“Novel Approaches to Weight Loss”

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Keystone, July 2014

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Duality of Interests

None
Novel Approaches to Weight Loss

- Gastric aspiration
- Endoluminal barrier
- Gastric balloon
- Transoral gastric suturing
Aspiration Therapy Overview

- A-shunt® implantation-outpatient 15-min endoscopic procedure, no general anesthesia
- 30-years experience with PEG tubes; 250,000/yr
- Provides “portion control” at the stomach
- Easy, aspirate stomach contents ~20-min after meal-takes ~ 5-10 minutes
- Removes 25%-30% of consumed calories
- Lowers threshold for achieving successful weight loss which empowers patients
- Provides safe, gradual, and controlled weight-loss, with the patient “in-control” –
- Counting device limited number of aspiration cycles (115), forcing patient back to physician
- Reversible; does not preclude bariatric surgery
Clinical Experience Overview

- Three trials to date, total of 24 obese patients (BMI 35.5-48.6 kg/m²) treated with Aspiration Therapy:
  - 3 in proof-of-principle trial in the US
  - 10 in pilot trial in Mexico
  - 11 in ongoing randomized controlled feasibility trial in the US.

- Safety confirmed by all three trials.
  - Careful monitoring for electrolytes, kidney & liver function, vitamins, etc.
  - Only serious adverse event reported: buried bumper

- Efficacy confirmed by all three trials.
  - Percent of patients** losing ≥25% excess weight loss (EWL*) at 52 wks = 94% (50% is FDA guideline)
  - Mean** %EWL* at 52 wks = 49.8% (25 % is FDA guideline)
  - Mean** %WL at 52 weeks=18.6%
US Pilot Study

Control Group (12 months)
- 15 session diet and behavioral weight loss program
- Two Town Hall Meetings
- Multivitamin & mineral supplement

AT Group
- A-Tube placed endoscopically
- Tube conversion at 10-14 days post placement
- Subjects instructed on aspiration procedure
- Proton pump inhibitor & potassium
- 15 session diet and behavioral weight loss program
- Two Town Hall meetings
- Multivitamin & mineral supplement
US Pilot Study

Control Group
Randomized n=7

Analyzied at week 52 n=4

Drop Out n=3

AT Group
Randomized n=11

Analyzied at week 52 n=10

Subjects with ≥25% EWL at 52 weeks allowed to continue therapy

Analysed at week 104 n=7

Drop Out n=1
## Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Control Group</th>
<th>AT Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (M/F)</td>
<td>4 (1/3)</td>
<td>10 (0/10)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>45.3 ± 2.8</td>
<td>38.7 ± 2.3</td>
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<tr>
<td>Weight (kg)</td>
<td>105.3 ± 2.5</td>
<td>112.2 ± 4.6</td>
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<tr>
<td>BMI (kg/m²)</td>
<td>39.3 ± 1.1</td>
<td>42.0 ± 1.4</td>
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<tr>
<td>Glucose (mg/dL)</td>
<td>86.8 ± 3.4</td>
<td>83.9 ± 1.9</td>
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<tr>
<td>HDL-C (mg/dL)</td>
<td>48.5 ± 4.1</td>
<td>53.6 ± 2.9</td>
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<tr>
<td>LDL-C (mg/dL)</td>
<td>116.0 ± 13.0</td>
<td>112.8 ± 6.9</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>139.3 ± 12.8</td>
<td>113.4 ± 18.8</td>
</tr>
<tr>
<td>ALT (IU/L)</td>
<td>26.8 ± 7.3</td>
<td>20.6 ± 2.6</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>121.8 ± 6.4</td>
<td>125.8 ± 3.5</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>80.5 ± 3.4</td>
<td>82.6 ± 1.2</td>
</tr>
<tr>
<td>Meal</td>
<td>Number of tests</td>
<td>Gastric Aspirate (gm)</td>
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<tr>
<td>----------------------</td>
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<td>-----------------------</td>
</tr>
<tr>
<td>450 kcal, 20 minute wait</td>
<td>6</td>
<td>1747 ± 186</td>
</tr>
<tr>
<td>450 kcal, 60 min wait</td>
<td>6</td>
<td>1761 ± 196</td>
</tr>
<tr>
<td>800 kcal, 20 min wait</td>
<td>7</td>
<td>2080 ± 240</td>
</tr>
<tr>
<td>800 kcal, 60 min wait</td>
<td>7</td>
<td>2034 ± 200</td>
</tr>
</tbody>
</table>
Effect of Aspiration Therapy on BODY WEIGHT

Time (Weeks)

Percent Weight Loss

Control

AT 52 week
n=10

AT 104 week
n=7
Percent of Subjects Who Achieved ≥25% EWL at week 52

![Bar chart showing percent of subjects achieving ≥25% EWL at week 52. The chart compares 'Control' and 'AT' groups. The 'AT' group has a significantly higher percentage compared to the 'Control' group.]
Quality-of-Life: IWQOL

- Physical Functioning
- Self-Esteem
- Sexual Life
- Public Distress
- Work
- Total

Comparison between AT Group and Control.
Behavior Outcomes

❖ Subject Self-Report
  • Change in meal-time activities
    ➢ Increased water consumption with meals
    ➢ Increased chewing time
  • Decreased anxiety with meals and eating out
  • Healthier food choices

❖ Eating Disorders Examination:
  • No episodes of binging or excessive eating in the AT group
  • No adverse effects on dietary restraint, body image, desired weight and shape
**Patient Acceptance**

