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 anaphyl$.af. OR allerg$.af]) LIMIT to human AND English language.

<table>
<thead>
<tr>
<th>Author, date, and country</th>
<th>Patient group</th>
<th>Study type (level of evidence)</th>
<th>Key results</th>
<th>Outcomes</th>
<th>Study weaknesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zaloga GP et al, 1986, USA</td>
<td>A 75 year old male with refractory anaphylactic shock following injection of a radiocontrast dye. Daily medications included atenolol 50 mg daily.</td>
<td>Case report</td>
<td>Improvement in BP following administration of glucagon</td>
<td>Resolution</td>
<td>Case report</td>
</tr>
<tr>
<td>Javeed N et al, 1996, USA</td>
<td>A 52 year old male with refractory anaphylactic shock following injection of a radiocontrast dye. Daily medications included atenolol 50 mg daily.</td>
<td>Case report</td>
<td>Improvement in BP following administration of glucagon</td>
<td>Resolution</td>
<td>Case report</td>
</tr>
</tbody>
</table>
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

Abstract
A short cut review was carried out to establish whether topical local anaesthetic reduces the pain of arterial puncture. 431 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 56 year old man presents to the emergency department with a 2 day history of pleuritic chest pain and shortness of breath. Pulse oximetry reveals oxygen saturations of 92%, although he does not appear to be acutely short of breath. The patient has had routine blood samples sent to the laboratory but is hesitant to agree to any other blood tests. You wonder therefore, if prior to taking an arterial blood gas sample, application of a topical local anesthetic, would reduce pain and discomfort.

Three part question
In [patients who require non-urgent arterial blood gas analysis] does [topical anesthetic] reduce [pain and discomfort]?

Search strategy
Medline 1966-12/04 using the OVID interface. [(exp lidocaine OR lidocaine.mp OR exp topical, administration OR exp anesthetics, local OR exp anesthesia, local OR emla.mp OR ametop.mp OR tetracaine OR lignocaine.mp OR prilocaine OR amethocaine.mp) AND (exp arterial puncture.mp OR exp arterial puncture to procurement of 1 ml of arterial blood OR exp difficulty performing the test (graded scale) OR exp side effects of the gel OR exp heart rate before, during and after arterial puncture OR exp primary outcome was pain experienced (measured on a visual analogue scale, 0–100))]

Table:

<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) Placebo group-mean score 20.7 (SD 18.5)</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></td>
<td></td>
<td></td>
<td>Number of passes through the skin</td>
<td>These differences were not statistically significant</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Heart rate before, during and after arterial puncture</td>
<td>These differences were not statistically significant</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Side effects of the gel</td>
<td>Small number of minor irritations reported in both groups. Tetracaine group-mean score 26.2 +/- 32.6 The placebo group-mean score 23.8 +/- 27.4 (p = 0.78)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mean time from skin puncture to procurement of 1 ml of arterial blood</td>
<td>Mean time from skin puncture to procurement of 1 ml of arterial blood: 48 seconds. Placebo group-mean time 49.6 +/- 48 seconds (p = 0.40)</td>
<td>Tetracaine group-mean time 70 +/- 103 seconds. Placebo group-mean time 49 +/- 48 seconds (p = 0.86)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Difficulty performing the test (graded scale)</td>
<td>Identical for both groups (p = 0.86)</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Author, date and country</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Aaron AD, et al, 2003, Canada</td>
<td>Fifty patients randomised, 24 to receive tetracaine and 26 placebo, 45 minutes prior to elective radial arterial puncture</td>
<td>RCT</td>
<td>Patient’s perception of pain (visual analogue scale, 0–100)</td>
<td>Patient’s perception of pain (visual analogue scale, 0–100)</td>
<td></td>
</tr>
</tbody>
</table>
blood gas analysis OR exp blood specimen collection OR arterial blood.mp NOT (BestBETs paediatric filter)] LIMIT to English language AND human.

**Search outcome**
Altogether 431 papers were identified, of which 429 were found not to answer the question directly, the remaining two papers were found to be relevant.

**Comment(s)**
Previous studies looking at the use of EMLA in pain reduction with venepuncture have highlighted that an application time of 60–90 minutes is necessary for adequate anaesthesia; the manufacturers of tetracaine recommend 45 mins application prior to venepuncture. It may be necessary that longer application times are needed for deeper structures.

► CLINICAL BOTTOM LINE
The papers found in this search provide little evidence for the effectiveness of topical analgesia in reducing the pain and discomfort of arterial puncture. Further studies with longer application times would be useful.


**Antifibrinolytics for the initial management of subarachnoid 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 subarachnoid 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 Aminocaproic Acids/OR aminocaproic acid.mp OR exp 6-Aminocaproic Acid/OR epsilon aminocaproic acid.mp OR epsilon amino-caproic 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.

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<table>
<thead>
<tr>
<th>Outcome</th>
<th>Key Results</th>
<th>Study Weaknesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor outcome (defined as death, vegetative state or severe disability)</td>
<td>Non significant. OR = 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>
<tr>
<td>Rebleeding at end of follow up</td>
<td>Less with treatment OR = 0.55 (CI 0.42–0.71)</td>
<td></td>
</tr>
<tr>
<td>Risk of cerebral ischaemia</td>
<td>Worse with treatment OR = 1.39 (CI 1.07–1.82)</td>
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<tr>
<td>Risk of death</td>
<td>Non significant. OR = 0.99 (CI 0.79–1.24)</td>
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<tr>
<td>Rate of hydrocephalus</td>
<td>Non significant. OR = 1.14 (CI 0.86–1.51)</td>
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Anticoagulation before cardioversion of acute atrial fibrillation in the emergency department

Report by Katherine Potier, Specialist Registrar in Emergency Medicine
Checked by Richard Parris, Locum Consultant

doi: 10.1136/emj.2005.023531

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 bemiaparin.mp OR certoparin.mp OR dalteparin.mp OR oxaparin.mp OR reviparin.mp OR tinzaparin.mp OR fragmin.mp OR cleaxene.mp] LIMIT to human AND English language.
Cochrane: ([atrial fibrillation) AND (anticoagulation) AND (cardioversion)]

Search outcome
Altogether 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
Checked by Richard Parris, Locum ED Consultant
doi: 10.1136/emj.2005.023549

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

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- Selecting from a validated, screened search (performed by in-house Information Specialists) epidemiologically sound studies for inclusion.
- 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.
- Updating the text every six months using any new, sound evidence that becomes available.

The Clinical Evidence in-house team will conduct the searches for contributors; your task is simply to filter out high quality studies and incorporate them in the existing text.

**To expand the topic to include a new question about once every 12–18 months.**

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