Optimizing the management of central retinal artery occlusion

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A thesis submitted in fulfilment of the requirement for the degree of PhD by published work

May 2011
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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-thrombolytic 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 ………………………
ACKNOWLEDGMENT

I would like to thank my mentors and supervisors, Professor Keryn A. Williams and Douglas J. Costers for their support and advise. I would like to acknowledge

- The American Australian Association Education Fellowship, for funding support for the study performed at the Johns Hopkins Hospital outlined in Chapter 5
- Perpetual Trustee : The Lindsay & Heather Payne Medical Research Charitable Foundation for partial funding for the randomized controlled clinical trial in Australia.

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:


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


**LIST OF ABBREVIATION**

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