SURGICAL GRAND ROUNDS
February 12, 2007

Octreotide/ Somatostatin,
Pancreatic Stents, Fibrin
Glue, Etc. to Prevent
Pancreatic Fistula

Guillermo Escobar, M.D.
How can it be fair for me to debate this topic?

- Who ever picks the topics dislikes baby seals
- Who ever picks the topics is testing me
- Who ever picks the topics knows that I can beat Dr. Gries at ANYTHING
What’s so hard about pancreatic surgery?
What’s so hard about pancreatic surgery?
Can you improve fistula rates?

The Other Side of the Argument

Pancreatic fistulas are inevitable

FALSE
Who cares about PF???

- Considered the #1 or #2 most common cause of morbidity, LOS and causative to mortality!
- Appear when there is a fault in healing/sealing between the pancreatic anastomosis or a leak from the pancreas uninvolved with the anastomosis.
What is a pancreatic fistula?

- There are >26 “definitions” found between 1994-2004!
- The incidence ranges from 5%-40%
- Considering only output and duration on the same 242 patients led to a “fistula” rate between 10%-28.5% (p<0.05)

Bassi C. Pancreatic fistula rate after pancreatic resection: the importance of definitions, *Dig Surg* 21;2004
What is a pancreatic fistula?

- Consensus statement defined a PF:
  - Any fluid >= POD #3 with amylase 3x Serum
- They are graded A-B-C according to
  - Clinical appearance, duration >3 weeks, infection or requiring additional Rx

Octreotide

European experience

Germany

• Randomized, double-blind, placebo-controlled, multicenter trial in 246 patients w/100mcg TID
  – All complications were lower in high risk pancreatic procedures (32% vs. 55%) and PF rate was 18% vs. 38% in placebo!

Octreotide

European experience

Italy

- Randomized, double-blind, placebo-controlled, multicenter trial in 252 patients w/100mcg TID
  - All complications were lower (15.6% vs. 29.2% p<0.05) and PF rate was 9% vs. 19% in placebo!

Octreotide

European experience

Italy II

- Randomized, double-blind, placebo-controlled, multicenter trial in 218 patients w/100mcg TID
  - All complications were lower (22% vs. 36% p=0.05) in high risk pancreatic procedures and PF rate was 9% vs. 20% (p<0.05) in placebo!

Octreotide

Hopkins 2000

- 211 pts underwent pancreaticoduodenectomy with pancreatic-enteric anastomosis
- PF were >50 mL after day 10 (no amylase)
- **250 μg** TID of octreotide (??)
- The pancreatic fistula rates were 9% in the control group and 11% in the octreotide group.
- The median postoperative length of hospital stay was 9 days in both groups.

Octreotide

- In the discussion after this paper and in one prior*, the primary author admits bias that he expected a negative trial.
- The study was terminated after recruitment of only 64% of the patients.
- In the fistula rate of 10%, it would require approximately 500 patients in each group to lower that rate to 5%.
- Pancreatic fistula was determined > POD 10 but >50% discharged on <POD 9
- Withdrawal rate was 45% (172 of 383). 40 patients were excluded because they didn’t get “at least a 5-day course of octreotide study drug.”

Why you can’t trust Hopkins

The New York Times

Johns Hopkins University
ARTICLES ABOUT JOHNS HOPKINS UNIVERSITY

A NATION CHALLENGED: THE RESPONSE; Many Lessons To Be Learned With Anthrax
By GINA KOLATA

Scientists and government officials are having to rethink everything they thought they knew about and cases of deadly inhalation anthrax, and they candidly admit that much of what they thought is wrong; that despite years of discussing and imagining how bioterrorism attack might occur, and how it might everyone by surprise; Centers for Disease Control and Prevention director Dr Jeffrey Koplan ...

October 28, 2001 Health News

Family of Fatality in Study Settles With Johns Hopkins

The family of a lab worker who died in an asthma study has reached a settlement with the university, a

October 12, 2001 News

National Briefing | Science And Health: Challenge To Research Limits

Johns Hopkins University, Kennedy Krieger Institute and University of Maryland Medical System ask
limits it imposed on medical research involving minors

September 19, 2001 Health News

Report on a Research Death Faults Review Board

A report on the death of a healthy volunteer in an asthma study at Johns Hopkins University found the board was inadequate to handle its thousands of studies and that some researchers had adversarial ...

August 31, 2001 News

U.S. Investigating Johns Hopkins Study of Lead Paint Hazard
By TAMAR LEWIN
Octreotide

MD Anderson 1997

- Prospective, randomized trial
- 120 patients undergoing Whipple for malignancy
- 150 mcg SC octreotide TID for 5 days
- PF was clinically significant after POD 3 if
  >2.5x serum amylase, leukocytosis, septic shock or needing drainage
- 12% PL in octreotide vs. 6% in ctrl (p = 0.23).

Octreotide

MD Anderson 1997

- Clinical PL in 7(12%) vs. 3(6%) with octreotide
- “Biochemical” PL in 9(16%) vs. 8(15%) with octreotide

Criticism

- They expected 30% leak rate (only 21% in control) and calculated 108 patients needed to detect a drop to 10% (66%).
- They needed >100 more patients!

Japan

- Prospective, randomized 56 patients undergoing distal pancreatectomy
- PF = fluid > POD 7 with 3x Amylase
- Overall incidence of PF was 26%, but occurred in 4 (15.4%) in the fibrin group vs. 12 (40.0%) in control (p= .04).

Suzuki Y Fibrin glue sealing for the prevention of pancreatic fistulas following distal pancreatectomy. Arch Surg. 1995 Sep;130(9):952
Fibrin Glue

Hopkins

- 125 patients randomized if high risk pancreas was found (soft/small duct)
- Attempted to lower fistulas from 25-10% (needed 224pts)
- Some were stented, some were not. Some were side to side, some were end to end. 1 or 2 drains were placed.
- PF = >50cc 3x Amylase >POD 10
- Stopped early with fistulas in “26%” of glued vs. “30%”

## Fibrin Glue

### Table 4. Postoperative complications and course

<table>
<thead>
<tr>
<th>Postoperative Complications and Course</th>
<th>Fibrin Glue (n = 58)</th>
<th>No Fibrin Glue (n = 66)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>0 (0%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Reoperation</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Percutaneous radiologic intervention</td>
<td>3 (5%)</td>
<td>6 (9%)</td>
</tr>
<tr>
<td>Any complication</td>
<td>15 (26%)</td>
<td>20 (30%)</td>
</tr>
<tr>
<td>Pancreatic fistula</td>
<td>8 (14%)</td>
<td>16 (24%)</td>
</tr>
<tr>
<td>Early delayed gastric emptying</td>
<td>5 (9%)</td>
<td>6 (9%)</td>
</tr>
<tr>
<td>Wound infection</td>
<td>3 (5%)</td>
<td>3 (5%)</td>
</tr>
</tbody>
</table>

Fistulas in “26%” of glued vs. “30%”
The truth is:

1. The data is hard to interpret prior to the consensus 2005
2. Not everyone uses drains - ? Fistula rates
3. Whipple had a PL rate of 19.5% in 41 patients
4. JH has PF varying from 7% (1980’s) to 47%. Stopping studies is irrational and bias is admitted repeatedly.
5. JH published that erythromycin made no clinical difference, yet they still use it – bias, bias, bias!!!
6. Octreotide at 100mcg TID is USEFUL.
7. Mostly in periampullary adenomas or islet cell tumors (soft pancreas)

Any technique utilized that includes:
• Experience
• Care
• Fine sutures
• Minimal handling
• Good blood supply
• No tension

Thank you