- **AT overwhelmingly accepted by patients**
  - Able to eat normally
  - Minimal invasiveness
  - Reversibility—and no anatomical rearrangement
  - No general anesthesia
  - Discrete/Private
  - Clear mechanism of action

- **Some people dislike having an object attached to their abdomen**

- **Some people fear criticism of therapy**

- **Family acceptance increased over time after weight loss was achieved**
Acceptability of AspireAssist™

Believe AT will help achieve weight loss

88%

Want to participate in clinical trial

82%

Anonymous survey obtained after Information Session in obese people (N=78) interested in weight loss studies
Acceptability of AspireAssist™

- Time spent performing AT is worth it: 81% Agree, 15% Disagree, 4% No Opinion
- Permanent Skin-Port is acceptable: 75% Agree, 21% Disagree, 4% No Opinion

Anonymous survey obtained after Information Session in obese people (N=78) interested in weight loss studies
AspireAssist™ vs. Bariatric Surgery

% of Obese People Preferring AspireAssist to Bariatric Surgery

- Strongly Agree: 76%
- Somewhat Agree: 26%
- Do not agree or disagree: 4%
- Somewhat Disagree: 8%
- Strongly Disagree: 0%

Anonymous survey obtained after Information Session in obese people (N=78) interested in weight loss studies
Conclusions

- Aspiration Therapy results in successful long-term weight loss
- No evidence of abnormal eating behaviors, attitudes towards eating, or perceived hunger/satiety (some psychological and eating behaviors improved)
- No compensation for decreased calorie absorption by increasing food intake.
- Psychosocial factors are important drivers of food intake in obese people (not a physiological signal for more calories or drive to meet a set point). Removing food contents after eating allowed subjects to satisfy their drive to eat without the consequence of excessive energy absorption.
- Patient acceptance of therapy is very high
EndoBarrier Gastrointestinal Liner:
GI Dynamics

Endoluminal Barrier

The duodenojejunal bypass sleeve mimics the physiology of intestinal bypass and shares the metabolic advantages of intestinal diversion. A high rate of premature device withdrawal has been its major limiting factor.
An Endoluminal Sleeve Induces Substantial Weight Loss and Normalizes Glucose Homeostasis in Rats with Diet-Induced Obesity

Vincent Aguirre¹, Nicholas Stylopoulos¹, Ronit Grinbaum¹ and Lee M. Kaplan¹

To investigate the contributions of two surgical gut manipulations—exclusion of the proximal intestine from alimentary flow and exposure of the jejunum to partially digested nutrients—to body weight regulation and metabolism, we have developed a rat model of an investigational device, the endoluminal sleeve (ELS). The ELS is a 10 cm, nutrient-impermeable, flexible tube designed for endoluminal implantation. ELS devices were surgically implanted in the duodenal bulb of rats with diet-induced obesity. Body weight, food intake, stool caloric content, and glucose homeostasis were subsequently evaluated. ELS-implanted rats demonstrated a 20% reduction of body weight compared to sham-operated (SO) controls. ELS-treated animals consumed an average of 27% fewer kcal/day than SO, and there was no evidence of malabsorption. ELS treatment improved fasting glycemia and glucose tolerance after oral and intraperitoneal (IP) administration. ELS treatment enhanced insulin sensitivity, as demonstrated
Gastric Balloon
Gastric Balloon

- Soft silicon sac placed in stomach
- Not a surgical procedure
  - Placed by endoscopy
  - Filled with 500-700 ml of normal saline
- Rapid transition from liquid to soft or normal diet
- Inflated to produce a sensation of satiety
- Remove at 6 months
Gastric Balloon Results: Italian Multicenter Study

- January 2005 to December 2009
- n = 1357 patients
- BMI: 44.9 ± 8.4 kg/m² (range 29-82.5)
- At 6 months 39.4 ± 7.3 kg/m²
- Intragastric balloon results also predicted 3 and 5 year benefit from LAP band procedure to follow.

Transoral Gastric Suturing

Transoral Gastric Suturing

Transoral Gastric Suturing: Effect at 12 Months

Mean Age – 40 years, BMI 38 kg/m²,

<table>
<thead>
<tr>
<th>Δ Wt</th>
<th>Δ BMI</th>
<th>Δ WC</th>
<th>Δ EWL</th>
<th>Δ Syst BP</th>
<th>Δ Diast BP</th>
</tr>
</thead>
<tbody>
<tr>
<td>-11.0 ± 10.0 kg</td>
<td>-4.0 ± 3.5 kg/m²</td>
<td>-12.6 ± 9.5 cm</td>
<td>-27.7 ± 21.9%</td>
<td>-15.2 mm</td>
<td>-9.7 mm</td>
</tr>
</tbody>
</table>

And too good to be true?

I’m definitely impressed, absolutely,” Dr. Arne V. Astrup, head of the department of nutrition, exercise and sports at the University of Copenhagen in Denmark and the lead investigator in the study, said.

But Dr. Daniel H. Bessesen, an endocrinologist at the University of Colorado who was not involved in the study, said weight loss of 2 percent beyond that provided by a placebo was “very modest. It doesn’t look like a game changer,”
So What Have We Learned Here?

• Have we really changed body weight regulation by these novel approaches?
  – Aspiration seems to create a CNS-mediated mechanism. **YES**
  – The endoluminal barrier also resembles the metabolic benefits of surgery. **Likely**
  – The gastric balloon by restricting food intake, more resembles the LAP band. **No**
  – Transoral gastric suturing (plication) might mediate effects by modifying blood supply to the greater curvature – data from pigs.
  • Cells that produce ghrelin. **Perhaps**
Thank You!