1.3 Proton pump inhibitor medicines dispensing, 1 year and under

Why is this important?

Proton pump inhibitor (PPI) medicines have become increasingly prescribed for managing gastro-oesophageal reflux in infants. They are also prescribed for general symptoms such as irritability and crying (or colic) on the basis that reflux might be causing these symptoms. This is despite a lack of evidence of effectiveness, as well as uncertainty about the long-term effects of these medicines in the very young. In particular, there is concern about the potential for increased susceptibility to infections and food allergies that may result from the alteration of normal gut bacteria.[1-3]

What did we find?

There was about a four-fold difference between the lowest and highest state and territory rates in Pharmaceutical Benefits Scheme (PBS) dispensing of PPI medicines for infants aged 1 year and under in Australia.

What can be done?

Greater clarity and consistency of guidelines on gastro-oesophageal reflux and colic in infants, with a focus on alternative approaches to managing symptoms that lead to PPI medicine prescribing by general practitioners (GPs) and specialists, could help to reduce the rate of inappropriate use of PPI medicines in infants in Australia. Ensuring that support is available for new parents, and that information about the potential risks and likelihood of benefits of PPI medicines use in infants is more readily available, may also reduce inappropriate use. Introducing an authority requirement for prescribing PPI medicines for infants could also reduce inappropriate use.

Proton pump inhibitor medicines dispensing, 1 year and under

Context

PPIs are a group of medicines that reduce acid production in the stomach.[4] Medicines in the PPI group include omeprazole, pantoprazole, lansoprazole, rabeprazole and esomeprazole.[5] This data item analyses PPI medicines use in infants (aged 1 year and under). See Chapter 2, page 117, for analysis of PPI medicine use in adults (aged 18 years and over).

Use of PPI medicines for gastro-oesophageal reflux and gastro-oesophageal reflux disease (GORD) in infants is common and increasing in Australia[6,7], despite concerns about side effects and evidence that PPI medicines are not effective in this age group for these conditions or for colic.[8-10] Most guidelines recommend non-medical therapy for simple reflux in infants aged 1 year and under (0–12 months)[11-13], but guidelines for the management of infant GORD (which involves complications, such as oesophagitis) are unclear in some cases and inconsistent.[6] Australian advice includes:

- Do not routinely treat GORD in infants with acid suppression therapy[11]
- Consider PPI therapy if there are concerns that excessive GORD of long duration is the cause of irritability in infants.[13]

Although a trial of PPI therapy has become a common recommendation for infants for problematic reflux symptoms, or for those with complications, trials have shown it is no better than placebo for symptoms of infant reflux.[14]

An Australian study of children treated in 2012–2013 either by a GP, by a paediatrician in an emergency department or as an inpatient reported that 41% of healthy, thriving infants presenting with irritability or unexplained crying were prescribed an acid suppression medicine at first presentation.[15] A study of Australian GPs found that the proportion of infants with gastro-oesophageal reflux that they managed by prescribing a PPI medicine increased from 12% in 2006–2008 to 28% in 2014–2016.[6] The proportion of infants with GORD managed by prescribing a PPI medicine increased from 33% to 50% over the same period.[6]

Gastric acid is an important factor in infection resistance and the composition of gastrointestinal flora.[1] A prospective study of 91 otherwise healthy young children (average age 10 months) taking either omeprazole or ranitidine (another type of acid suppression medicine) for GORD found that they were significantly more likely to develop acute gastroenteritis or pneumonia than the control group.[1] Retrospective studies have also found an association between PPI medicine use in infants and children and an increased risk of developing allergies.[2,3]

About the data

Data are sourced from the PBS dataset which includes all prescriptions dispensed under the PBS or the Repatriation Pharmaceutical Benefits Scheme. This includes prescriptions that do not receive an Australian Government subsidy and prescriptions dispensed under the Closing the Gap scheme.

The dataset does not include prescriptions dispensed for patients during their admission to public hospitals, discharge prescriptions dispensed from public hospitals in New South Wales and the Australian Capital Territory, direct supply of medicines to remote Aboriginal health services, over-the-counter purchase of medicines, doctor's bag medicines or private prescriptions.

Rates are based on the number of prescriptions dispensed for PPI medicines per 100,000 infants aged 1 year and under in 2016–17.

The analysis and maps are based on the residential address of the patient recorded in the PBS prescription claim and not the location of the prescriber or the dispensing pharmacy.

Rates are sex standardised to allow comparisons between populations with different sex structures.

Because of small numbers, data are reported only at state level. Reporting by smaller geographical area, remoteness and socioeconomic disadvantage is not possible.

This analysis was not undertaken by Aboriginal and Torres Strait Islander status because this information was not available for the PBS data at the time of publication.

What do the data show?

Magnitude of variation

In 2016–17, there were 22,810 PBS prescriptions dispensed for PPI medicines to infants aged 1 year and under, representing 3,628 prescriptions per 100,000 infants aged 1 year and under (the Australian rate).

