Does Oral Antibiotic Prophylaxis Reduce Surgical Site Infection after skin lesion excision from lower limb?

A Prospective Double-Blind Randomised Controlled Trial

Clare Heal, Samuel Smith, Petra Buttner
Background: Skin cancer

- highest skin cancer incidence in the world[1-3]
- 70% men; 58% women by 70yrs
- Higher burden in North Queensland[3,4]
- Majority managed in general practice: 25% by QLD GP
Surgical Site Infection (SSI)

- Overall incidence w/dermasurgery 1-3%\textsuperscript{[9-15]}

- Overall incidence in Mackay 8.6%\textsuperscript{[16]} and 8.7%\textsuperscript{[17]}

- Potential consequences of SSI:
  1. Delayed healing and increased costs
  2. Impaired cosmetic outcome
Risk Factors

- **Risk factors associated with SSI:**
  - Lower limb and groin (6.92-18.8%)\(^{[13,15-17]}\)
  - Excision length (>2.5 cm – 14.6%)\(^{[17]}\)
  - Skin cancer (7.6-18.7%)\(^{[10,11,16,17]}\)
  - Diabetes (4.2-18.2%)\(^{[14,16]}\)

- Mackay: up to **18.8%\(^{[17]}\)** after lower limb excisions
Antibiotic Prophylaxis & Skin Lesion Excision

Systemic – All in specialist surgical units

<table>
<thead>
<tr>
<th>Study</th>
<th>Prophylaxis</th>
<th>Relative Reduction (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amland et al, 1994&lt;sup&gt;[22]&lt;/sup&gt;</td>
<td>PO Azithromycin – single dose night before surgery</td>
<td>64.3% (0.223)</td>
</tr>
<tr>
<td>Bencini et al, 1994&lt;sup&gt;[23]&lt;/sup&gt;</td>
<td>IM Cephazolin</td>
<td>76.8% (0.0005)</td>
</tr>
<tr>
<td>Czarnecki, D. 1992&lt;sup&gt;[24]&lt;/sup&gt;</td>
<td>PO Cephalexin - 3 day course</td>
<td>87.5% (0.076)</td>
</tr>
<tr>
<td>Bencini et al, 1991&lt;sup&gt;[25]&lt;/sup&gt;</td>
<td>IM Cephazolin</td>
<td>80.4% (&lt;0.0001)</td>
</tr>
</tbody>
</table>

Guidelines

Mayo Clinic 2008; Consider 2g cephalexin 30-60mins before excisions lower limb and groin
Clinical Question

Does a single 2g prophylactic dose of cephalexin 30 – 60mins prior to skin lesion excision from the lower limb and groin reduce the incidence of surgical site infection?
Design

Prospective double-blind randomised controlled trial
Setting

- JCU - Mackay Rural Clinical School
- Mackay’s population about 80,000
- 104 practicing GPs
- No resident dermatologist or plastic surgeon
Recruitment and Participants

- 8 GPs in 2 practices
- Data collection June 2011 to May 2012
- Consecutive patients presenting for minor skin excision
- GP nurses: recruitment, randomisation, data collection
Data Collection

- Demographic details
- Current medical conditions
- Body site, histology
## Eligibility criteria

### Inclusion Criteria
- >18 yrs old and capable of informed consent
- Presenting for excision of a minor skin lesion from lower leg or groin

### Exclusion criteria
- Currently taking antibiotics or clinically indicated for antibiotic treatment following excision
- Repair of lacerations or lesions considered contaminated/infected prior to surgery
- Excision not requiring sutures (E.g. shave biopsy or curette)
- Excision of sebaceous cyst
- Patient unable to return for suture removal
- Penicillin or cephalosporin allergy

## Surgical wound management protocol
Intervention

**Double Blind Randomised Placebo-Controlled Trial**

**Randomisation:** numbered jars (computer generated sequence randomised in permuted blocks of 20 with 1:1 ratio)

**Blinding:** identical capsules, identity known only to principle investigator

**Intervention**
2g cephalexin PO 30-60 minutes before skin lesion excision

**Control**
Identical placebo (rice flour) taken PO 30-60 minutes before skin lesion excision
Clinical outcome measure

CDC NNISS definition of superficial surgical site infection standardized surveillance criteria:

1. Infection within 30 days

2. a. Purulent discharge from wound, or
   b. Positive culture, or
   c. Doctor diagnoses infection

3. Stitch abscess does not count as infection

Rather vague – but “gold standard”
Sample size

- Based on previous infection rate lower limb: **15%**

- *absolute reduction of 10% to infection rate 5% “clinically significant”*

- Sample size **282** power 80%; alpha 0.05

- Convenience sample 50-100 excisions
Patients presenting during study period n = 84

Randomisation n = 58

Cephalexin n = 27
(Non complier n = 2)

Lost to follow-up: n = 0
Analysed: n = 25
Infections = 2

Placebo n = 31
(Non complier n = 5)

