Anal fissure best choice

SR Brown Colorectal Surgeon Sheffield Teaching Hospitals
Overview

- What we are taught in medical school
- The evidence for non-surgical therapy
- The evidence for surgery
- Why do some treatments not work
Acute fissure

- Passage hard stool
Acute fissure treatment

- Diet
- Analgesia
Excoriation
Treatment

- Avoid soap
- Barrier creams
Crohn’s fissure

- Atypical position
- Associated disease
  - Fleshy tags
  - Fistulae
Nicorandil associated ulceration

- Well circumscribed
- Skin undermining
- Cardiac cripples
Definition of a chronic fissure

- >6 week history
- Wider and deeper than acute fissure (IAS fibres)
- Midline
- Skin tag
Classic aetiology of a chronic fissure

- High sphincter tone
- Poor midline anal blood supply
Post-partum fissure

- Usually anterior
- No sphincter spasm
- ?hormonal, constipatory, perineal dynamic changes
Historical therapies

1920s
- Cocaine
- Opium
- Mercury
Historical therapies

1930s

- Hot water bath and brick
Historical therapies

1950s
• Silver nitrate
Historical therapies

1970s

- Lignocaine, steroids and St Mark’s dilator
Current non-surgical therapies

- Designer drugs for the anus
  - GTN, CCB, Botox etc.
- Others
  - Hyperbaric oxygen.
Current non-surgical therapies

- 75 RCTs
- 5031 participants
- 17 different agents
Mechanism of action
Designer drugs for the anus
Nitric oxide donors

Diagram:
- NANC
- NO VIP
- β2-ARs
- cGMP↑
- cAMP↑
- Contraction
- Relaxation
- K+ channel
- Ca2+
- SR
- G protein
- α1-ARs
GTN
# GTN versus Placebo

Non-healing

## Review: Non surgical therapy for anal fissure

**Comparison:** GTN versus Placebo  
**Outcome:** NON - Healing of fissure (persistance or recurrence)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>GTN n/N</th>
<th>Placebo n/N</th>
<th>Odds Ratio M-H,Random,95% CI</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Altomare 2000</td>
<td>42/88</td>
<td>33/64</td>
<td>1.52 [0.76, 3.03]</td>
<td>8.3%</td>
</tr>
<tr>
<td>Bailey 2002</td>
<td>162/266</td>
<td>19/38</td>
<td>1.56 [0.79, 3.08]</td>
<td>8.3%</td>
</tr>
<tr>
<td>Carapeti 1999</td>
<td>26/48</td>
<td>18/22</td>
<td>0.26 [0.08, 0.80]</td>
<td>5.6%</td>
</tr>
<tr>
<td>Chaudhuri 2001</td>
<td>5/12</td>
<td>11/13</td>
<td>0.13 [0.02, 0.86]</td>
<td>7.2%</td>
</tr>
<tr>
<td>Kennedy 1999</td>
<td>13/24</td>
<td>18/19</td>
<td>0.22 [0.05, 0.97]</td>
<td>6.5%</td>
</tr>
<tr>
<td>Kenny 2001</td>
<td>12/20</td>
<td>8/20</td>
<td>3.50 [0.94, 12.97]</td>
<td>6.9%</td>
</tr>
<tr>
<td>Lund 1997</td>
<td>16/39</td>
<td>38/41</td>
<td>0.05 [0.01, 0.21]</td>
<td>6.9%</td>
</tr>
<tr>
<td>Oglesby 2001</td>
<td>10/15</td>
<td>6/15</td>
<td>3.00 [0.88, 13.31]</td>
<td>6.5%</td>
</tr>
<tr>
<td>Sonmez 2002</td>
<td>9/26</td>
<td>20/21</td>
<td>0.03 [0.00, 0.23]</td>
<td>5.0%</td>
</tr>
<tr>
<td>Tander 1999</td>
<td>5/31</td>
<td>11/17</td>
<td>0.10 [0.03, 0.42]</td>
<td>6.8%</td>
</tr>
<tr>
<td>Scholefield 2003</td>
<td>71/149</td>
<td>30/51</td>
<td>0.64 [0.33, 1.21]</td>
<td>8.4%</td>
</tr>
<tr>
<td>Werre 2001</td>
<td>5/20</td>
<td>16/20</td>
<td>0.08 [0.02, 0.37]</td>
<td>6.5%</td>
</tr>
<tr>
<td>Maan 2004</td>
<td>1/16</td>
<td>21/48</td>
<td>0.09 [0.01, 0.70]</td>
<td>5.1%</td>
</tr>
<tr>
<td>Tankova 2002</td>
<td>2/10</td>
<td>7/9</td>
<td>0.07 [0.01, 0.65]</td>
<td>4.9%</td>
</tr>
<tr>
<td>Weinstein 2004</td>
<td>20/32</td>
<td>9/16</td>
<td>1.30 [0.38, 4.39]</td>
<td>7.2%</td>
</tr>
</tbody>
</table>

