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Waitemata District Health Board
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OMEPRAZOLE FOR CHILDREN – SAFE PRESCRIBING – THE INS AND OUTS

- EXPLAIN TO CAREGIVERS THAT MANY INFANTS WITH REFLUX/GORD IMPROVE WITHOUT MEDICATION
- REASSURE CAREGIVERS THAT IRRITABILITY, CRYING AND FUSSING ARE COMMON – OMEPRAZOLE DOES NOT CHANGE THESE BEHAVIOURS
- CONSIDER THE POTENTIAL INCREASED RISK OF INFECTIONS BEFORE PRESCRIBING
- USE MEDICATION FOR A LIMITED TIME

Uncomplicated infant reflux is common, and often due to large quantities of milk being ingested relative to the size of the infant's stomach. Almost all preterm infants show some degree of reflux which usually improves as the infant grows and the digestive system matures.[1]

GORD (Gastro-Oesophageal Reflux Disease) has been defined by the North American and European Societies of Paediatric Gastroenterology, Hepatology and Nutrition as 'when the reflux of gastric contents causes troublesome symptoms and/or complications'.[2]

EXPLAIN TO CAREGIVERS THAT MANY INFANTS WITH REFLUX/GORD IMPROVE WITHOUT MEDICATION

Most children under 12 months of age who are thriving and have uncomplicated reflux will not require any medical intervention.[3,4] Approximately 40% of infants under 1 year, regurgitate at least once a day.[5] All that is usually required for uncomplicated reflux is reassurance and conservative management such as adequate burping, increased frequency and reduced volume of feeds or thickened feeds on the advice of a dietician.[6,7]

Omeprazole reduces gastric acidity, not the frequency of reflux events. In addition, the gastric contents of milk-fed infants are non-acidic during a large part of the day.[8] Omeprazole is not considered effective for treating symptoms of irritability.[9] Reassure caregivers that most cases will spontaneously resolve regardless of medication, usually when the child begins to adopt an upright posture or consume solids.[3] Simple measures such as avoiding overfeeding may also improve symptoms.

There is a lack of robust evidence to support the optimal management of infant reflux or GORD because most studies have been conducted in children over the age of 2 years. In New Zealand, *proton pump inhibitors (PPIs) are not approved for use in infants under 1 year of age.*

Infants who are treated with PPIs may not experience a decrease in symptoms that are perceived to be caused by reflux.[9] In a study of 19 infants with confirmed GORD, symptoms improved in 10 infants without the use of pharmacotherapy.[10]

Clinical guidelines from Starship Children's Hospital regard acid-reducing agents such as PPIs as being ineffective for uncomplicated gastroesophageal reflux in infancy.[6]

REASSURE CAREGIVERS THAT IRRITABILITY, CRYING AND FUSSING ARE COMMON - OMEPRAZOLE DOES NOT CHANGE THESE BEHAVIOURS

Omeprazole does not suppress irritability, crying or fussing compared to placebo.[9] Although GORD and persistent crying may occur together, a significant association has not been established.[11]

Reassure caregivers that crying patterns vary with age during infancy; 20% of parents report a problem with infant crying in the first 3 months.[5] Crying frequency usually peaks between 6 weeks and 3 months; 3 hours per day can be considered 'normal', especially in the late afternoon to early evening. In a study of 37 infants with symptoms of GORD who were given conservative treatment alone (eg feeding modification and positioning), improvement of regurgitation

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and crying was observed in 78%, and 24% of them had 'normalised' by their two-week follow up.[12]

The benefits of simple, conservative treatment (eg adequate burping, thickened feeds, and avoidance of passive smoking) should be explored before pharmacological measures are considered.

CONSIDER THE POTENTIAL INCREASED RISK OF INFECTIONS BEFORE PRESCRIBING

Emerging evidence suggests that omeprazole may increase the risk of community acquired pneumonia (CAP) and gastroenteritis.[13]

A study investigating children aged from 4-36 months revealed that the rate of acute gastroenteritis and CAP significantly increased in children receiving either omeprazole or ranitidine, compared to healthy controls at their 4-month follow-up. This may be due to the role of gastric acid as a means of limiting the survival of microorganisms and regulation of gastrointestinal microflora.[13] The potential for an increased risk of infections from CAP or gastroenteritis should be considered before prescribing a PPI.

Due to the lack of evidence for the effectiveness of the use of omeprazole for uncomplicated reflux in infants, and concerns about safety,[8] it is recommended that it should only be considered for severe infantile reflux oesophagitis, or if there are related complications such as failure to thrive.[1] The decision to prescribe should be in consultation with a paediatrician or paediatric gastroenterologist.

USE MEDICATION FOR A LIMITED TIME

If the decision is made to prescribe a PPI, it is advisable to reassess symptoms after 2 to 4 weeks.[3,4] If there is no benefit, consider other options with a specialist.

Note: Please inform caregivers that omeprazole suspension will need to be prepared at a community pharmacy. The recommended formula is for 2mg/mL and has a 15 day expiry when kept in the fridge.

Side effects of omeprazole include nausea and vomiting, constipation, diarrhoea and abdominal pain.[14] Persistent crying may be related to these side effects, thus adding to the irritability. If symptoms worsen with treatment refer to a paediatric gastroenterologist.

Medication should be discontinued when symptoms improve, and the child monitored for signs of recurrence. Be aware that short-term acid rebound may occur upon discontinuation of a PPI.[14]

Information for parents and carers about omeprazole is www.nzfchildren.org.nz/nzf/resource/MFC/MfC_Omeprazole_for_GORD.pdf

Note: If the child has reflux with poor weight gain, and a strong family history of atopic disease, then allergic gastroenteritis (or dietary protein-induced gastroenteropathy) may be the cause.