The number of PBS prescriptions dispensed for PPI medicines varied across states and territories, from 2,195 per 100,000 infants in the Northern Territory to 8,066 per 100,000 in South Australia (Figure 1.9).

Analysis by prescriber type

GPs prescribed 66% of the PBS prescriptions dispensed for PPI medicines in infants, paediatricians prescribed 27%, and other health professionals prescribed 7%. The proportion prescribed by GPs varied across states and territories from 30% in the Northern Territory to 80% in Western Australia (Figure 1.9).

Interpretation

Variation in rates of PPI medicines dispensing is likely to be due to geographical differences in the factors discussed below.

Clinical decision-making

Variation in awareness of, and adherence to, guidelines for management of simple reflux symptoms in infants is likely to influence the pattern of use, as could over-diagnosis of reflux in infants presenting with irritability and unexplained crying (colic).

Use of other medicines

Use of other types of acid suppression medicines, such as H2 blockers, for reflux symptoms in infants is likely to influence the patterns of PPI medicines use.[6]

Access to medical care

Access to GPs, paediatricians and gastroenterologists may influence the likelihood of consumers seeking care for gastro-oesophageal reflux and GORD for their children, and therefore affect rates of PPI medicines use. Access to programs that provide education and support for parents may also affect rates of consultation for unexplained crying in infants, and affect rates of PPI medicines use.

As well, variations between states/territories may not directly reflect the practices of the clinicians who are based in these areas. The analysis is based on where people live rather than where they obtain their health care. Patients may travel outside their local area to receive care.

Proton pump inhibitor medicines dispensing, 1 year and under

Promoting appropriate care

The quality of evidence on long-term risks of PPI medicines is generally low[16], but these possible risks are important when seen in the context of large-scale inappropriate use and the potential for effects on health over an infant's life course. Limiting use to appropriate indications would also reduce patient costs and waste of health resources.[16,17]

The Pharmaceutical Benefits Advisory Committee recently proposed reconsidering the PBS restriction levels for PPI medicines.[18] Introducing an authority requirement for prescribing PPI medicines for infants could reduce inappropriate use in Australia.

Educational campaigns for family and child health nurses, GPs and parents, as well as greater clarity and consistency of guidelines for managing gastro-oesophageal reflux and colic in infants, could also help to reduce the rate of inappropriate use of PPI medicines in infants in Australia.[6,19] Further research to give a better understanding of the influences on PPI medicines prescribing would also be helpful for informing strategies.[6]

Misinformation about the appropriate use of PPI medicines in infants – in both medical and consumer publications – poses a risk to children.[20] Providing evidence-based information is vital, especially in widely read publications that family and child health nurses and GPs may rely on for continuing education.

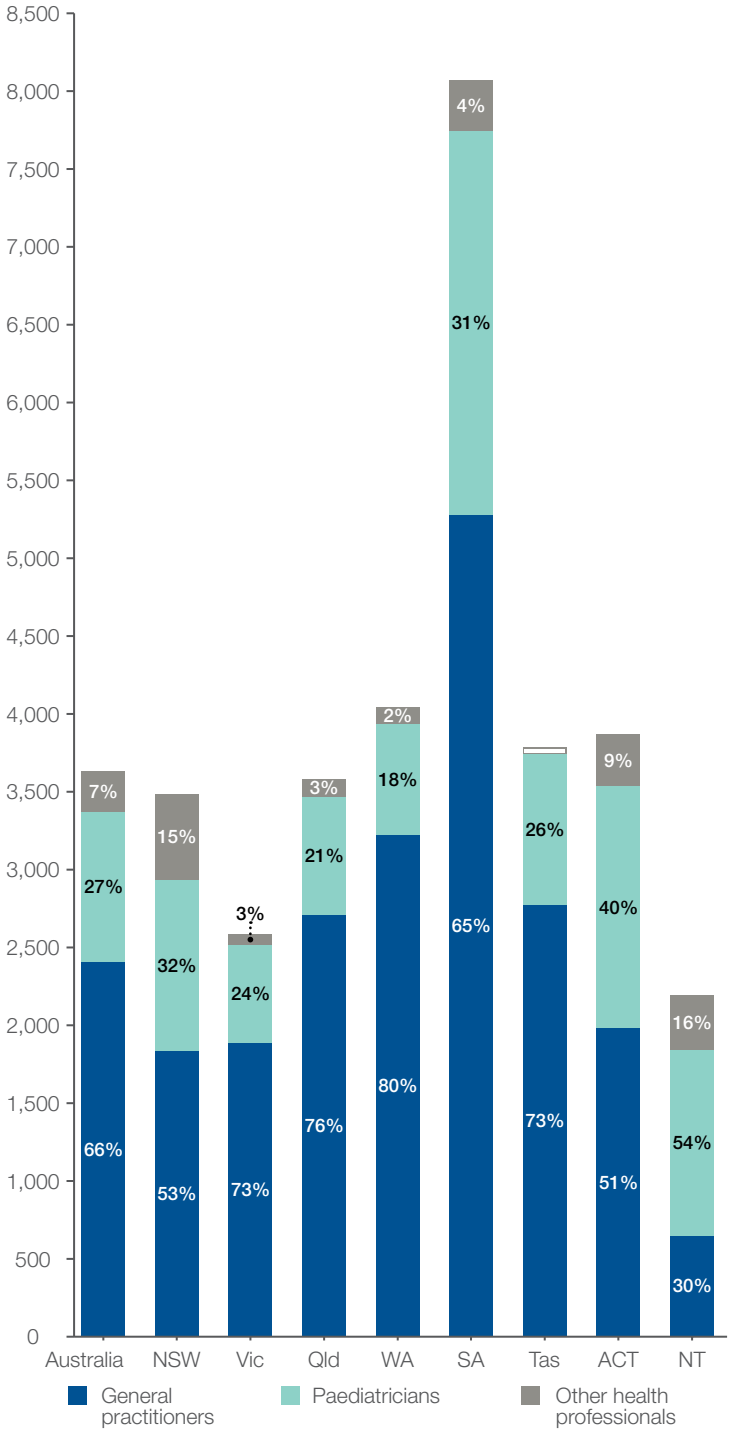
Infants may be over-diagnosed with GORD, which could lead to other causes of symptoms not being addressed, as well as overuse of PPI medicines.[21,22] The great majority of infants will respond to non-pharmacological measures, or get better with time, and a stepwise approach to investigation and management will reduce the number of infants exposed to PPI medicines.[20] Irritable infants with uncomplicated GORD are recommended to continue lifestyle modifications and to avoid acid suppression therapy.[23] Further research is needed to determine how best to support parents to manage gastro-oesophageal reflux in infants, and to get to the root cause of their reasons for seeking medical help.[21]