**Total (95% CI):** 776/414  
**Total events:** GTN 261 (Placebo)  
**Heterogeneity:** Tau² = 1.50, Chi² = 74.25, df = 14 (P<0.00001); I² = 81%  
**Test for overall effect:** Z = 2.84 (P = 0.0044)
Summary for GTN

• Healing rate 49% vs. 36%
• About 50% recur
• Side effects (headache)
Variations in delivery

• Higher doses (0.4% vs 0.2%)
  – No difference

• Patches
  – No difference

• Intra-anal application
  – Less headaches?
Calcium Channel Blockers

Diagram showing the effects of NANC, NO, Vip, K+ channel, K+, Ca2+, cGMP↑, cAMP↑, Relaxation, Contraction, SR, Ca2+, G protein, and α1-ARs on internal anal sphincter smooth muscle cell.
Calcium Channel Blockers

• Topical
  – Diltiazem
  – Nifedipine

• Oral
  – Nifedipine
  – Lacidipine
Botox Injection
Mechanism of action

- Sympathetic blockade
- Antinociceptive
  - Immediate effect despite lack of healing
What dose?

2.5 U  100 U
• “injected into the external anal sphincter on both sides lateral to the fissure” Jost 1997

• “The internal anal sphincter was easily palpated and injected with a 27-gauge needle” Maria 1998

• “…the injection was always done through the intersphincteric groove…” Minguez 1999
Summary of Botox and CCB efficacy

• Similar to GTN
• Less side effects
Disadvantages of Botox

- Cost
- Requires GA/sedation
- ?Incontinence
Other designer drugs

- L-arginine
  - Precursor NO
  - No headache
  - RCT no different to placebo
Other designer drugs

- K channel openers (Minoxidil)
Other designer drugs

- **K channel openers**
  - No difference to placebo
  - May cause ulcers

(Minoxidil)
Other designer drugs

- Alpha-1 adrenoceptor blockers
  - Same as placebo
  - Many side effects
Other designer drugs

- Phosphodiesterase-5 inhibitors (Viagra)
Other designer drugs

- **Phosphodiesterase-5 inhibitors (Viagra)**
  - No RCT evidence
Other designer drugs

- Clove oil
  - Anaesthetic
  - Antimicrobial
  - Vaso-active
  - Smooth muscle relaxant
Other designer drugs

- Clove oil
  - Healing in 60%
  - RCT evidence.
Other designer drugs

- Captopril
- Aloe Vera
- Emugel
- Topical Metronidazole
- Injection sclerotherapy
Other therapies

• Hyperbaric oxygen
Perineal support toilet
What about surgery?
Surgical interventions

17 procedures

• Anal stretch
  – Lord’s/balloon/controlled/sphincterolysis

• Sphincterotomy
  – Closed/open/lateral/bilateral/tailored/radial/circumferential/segmental/caudal/cranial

• Advancement flap

• Fissurectomy

• Perineoplasty
What about surgery?
Non-healing
What about surgery?

Long term healing

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Surgery n/N</th>
<th>Medical Therapy n/N</th>
<th>Odds Ratio M-H, Random 95% CI</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arroyo 2005</td>
<td>3/40</td>
<td>22/40</td>
<td>0.07 [0.02, 0.25]</td>
<td>70.9 %</td>
</tr>
<tr>
<td>Libertiny 2002</td>
<td>0/35</td>
<td>16/35</td>
<td>0.02 [0.00, 0.29]</td>
<td>15.3 %</td>
</tr>
<tr>
<td>Parellada 2004</td>
<td>0/27</td>
<td>3/27</td>
<td>0.13 [0.01, 2.59]</td>
<td>13.8 %</td>
</tr>
</tbody>
</table>

Total (95% CI) 102 102
Total events: 3 (Surgery), 41 (Medical Therapy)
Heterogeneity: Tau² = 0.0; Chi² = 1.08, df = 2 (P = 0.58); I² = 0.0%
Test for overall effect: Z = 4.96 (P < 0.00001)
Current gold standard
Sphincterotomy

• Healing rates >85%
• Long lasting effect

BUT

• Incontinence
Is incontinence a big issue?