When to Refer[5]

Refer to a paediatrician if the infant has excessive reflux **and**:

- Conservative treatment has failed (burping, small volume feeds, smoke-free environment, thickened feeds) or
- Extreme parental anxiety or
- Diagnostic uncertainty or
- Presence or suspicion of complications:
  - Failure to thrive
  - Oesophagitis
  - Respiratory complications
  - Neurobehavioural symptoms

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OMEPRAZOLE COMPOUNDING FOR PHARMACISTS

Omeprazole is unstable in acidic conditions; a suspension in sodium bicarbonate solution can be prepared as below.

Note: There are enteric coated pellets inside the capsules. The capsules should not be dissolved in milk or water.

Formula[15,16]

Omeprazole suspension 2mg/mL

Omeprazole powder	100mg
(**Or** omeprazole capsules	20mg x 5)
Sodium bicarbonate powder	4.2g
Water	50ml

Method

- Weigh sodium bicarbonate powder and grind in mortar and pestle to remove lumps
- Add powder to approximately 40ml water and stir until dissolved
- Put omeprazole powder into mortar (OR If using capsules, empty capsule contents into mortar and use pestle to crush the granules into a fine powder)
- Add a small volume of sodium bicarbonate solution, triturate to make a paste
- Transfer paste to measure and make up to final volume with sodium bicarbonate solution

Expiry: 15 days under refrigeration

Storage: Omeprazole is light sensitive. Store in amber plastic or glass containers. A colour change (to orange or black) may occur on exposure to light.

SHAKE THE BOTTLE because omeprazole is incompletely dissolved and partly in suspension.

Alternatively, if exactly 10mg or 20mg is prescribed, the capsule can be carefully opened and the granules mixed with a small amount of soft food (yoghurt/fruit puree). It is important the total amount is given straight away. The granules must not be crushed or chewed.

Capsule contents must not be directly placed on the child's tongue.

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REFERENCES

1. Reith D, Leathart C, Alderton A. Irritable infants, reflux and GORD. Best Practice Journal 2011; 40: 30-37 www.bpac.org.nz/BPJ/2011/november/infant-reflux.aspx (Accessed 20-05-16)
2. Vandenplas Y, Rudolph CD, Di Lorenzo C et al. Pediatric Gastroesophageal Reflux Clinical Practice Guidelines: Joint Recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN). Journal of Pediatric Gastroenterology and Nutrition 2009;49:498–547
3. www.naspghan.org/files/documents/pdfs/position-papers/FINAL%20-%20JPGN%20GERD%20guideline.pdf (Accessed 04-07-16)
4. Borton C. Childhood gastro-esophageal reflux. Egton Medical Information Systems Limited. 2015;1591(4) www.patient.co.uk/doctor/childhood-gastro-oesophageal-reflux (Accessed 04-07-16)
5. Winter HS. Gastroesophageal reflux in infants. UpToDate 2016;5876(34.0). www.uptodate.com/contents/gastroesophageal-reflux-in-infants?source=search_result&search=gastroesophageal+reflux+disease&selectedTitle=1%7E150 (Accessed 04-07-16)
6. Best Practice Advocacy Centre reports. The use of omeprazole in infants is still high. 2013 update. (Accessed 20-05-16)
7. Starship Hospital Clinical Guidelines. Gastro-oesophageal Reflux 2012.
8. www.adhb.govt.nz/starshipclinicalguidelines/_Documents/Gastro-Oesophageal%20Reflux.pdf (Accessed 20-05-16)
9. New Zealand Formulary for Children. Gastro-oesophageal reflux disease. www.nzfchildren.org.nz/nzf_655 (Accessed 04-07-16)
10. Van der Pol RJ, Smits MJ, van Wijk MP et al. Efficacy of proton-pump inhibitors in children with gastroesophageal reflux disease: A systematic review. Pediatrics 2011; 127(5):925-35 http://pediatrics.aappublications.org/content/pediatrics/127/5/925.full.pdf (Accessed 04-07-16)
11. Moore DJ, Tao SKB, Lines DR et al. Double-blind placebo-controlled trial of omeprazole in irritable infants with gastroesophageal reflux. Journal of Pediatrics 2003;143:219-23.
12. Orenstein SR, Shalaby TM, Kelsey SF, Frankel E. Natural history of infant reflux esophagitis: Symptoms and morphometric histology during one year without pharmacotherapy. American Journal of Gastroenterology 2006; 101:628-40.
13. Heine RG, Jordan B, Lubitz L et al. Clinical predictors of pathological gastro-oesophageal reflux in infants with persistent distress. Journal of Paediatrics and Child Health 2006;42:134-9.
14. Ornstein SR, McGowan JD. Efficacy of conservative therapy as taught in the primary care setting for symptoms suggesting infant gastroesophageal reflux. Journal of Pediatrics 2008;152(3):310-4 www.jpeds.com/article/S0022-3476(07)00854-2/pdf (Accessed 05-07-16)
15. Canani RB, Cirillo P, Roggero P et al. Therapy with gastric acidity inhibitors increases the risk of acute gastroenteritis and community-acquired pneumonia in children. Pediatrics 2006:117;e817-20.
16. New Zealand Formulary for Children. 1.3.5 Proton pump inhibitors. www.nzfchildren.org.nz/nzf_763 (Accessed 05-07-16)
17. New Zealand Formulary. Omeprazole suspension. www.nzf.org.nz/nzf_9669.html (Accessed 04-07-16)
18. PHARMAC Pharmaceutical Management Agency, New Zealand. The Pharmaceutical Schedule. www.pharmac.govt.nz/2017/05/01/Schedule.pdf (Accessed 10-05-17)

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