Overdiagnosis and dangerous overtreatment of irritable infants with “reflux”

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With acknowledgement to many of the academic staff of the dept of Paediatrics, Christchurch
Overdiagnosis and dangerous overtreatment of irritable infants with “reflux” A rapidly emerging non illness: A case study of an effective multi-modal educational solution
What Will You Say To Charlie’s Mum?
A Common Scenario

• New baby to the practice, Charlie - six weeks old
• Crying excessively
• Arches back, seems to be in pain
• Brings back milk/spilling
• Difficult to comfort
• Distressed parents
• “Surely there is something wrong? Two of the babies in my coffee group have been put on Losec (omeprazole) and it has worked wonders, we are at our wits end, please, please can you prescribe this for Charlie.”
What Do We Know?

• Many babies and infants cry more than their parents are comfortable with
• Crying is generally thought to be associated with pain or discomfort
• Babies frequently regurgitate milk after feeding
• Many babies do both
What Have We Been Taught?

• Regurgitation of stomach contents into the adult oesophagus is associated with pain and called gastro oesophageal reflux (+/- the Disease label GORD)

• GOR is effectively treated with stomach acid reduction

• PPIS are the most effective and are safe
It Makes Perfect Sense Then, That:

Irritable infants who bring back milk have GER(D), are in pain which thankfully can be safely and effectively treated with omeprazole
Omeprazole Use In Canterbury Infants

Patients under 1yr old dispensed omeprazole
Canterbury region 2005-2010
Regional Variation in PPI use < 1yr old
2005-2010

% Unique Patients per Live Births March-March 2005-2010

- Taumarunui
- Whanganui
- Lakes
- Northland
- Hawke's Bay
- Canterbury
- Counties Manukau
- Taranaki
- Southern Capital and Coast
- Midcentral
- West Coast
- Hutt
- South Canterbury
- Wairarapa
- Auckland
- Nelson Marlborough
- Waitemata
- Bay of Plenty
- Waikato
Canterbury Infants Exposed To PPI as % of National Prescribing

Canterbury has approx 10% of NZ live births
HealthPathways algorithm 2009
# Evidence for (non) efficacy

<table>
<thead>
<tr>
<th>Researcher</th>
<th>Drug</th>
<th>Findings</th>
</tr>
</thead>
</table>
| Moore et al (2003)                 | Omeprazole | - Omeprazole group had significant reduction in reflux index (9% with omeprazole vs. 2% with placebo)  
- No difference in improvement in cry/fuss time between omeprazole and placebo  
- No difference in visual analogue scale of intensity of infant irritability (parental impression) between omeprazole & placebo  
- Significant improvement in irritability & visual analogue score independent of treatment |
| Omari et al (2007)                 | Omeprazole | - Omeprazole significantly reduced gastric acidity, oesophageal acid exposure & number of acid reflux episodes  
- No difference in irritability, fussing & crying, vomiting, apnoea, choking between omeprazole and placebo |
| Orenstein et al (2009)             | Lansoprazole | - No difference in GORD symptoms between lansoprazole & placebo |
| Winter et al (2010)                | Pantoprazole | - No significant change between pantoprazole & placebo in weekly GORD symptom scores |
## Evidence for harm

<table>
<thead>
<tr>
<th>Study</th>
<th>Medication</th>
<th>Findings</th>
</tr>
</thead>
</table>
| Canani et al (2006)   | Omeprazole, Ranitidine| - Increase of acute gastroenteritis (3 x more likely) & community acquired pneumonia (6x more likely) in those treated with omeprazole or ranitidine compared to healthy children during 4 month follow up  
- In those treated with omeprazole or ranitidine, incidence of gastroenteritis & pneumonia increased comparing pre and post treatment |
| Orenstein et al (2009)| Lansoprazole          | - Serious adverse events occurred 6 times more frequently in those receiving lansoprazole compared to placebo  
- Most frequent serious adverse event lower respiratory tract infection |
## Numbers Needed to Harm

<table>
<thead>
<tr>
<th>Condition</th>
<th>NNH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastroenteritis</td>
<td>4</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>10</td>
</tr>
</tbody>
</table>
CONCLUSIONS

If the primary aim is to treat GERD symptoms in infants, PPIs should not be prescribed. Despite PPIs seeming to be well tolerated in the short-term, there is insufficient evidence to support the effectiveness and safety of PPIs in the treatment of GERD in children and adolescents. Therefore, physicians should be careful when prescribing PPIs, medications that are not approved for infants and have potential adverse effects, unless there is documented disease or with careful monitoring. Large, well-designed, placebo-controlled, randomized trials with well-chosen end points are necessary to evaluate the effect and safety of PPIs in the entire pediatric age range. Furthermore, we recommend more pathophysiological research on symptom genesis to be able to clearly define homogeneous patient groups and to enable the development of a therapy to tackle this growing health care problem.

