. Chen CS, Lee AW. Management of acute central retinal artery occlusion. Nature Clinical Practice Neurology. 2008; 4:376-83.
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4. Rudkin AK, Lee AW, Chen CS. Vascular risk factors for central retinal artery occlusion. Eye (Lond). 2010;24:678-81
5. Aldrich EM,* Lee AW,* Chen CS,* Gottesman RF, Bahouth MN, Gailloud P, Murphy K, Wityk R, Miller NR. Local Intraarterial Fibrinolysis Administered in Aliquots for the Treatment of Central Retinal Artery Occlusion. The Johns Hopkins Hospital Experience. Stroke. 2008; 39:1746-50. *first authors contributed equally
6. Rudkin AK, Lee AW, Chen CS. Central retinal artery occlusion: timing and mode of presentation. Eur J Neurol. 2009; 16:674-7.
7. Chen CS, Lee AW, Campbell B, Lee T, Paine M, Fraser C, Grigg J, Markus R, Williams KA, Coster DJ. Study of the efficacy of intravenous tissue plasminogen activator in central retinal artery occlusion. Int J Stroke; 2011;6(1):87-9.
8. Chen CS, Lee AW, Campbell B, Lee T, Paine M, Fraser C, Grigg J, Markus R. Efficacy of intravenous tissue plasminogen activator in central retinal artery occlusion : report of a randomized controlled trial. Stroke. Accepted for publication February 2011.

The following are publications authored by the candidate on ischemic retinovascular disorders :

1. **Chen CS,** Miller NR. Ocular ischemic syndrome : review of clinical presentations, etiology, investigation and management. Compr Ophthalmol Update 2007; 8:17-28.
2. **Chen CS**, Johnson MA, Flower RW, Slater BJ, Miller NR, Bernstein SL. A novel primate model of non-arteritic anterior ischemic optic neuropathy (pNAION). Invest Ophthalmol Vis Sci. 2008 49(7):2985-92.
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5. **Chen CS**, Lee AW, Kelman S, Wityk R. Ischemic optic neuropathy in moyamoya disease. European Journal of Neurology 2007; 14:823-825.
6. Luu S, Lee AW, Chen CS. Bilateral occipital lobe infarction with altitudinal field loss following radiofrequency cardiac catheter ablation. BMC Cardiovascular disorder 2010, **10**:14.
7. Luu S, Lee AW, Daly A, Chen CS. Visual field defects after stroke--a practical guide for GPs. Aust Fam Physician. 2010;39:499-503.
8. Matti AI, Lee AW, Chen CS. Concurrent branch retinal vein occlusion and cerebral venous thrombosis from oral contraceptive pill use. Can J Ophthalmol. 2010;45(5):1
9. Matti AI, Lee AW, Chen CS. Traumatic vertebral artery dissection presenting with incomplete congruous homonymous quadrantanopia. BMC Ophthalmol. 2010;10(1):14.

10. Chu ERL, Lee AW, **Chen CS**. Resolution of visual field constriction with verapamil in a patient with bilateral optic neuropathy, migraine and Raynaud's phenomenon. Internal Medical Journal 2009; 39:851-852.
11. Luu S, Lee AW, **Chen CS**. Transient Monocular Visual Loss following administration of topical latanoprost: a case report. Canadian Journal of Ophthalmology. 2009;44(6):715.
12. **Chen CS**, Gailloud P, Miller NR. Bitemporal hemianopia caused by an intracranial vascular loop. Archives of Ophthalmology 2008;126:274-6.

LIST OF ABBREVIATION

BCVA	best corrected visual acuity
CF	counting fingers
CRAO	central retinal artery occlusion
CRP	C-reactive protein
ESR	erythrocyte sendimentation rate
FMC	Flinders Medical Centre
GP	general practitioner
HM	hand movement
JHH	Johns Hopkins Hospital
ICH	intracerebral hemorrhage
IOP	intraocular pressure
IV	intravenous
LIF	local intra-arterial fibrinolysis
LP	light perception
MRI	magnetic resonance imaging
NIHSS	National Institute of Health Stroke Scale
NLP	no light perception
NV	neovascularization
NVD	neovasularization at the disc
NVG	neovascular glaucoma
NVI	neovascularization of the iris
PRP	panretinal photocoagulation
PTT	partial thromboplastin time
RCT	randomized controlled trial
tPA	tissue plasminogen activator
VA	visual acuity