Glucagon infusion in refractory anaphylactic shock in patients on beta-blockers

Report by Martin Thomas, Specialist Registrar
Checked by Ian Crawford, Senior Clinical Fellow
doi: 10.1136/emj.2005.023507

Abstract
A short cut review was carried out to establish whether a glucagon infusion is of benefit in patients with refractory anaphylaxis. 62 papers were found using the reported search, of which two presented the best evidence to answer the clinical question. The author, date and country of publication, patient group studied, study type, relevant outcomes, results, and study weaknesses of these best papers are tabulated. A clinical bottom line is stated.

Clinical scenario
A 53 year old man attends the emergency department with a severe allergic reaction, having been stung by a wasp. You note that he takes atenolol for angina. Despite adequate treatment with adrenaline and intravenous fluids, he remains hypotensive and subsequently dies. Afterwards, you hear that a glucagon infusion may have been of benefit and wonder if there is any evidence for this.

Three part question
In [anaphylactic shock for patients on regular beta-blockers] does [the use of a glucagon infusion] improve [outcome]?

Search strategy
Medline 1966-12/04 using the OVID interface. ([exp Glucagon OR glucagon.af] AND [exp Hypersensitivity OR anaphyla$.af. OR allerg$.af]) LIMIT to human AND English language.
Search outcome
Altogether 62 papers were found, of which two were directly relevant to the three part question.

Comment(s)
Although there is a pathophysiological rationale for the use of glucagon in anaphylactic patients on beta-blockers, the clinical evidence is limited to case reports only. This is not surprising as the situation rarely arises and it is probably unlikely that large series will be published. Although the two reports indicate success, such reports are subject to publication bias and as such should be interpreted with caution.

**Topical analgesia for pain reduction in arterial puncture**

**Report by Debbie Dawson, Clinical Research Nurse**
**Checked by Kerstin Hogg, Clinical Research Fellow**

doi: 10.1136/emj.2005.023515

<table>
<thead>
<tr>
<th>Author, date and country</th>
<th>Patient group</th>
<th>Study type (level of evidence)</th>
<th>Outcomes</th>
<th>Key results</th>
<th>Study weaknesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tran NQ, et al, 2002, Australia</td>
<td>Topical use of 4% amethocaine gel applied for 30 mins prior to arterial puncture for blood gas analysis</td>
<td>RCT</td>
<td>Primary outcome was pain experienced (measured on a visual analogue scale, 0–100)</td>
<td>Amethocaine group-mean score 16.0 (SD 23.3)</td>
<td>Amethocaine can cause blanching to the skin, which may affect blinding by introducing bias, though this was not commented on in the paper as one of the reported side effects. Women of ‘child bearing potential’ were excluded from the study. Does this mean that all pre-menopausal women were not included, and if so why?</td>
</tr>
<tr>
<td>81 adult patients. 42 received amethocaine gel and 39 received a placebo gel</td>
<td>Number of passes through the skin</td>
<td>These differences were not statistically significant</td>
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<tr>
<td>Heart rate before, during and after arterial puncture</td>
<td>These differences were not statistically significant</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Small number of minor irritations reported in both groups</td>
<td></td>
<td></td>
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</tbody>
</table>

| Tetracaine group-mean score 26.2+/−32.6 The placebo group-mean score 23.8+/−27.4 (p=0.78) |
| Aaron AD, et al, 2003, Canada | Fifty patients randomised, 24 to receive tetracaine and 26 placebo, 45 minutes prior to elective radial arterial puncture | RCT | Patient’s perception of pain (visual analogue scale, 0–100) | Tetracaine group-mean time 70+/−103 seconds. Placebo group-mean time 49+/−48 seconds (p=0.40) |
| Mean time from skin puncture to procurement of 1 ml of arterial blood | Tetracaine group-mean time 49+/−48 seconds |
| Difficulty performing the test (graded scale) | Identical for both groups (p=0.86) |
Antifibrinolytics for the initial management of sub arachnoid haemorrhage

Report by Simon Carley, Locum Consultant in Emergency Medicine
Checked by Ayan Sen, Clinical Fellow
doi: 10.1136/emj.2005.023523

Abstract
A short cut review was carried out to gather the evidence for and against the use of tranexamic acid to patients who have suffered subarachnoid bleeding. 267 papers were found using the reported search, of which one presented the best evidence to answer the clinical question. The author, date, and country of publication, patient group studied, study type, relevant outcomes, results, and study weaknesses of this best paper are tabulated. A clinical bottom line is stated.

Clinical scenario
A 24 year old man presents to the emergency department following a sudden headache and collapse. He is GCS 14 on arrival with no localising signs. CT scan demonstrates a sub arachnoid haemorrhage. In a previous hospital you were advised to give tranexamic acid to prevent rebleeding. You suggest this to the neurosurgical SpR on call who thinks you are talking rubbish and strongly advises against it.

You wonder if he is an evidence based neurosurgeon ... or whether he is behind the times?

Three part question
[In patients with confirmed SAH] are [antifibrinolytics better than placebo] at [reducing rebleeding, improving survival, or improving morbidity]

Search strategy

Medline: [exp Subarachnoid Hemorrhage/OR subarachnoid haemorrhage.mp] OR exp Aneurysm, Ruptured/OR SAH.mp] AND [exp Antifibrinolytic Agents/OR antifibrinolytics.mp OR exp Tranexamic Acid/OR tranexamic acid.mp OR exp 6-Aminocaproic Acid/OR aminocaproic acid.mp OR epsilon aminocaproic acid.mp OR antifibrinolytics$.mp]

Cochrane: subarachnoid hemorrhage OR subarachnoid haemorrhage.