Lost to follow-up: n = 0
Analysed: n = 26
Infections = 9

Excluded (n = 26):
Refused to participate n = 4
Other reasons n = 15
Missed n = 7
Infections n = 9
Baseline comparison

<table>
<thead>
<tr>
<th></th>
<th>Intervention</th>
<th>Placebo</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>6 (20.7)</td>
<td>6 (22.2)</td>
<td></td>
</tr>
<tr>
<td>Median Age (IQR)</td>
<td>71 (60-77)</td>
<td>71 (60-70)</td>
<td>0.785</td>
</tr>
<tr>
<td>Male</td>
<td>18 (62.1)</td>
<td>13 (59.3)</td>
<td>0.420</td>
</tr>
<tr>
<td>Smoking Status Current Smoker</td>
<td>2 (6.9)</td>
<td>2 (7.4)</td>
<td>0.838</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>12 (12.9)</td>
<td>9 (33.3)</td>
<td></td>
</tr>
<tr>
<td>Never Smoked</td>
<td>15 (51.7)</td>
<td>16 (59.3)</td>
<td></td>
</tr>
<tr>
<td>Co-morbid Conditions</td>
<td>25 (86.2)</td>
<td>18 (66.7)</td>
<td>0.116</td>
</tr>
<tr>
<td>Site Below Knee</td>
<td>15 (51.7)</td>
<td>18 (66.7)</td>
<td></td>
</tr>
<tr>
<td>Above Knee</td>
<td>6 (20.7)</td>
<td>4 (14.8)</td>
<td>0.756</td>
</tr>
<tr>
<td>Other Sites</td>
<td>4 (13.8)</td>
<td>4 (14.8)</td>
<td></td>
</tr>
<tr>
<td>Skin Flaps</td>
<td>2 (6.9)</td>
<td>2 (7.4)</td>
<td>0.217</td>
</tr>
<tr>
<td>Histol NMSC</td>
<td>22 (75.9)</td>
<td>19 (70.4)</td>
<td></td>
</tr>
<tr>
<td>Melanoma</td>
<td>1 (3.4)</td>
<td>1 (3.7)</td>
<td>0.875</td>
</tr>
<tr>
<td>Other Benign</td>
<td>6 (20.7)</td>
<td>7 (25.9)</td>
<td></td>
</tr>
</tbody>
</table>
Infections

- Infection rate (Number of infections); 95% CI
  - Placebo 34.6% (9/26) 0.172-0.557
  - Intervention 8.0% (2/25) 0.010-0.260

  p-value 0.038 Fisher’s Exact test

- Absolute Reduction (95% CI):
  - 26.6% (4.2-31.7)

- Relative Reduction (95% CI):
  - 76.9% (12.7-95.1)

- Number Needed to Treat (95% CI):
  - 3.714 (3.15-23.62)
Discussion

- Infection rate $p = 0.038$
  - Placebo $34.6\%$
  - Intervention $8.0\%$

- Lucky to achieve statistical significance
- High baseline infection rate
Limitations & Generalisability

• Study Limitations
  • Small Sample Size
  • No Cluster Analysis
  • Surgical technique and training of GPs

• Factors potentially impairing generalisability
  • Location
  • High baseline infection rate
Antibiotic prophylaxis

- Efficacy, costs, adverse effects, resistance
- NNTT 3.7, 49% reduction antibiotic use
- Reduced follow up visits
Conclusion

- 2g of oral cephalexin 30-60mins prior to minor surgery from the lower limb produces a clinically and statistically significant reduction in infection rate

- Individual GPs could consider single dose oral prophylaxis before excisions from lower limb
Acknowledgements - Thank you!

- PHCRED JCU Townsville
- GPs and Practice Nurses in Mackay: Ms Toni Kelly, Ms Vicki Abdela, Ms Julie Sullivan, Ms Debbie Kimber, Dr Lutie Van De Berg, Dr Sheldon Browning, Dr Andrew O’Neill, Dr Andrea Cosgrove, Dr Luke Notley, Prof Herwig Drobetz
References


References


Questions
Implications

- Individual GPs might consider single dose oral prophylaxis before excisions from lower limb

- Promising area for future improvements in patient care and cost reduction

- Provides the first evidence to support recommendations which are increasingly put forward by expert groups

- May help direct the development of future guidelines
### Efficacy of Systemic Prophylaxis in Broader Clinical Context – Review of Meta-analyses