CONCLUSIONS: PPIs are not effective in reducing GERD symptoms in infants. Placebo-controlled trials in older children are lacking. Although PPIs seem to be well tolerated during short-term use, evidence supporting the safety of PPIs is lacking. Pediatrics 2011;127:925–935

PPIs are not effective in reducing GERD symptoms in infants.
Reflux, GORD and Irritability

- Reflux/spilling
- Irritability
- True GORD
In This Instance There Appeared To Be A Need To:

De-medicalise and reframe infant irritability and reflux as normal developmental stages, reducing parental anxiety and minimising iatrogenic harm.
Defining the Clinical Problem
The Portfolio of Project Work

• Education sessions to many groups, produced and presented by a team representing primary and secondary care including:
  • General practice teams,
  • Paediatricians,
  • Pharmacists
  • Child (Plunket) Nurses,
  • Midwives

• Publications in professional journals

• Local media interviews

• Provide alternative strategies to manage difficult developmental stage

• Revise and reframe HealthPathways (local web-based guidelines) from “reflux disease” to “management of irritable infants”
Presenter’s Notes

Irritable Infants
Reflux and Constipation

This material was prepared by the Education Team with help gratefully received from Susie Tannary, Jeanette Banks, and David Bui.

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Take Home Messages – Irritable Babies

• Reflux and crying are common, normal, and usually improve with time

• Reflux + Crying ≠ GORD

• Little quality evidence supporting PPIs in infants

• PPI safety concerns

• Parent-health professional communication, education and reassurance very important
Simple Refluxing is normal

Characteristics in infancy

- Transient Relaxation
- LOS
- Relatively short Oesophagus
- Short Intra Abdominal Oesophagus
Infant Crying is Universal

Curves of Early Infant Crying
2 Weeks to 4 – 5 Months

Length of Time Crying

High Crier
Average Crier
Low Crier

5 – 6 Hours
20 – 30 Minutes

Barr RG. www.purplecrying.info
The Period of Purple Crying

The Letters in PURPLE Stand for

<table>
<thead>
<tr>
<th>P</th>
<th>U</th>
<th>R</th>
<th>L</th>
<th>E</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEAK OF CRYING</td>
<td>UNEXPECTED</td>
<td>RESISTS SOOTHING</td>
<td>PAIN-LIKE FACE</td>
<td>LONG LASTING</td>
</tr>
<tr>
<td>Your baby may cry more each week. The most at 2 months, then less at 3-5 months</td>
<td>Crying can come and go and you don’t know why</td>
<td>Your baby may not stop crying no matter what you try</td>
<td>A crying baby may look like they are in pain, even when they are not</td>
<td>Crying can last as much as 5 hours a day, or more</td>
</tr>
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[www.purplecrying.info](http://www.purplecrying.info)
Use of omeprazole and ranitidine is not indicated in primary care as there is a lack of evidence for their efficacy and concern about their safety.
Omeprazole Use in Canterbury since Multi-Disciplinary Education

Canterbury Unique Patients Under 1yrs Old dispensed Omeprazole
Omeprazole use Nationally since Multi-Disciplinary Education

Unique Patient count by year - Under 1yr Old Dispensed Omeprazole

- National
- Canterbury
Omeprazole Use in Canterbury since Multi-Disciplinary Education

Canterbury Unique Patients Under 1yrs Old dispensed Omeprazole
Omeprazole use nationally since Multi-Disciplinary Education

Unique Patient count by year - Under 1yr Old Dispensed Omeprazole
Number of Omeprazole Prescriptions

Omeprazole Scripts by Quarter - under 1 yr old

- National excl CDHB
- Canterbury
Change by District Health Board

% Unique Patients per Live Births Dec – Dec selected years

Canterbu

2006 2010 Pre Education 2014 Post Education (Current)
Regional variation in PPI use < 1yr old
Dec-Dec 2014

% Unique Patients <1 given PPI per Live Births

Drop in PPI Rx

2014 Post Education(Current)  2010 Pre Education
Canterbury Infants Exposed to PPI as % of National Prescribing

Canterbury has approx 10% of NZ live births
Canterbury Infants Exposed to PPI as % of National Prescribing

Canterbury has approx 10% of NZ live births
Take home message

When there are locally promoted conflicting versions of the truth, leading to unrealistic patient expectation and a gap between evidence and clinical practice, a whole of system approach to education and behavioural change is needed to effect change.
Post Script
Recent NICE Guidance May Have Muddied The Waters

• 1.3.2 Consider a 4-week trial of a PPI or H2RA for those who are unable to tell you about their symptoms (for example, infants and young children, and those with a neurodisability associated with expressive communication difficulties) who have overt regurgitation with 1 or more of the following: unexplained feeding difficulties (for example, refusing feeds, gagging or choking) distressed behaviour faltering growth. NICE guideline Published: 14 January 2015
NICE use of language to denote strength of evidence

• We use 'consider' when we are confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.
Thank you, I feel Much Better