Search outcome
Altogether 267 references found including one recent Cochrane review. No papers after the publication of the Cochrane review were found. The summary of the Cochrane review is presented here.

Comment(s)
A well constructed review article answers the question. Although there appears to be a reduction in the rate of rebleeding this is not matched by an improvement in patient outcome. The authors of this review postulate that the increase in cerebral ischaemia seen in most of the trials may account for this.

From a clinical perspective there appears to be little to be gained from the administration of antithrombolytics in confirmed SAH.

<table>
<thead>
<tr>
<th>Patient group</th>
<th>Author, date, and country</th>
<th>Study type (level of evidence)</th>
<th>Outcomes</th>
<th>Key results</th>
<th>Study weaknesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roos YB, WEM et al, 2003, Netherlands</td>
<td>9 trials involving 1399 patients included. Papers sourced through electronic and hand searching methods. RCTs of IV or oral agents included. Only confirmed SAH patients.</td>
<td>Systematic review and Meta analysis</td>
<td>Poor outcome (defined as death, vegetative state or severe disability)</td>
<td>Non significant OR of 1.12 (CI 0.88–1.43) for poor outcome with treatment</td>
<td>This is a well researched review. The studies match the clinical problem well. Of 21 trials found only 9 satisfied the quality filter of the authors which suggests some rigour in the approach used. One of the review authors’ own study was included in the review.</td>
</tr>
</tbody>
</table>

Rebleeding at end of follow up
Less with treatment
OR = 0.55 (CI 0.42–0.71)
Risk of cerebral ischaemia
Worse with treatment
OR = 1.39 (CI 1.07–1.82)
Risk of death
Non significant. OR = 0.99 (CI 0.79–1.24)
Rate of hydrocephalus
Non significant. OR = 1.14 (CI 0.86–1.51)
Anticoagulation before cardioversion of acute atrial fibrillation in the emergency department

Report by Katherine Potier, Specialist Registrar in Emergency Medicine

Abstract
A short cut review was carried out to establish whether anticoagulation is indicated prior to emergency department cardioversion of a patient with acute onset atrial fibrillation. 54 papers were found using the reported search, of which none presented any evidence to answer the clinical question. It is concluded that there is no evidence available to answer this question. Further research is needed.

Clinical scenario
A 58 year old man presents to the emergency department with a 24 hour history of new onset AF. You decide to cardiovert him in the department (chemically or electrically) and wonder whether he needs to be anticoagulated prior to this to reduce any thromboembolic risks.

Three part question
In a patient with [acute atrial fibrillation undergoing cardioversion in the emergency department] does [anticoagulation immediately before cardioversion] [reduce the incidence of thrombo-embolism]?

Search strategy
Medline: [exp Atrial fibrillation OR AF.mp OR atrial fibrillation.mp] AND [exp electric countershock OR cardioversion.mp OR exp anti arrhythmia agents/OR chemical cardioversion.mp] AND [exp heparin OR heparin.mp OR exp heparin, low molecular weight OR low molecular weight heparin.mp OR fractionated heparin.mp OR bemiparin.mp OR certoparin.mp OR dalteparin.mp OR oxaparin.mp OR reviparin.mp OR tinzaparin.mp OR fragnin.mp OR clexane.mp] LIMIT to human AND English language.
Cochrane: (atrial fibrillation) AND (anticoagulation) AND (cardioversion)

Search outcome
Alltogether 54 papers were found, of which none are relevant to the question.

Relevant paper(s)
No relevant papers given.

Comment(s)
Anticoagulation is recommended before cardioversion of AF lasting more than 2 days to avoid thromboembolic complications. However there is little evidence from the literature to support its use in AF of shorter duration.

Anticoagulation post-cardioversion of acute atrial fibrillation in the emergency department

Report by Katherine Potier, Specialist Registrar, Emergency Medicine

Abstract
A short cut review was carried out to establish whether anticoagulation is indicated after emergency department cardioversion of a patient with acute onset atrial fibrillation. 243 papers were found using the reported search, of which none presented any evidence to answer the clinical question. It is concluded that there is no evidence available to answer this question. Further research is needed.

Clinical scenario
A 45 year old man who presented to your emergency department with new onset AF has been successfully chemically cardioverted. You wonder whether he needs anti-coagulating on discharge to prevent any longer term thromboembolic complications.

Three part question
In a [patient with acute atrial fibrillation who has cardioverted to sinus rhythm] does [anticoagulation post-cardioversion] [reduce the incidence of thromboembolic complications]?

Search strategy
Cochrane: (atrial fibrillation) AND (anticoagulation) AND (cardioversion)

Search outcome
A total of 243 papers were found, none of which answered the three part question.

Relevant paper(s)
No relevant papers given.

Comment(s)
It has been recommended that patients with AF lasting more than 2 days should be anticoagulated for at least 1 month post cardioversion. This is because of the formation of...
intratrial thrombus and the potential for embolic events with atrial stunning. However, there is no evidence to support this approach in AF of shorter duration as the likelihood of cardioversion related thromboembolism is thought to be very low.

**Clinical Bottom Line**

There is no evidence to support the anticoagulation of patients with new onset AF on discharge, who have been successfully cardioverted in the emergency department (whether this be chemically, electrically, or spontaneously).

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- Eye disorders: bacterial conjunctivitis
- Male health: prostate cancer (metastatic)
- Women’s health: pre-menstrual syndrome; pyelonephritis in non-pregnant women

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- Documenting your decisions about which studies to include on an inclusion and exclusion form, which we keep on file.
- Writing the text to a highly structured template (about 1500–3000 words), using evidence from the final studies chosen, within 8–10 weeks of receiving the literature search.
- Working with *Clinical Evidence* editors to ensure that the final text meets epidemiological and style standards.
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