<table>
<thead>
<tr>
<th>Meta-analysis</th>
<th>Surgery Type</th>
<th>Baseline Infection Rate</th>
<th>Absolute Risk Reduction</th>
<th>Relative Risk with Prophylaxis (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sanabria et al, 2006</td>
<td>Tube Thoracostomy</td>
<td>0.08</td>
<td>0.06</td>
<td>0.19 (0.07-0.50)</td>
</tr>
<tr>
<td>Barker FG., 1994</td>
<td>Craniotomy</td>
<td>0.09</td>
<td>0.07</td>
<td>0.21 (0.13-0.35)</td>
</tr>
<tr>
<td>Glenny and Song, 1999</td>
<td>Total hip replacement</td>
<td>0.04</td>
<td>0.03</td>
<td>0.24 (0.14-0.43)</td>
</tr>
<tr>
<td>Stewart et al, 2006</td>
<td>Arterial Reconstructions</td>
<td>0.16</td>
<td>0.12</td>
<td>0.25 (0.17-0.38)</td>
</tr>
<tr>
<td>Da Costa et al, 1998</td>
<td>Pacemaker insertion</td>
<td>0.04</td>
<td>0.03</td>
<td>0.26 (0.10-0.66)</td>
</tr>
<tr>
<td>Sharma and Howden, 2000</td>
<td>Percutaneous Endoscopic Gastrostomy</td>
<td>0.24</td>
<td>0.18</td>
<td>0.27 (0.17-0.41)</td>
</tr>
<tr>
<td>Meijer et al, 1990</td>
<td>Biliary Tract Surgery</td>
<td>0.135</td>
<td>0.09</td>
<td>0.33 (0.26-0.41)</td>
</tr>
<tr>
<td>Song and Glenny, 2000</td>
<td>Colorectal Surgery</td>
<td>0.4</td>
<td>0.26</td>
<td>0.35 (0.20-0.56)</td>
</tr>
<tr>
<td>Andersen et al, 2005</td>
<td>Complicated Appendicitis</td>
<td>0.35</td>
<td>0.22</td>
<td>0.37 (0.29-0.48)</td>
</tr>
<tr>
<td>Barker FG, 2002</td>
<td>Spinal Surgery</td>
<td>0.06</td>
<td>0.03</td>
<td>0.38 (0.18-0.79)</td>
</tr>
<tr>
<td>Smaill and Gyte, 2010</td>
<td>Caesarean Section</td>
<td>0.095</td>
<td>0.059</td>
<td>0.39 (0.32-0.48)</td>
</tr>
<tr>
<td>Andersen et al, 2005</td>
<td>Simple Appendicitis</td>
<td>0.11</td>
<td>0.06</td>
<td>0.40 (0.32-0.49)</td>
</tr>
<tr>
<td>Mittendorf et al, 1993</td>
<td>Abdominal hysterectomy</td>
<td>0.21</td>
<td>0.12</td>
<td>0.43 (0.36-0.51)</td>
</tr>
<tr>
<td>Ratilal et al, 2006</td>
<td>Intracranial Ventricular Shunts</td>
<td>0.11</td>
<td>0.05</td>
<td>0.55 (0.38-0.76)</td>
</tr>
<tr>
<td>Southwell-Keely et al, 2004</td>
<td>Hip Fractures</td>
<td>0.1</td>
<td>0.05</td>
<td>0.58 (0.38-0.86)</td>
</tr>
<tr>
<td>Gillespie and Walenkamp, 2010</td>
<td>Proximal Femur and other Long Bone Fractures</td>
<td>0.055</td>
<td>0.022</td>
<td>0.6</td>
</tr>
<tr>
<td>Cunningham and Handscomb, 2008</td>
<td>Breast Surgery</td>
<td>0.094</td>
<td>0.027</td>
<td>0.72 (0.53-0.97)</td>
</tr>
<tr>
<td>Sanchez-Manuel et al, 2007</td>
<td>Inguinal Hernia Repair</td>
<td>0.04</td>
<td>0.011</td>
<td>0.73</td>
</tr>
<tr>
<td>Sanabria et al, 2010</td>
<td>Laproscopic Cholecystectomy</td>
<td>0.033</td>
<td>0.006</td>
<td>0.82</td>
</tr>
</tbody>
</table>
Results

Total Eligible for Trial during Study Period
95

Randomised
64

Excluded after randomisation
1
Reasons:
Number of trial medication not recorded
Infections: 0

Intervention

Excluded after randomisation
1
Reasons:
Patient forgot to take tablets
Infections: 1

Analysed
29
Infections: 2

Control

Excluded after randomisation
4
Reasons:
Lesion became infected pre-op – 1
Patient forgot to take tablets – 1
Excision cancelled – 1
Shave biopsy performed instead – 1
Infections: 0

Analysed
27
Infections: 9

Excluded
31
Reasons for exclusion:
Allergy – 5
Already on antibiotics – 8
Doctor felt antibiotics were indicated – 2
Missed – 9
Did not wish to take trial medication – 5
Removal Sutures Elsewhere – 1
Unable to Consent – 1
Infections: 9

Drop Out after Excision
2
Reasons:
Patient treated wound with antiseptic – 1
Topical antibiotic applied to wound– 1
Infections: 0
Surgical wound management protocol

- Skin preparation - chlorhexidine
- Sterile technique, including sterile gloves
- Local anaesthetic – type and volume recorded
- Suture material – nylon
- Dressing – melolin and tape
- No antibiotics, neither topical nor oral; no topical antiseptics; no antiseptic washes; no medicated soaps
- Removal of sutures – back 10 days, other sites 7 days