• Cochrane review
  – 1030 underwent lateral sphincterotomy
  – Minor incontinence in 5%

• Meta-analysis (4532 patients) (Garg 2013)
  - 9% seepage
  - <1% major incontinence
Can you improve sphincterotomy?

- Incontinence reduced with
  - ?Tailoring
  - ?avoiding in post-partum women/previous surgery
Does tailoring make any difference?

### 3.2 Anal Incontinence Score

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Dentate Line</th>
<th>Fissure Apex</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Total</td>
<td>Mean</td>
</tr>
<tr>
<td>Mentes 2008</td>
<td>0.13</td>
<td>0.34</td>
<td>30</td>
<td>0.35</td>
</tr>
<tr>
<td>Elsebae 2007</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Mentes 2005</td>
<td>0.58</td>
<td>1.13</td>
<td>38</td>
<td>0.42</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>0.58</td>
<td>1.13</td>
<td>69</td>
<td>0.42</td>
</tr>
</tbody>
</table>

Heterogeneity: Chi² = 2.02, df = 1 (P = 0.16); I² = 51%

Test for overall effect: Z = 0.80 (P = 0.42)
Does tailoring make any difference?

### 3.1 Treatment Failure

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Dentate Line Events</th>
<th>Total Events</th>
<th>Fissure Apex Events</th>
<th>Total Events</th>
<th>Weight</th>
<th>Odds Ratio M-H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elsebae 2007</td>
<td>0</td>
<td>46</td>
<td>2</td>
<td>46</td>
<td>21.0%</td>
<td>0.19 [0.01, 4.10]</td>
</tr>
<tr>
<td>Mentes 2005</td>
<td>0</td>
<td>38</td>
<td>5</td>
<td>38</td>
<td>46.1%</td>
<td>0.08 [0.00, 1.48]</td>
</tr>
<tr>
<td>Mentes 2008</td>
<td>1</td>
<td>30</td>
<td>4</td>
<td>30</td>
<td>32.9%</td>
<td>0.22 [0.02, 2.14]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>1</td>
<td>114</td>
<td>114</td>
<td></td>
<td>100.0%</td>
<td>0.15 [0.03, 0.69]</td>
</tr>
</tbody>
</table>

Total events: 11

Heterogeneity: Chi² = 0.33, df = 2 (P = 0.85); I² = 0%

Test for overall effect: Z = 2.44 (P = 0.01)
Improving results of surgery

• High fibre diet and fluids
• Avoid chillies
  – RCT twice as much anal burning
• Sitz baths
  – RCT less burning
What about surgery?
Anal stretch
Anal stretch

Normal

Anal stretch
Anal stretch

- Probably less effective than sphincterotomy (OR 1.55 (0.85-2.86))
- 4 x higher risk of incontinence
- Still being done (papers from 2013)
‘Controlled anal stretch’

Precise Anorectal Sphincter Dilatation—Its Role in the Therapy of Anal Fissures

\[ C = 2\pi\sqrt{\frac{A^2+B^2}{2}} \]

\[ C = 11.99 \]
Advancement flap

- 2 RCTs (70 patients with flaps)
  - No incontinence
  - Healing in 80% (cf 98% sphincterotomy)
Other therapies

• Combinations of above
  – Fissurectomy and Botox
  – Sphincterotomy and flap
  – Botox and flap

• Nerve stimulation
  – Tibial
  – Sacral
Why don’t these therapies always work?
Aetiology of anal fissure

Spasm

Fibrosis

Chronicity
Fissurectomy-botulinum toxin

- Combine excision of the sentinel pile, fissure edges and curettage of base with injection of botulinum toxin
- 30 patients who failed conservative therapy
- 28 (93%) healed

Lindsey 2004
Fissurectomy and botox

- 44 patients (all female)
- 85% healed
- Subsequent recurrence in 50% at median 22 months
- Surgical intervention in 15%

Baraza, Brown 2008
Algorithm of care

- Make diagnosis
- Consent
  - Males
    - Non-surgical
    - Lateral sphincterotomy
  - Females
    - Non-Surgical
    - Botox and fissurectomy