United States research shows that adherence to guidelines recommending against empirical acid suppression for gastro-oesophageal reflux in infants is low in children's hospitals.[22,24] Quality improvement interventions in hospitals could improve appropriateness of care in this setting, and could have a flow-on effect to prescribing in the community, as hospital recommendations for PPI medicines use may influence PPI medicines use after discharge.[25]

Creating hospital-specific policies could improve adherence to the recommendations of national guidelines.[24] Implementing an evidence-based guideline in a United States neonatal intensive care unit correlated with a substantial decrease in non-indicated prescriptions of PPI medicines (from 7.5 per month to zero).[26] The intervention followed plan–do–study–act cycles of quality improvement, and included staff education and guideline revision based on staff feedback. Keys to the program's success were thought to include leadership involvement, staff incentives and real-time data tracking.[26] The intervention could be implemented in similar inpatient settings for newborns.[26]

Rates by state and territory and prescriber type

Figure 1.9: Number of PBS prescriptions dispensed for proton pump inhibitor medicines per 100,000 infants aged 1 year and under, sex standardised, by state and territory of patient residence, by prescriber type, 2016–17



The data for Figure 1.9 are available at www.safetyandquality.gov.au/atlas

Notes:
Unshaded data (Tasmanian other health professionals) are based on a small number of prescriptions dispensed.
For further detail about the methods used, please refer to the Technical Supplement.
Sources: AIHW analysis of Pharmaceutical Benefits Scheme data and ABS Estimated Resident Population 30 June 2016.

Proton pump inhibitor medicines dispensing, 1 year and under

Resources

- National Institute for Health and Care Excellence, *Gastro-oesophageal Reflux Disease in Children and Young People: Diagnosis and management* (clinical guideline)[12]
- Royal Children's Hospital Melbourne, 'Gastro-oesophageal reflux in infants'[13]
- Royal Children's Hospital Melbourne, *Reflux (GOR) and GORD*, fact sheet for parents[27]
- New South Wales Health, *Infants and Children: Acute management of the unsettled and crying infant*.[28]

Australian initiatives

The information in this chapter will complement work already under way to improve the appropriateness of PPI medicines use in Australia. At a national level, this work includes:

- Royal Australian College of Physicians, Paediatrics and Child Health Division top 5 low-value practices and interventions – EVOLVE recommendation 4: Do not routinely treat gastroesophageal reflux disease (GORD) in infants with acid suppression therapy.[11]
- Pharmaceutical Benefits Advisory Committee, recommendations in 2018 to change PBS restriction levels for some PPI medicines.[18]

Many state and territory initiatives are also in place to improve the appropriateness of PPI medicines use, including:

- Tasmanian HealthPathways web-based information portal, 'Gastro-oesophageal reflux in children'.[29]

References

1. Canani RB, Cirillo P, Roggero P, Romano C, Malamisura B, Terrin G, et al. Therapy with gastric acidity inhibitors increases the risk of acute gastroenteritis and community-acquired pneumonia in children. Pediatrics 2006;117(5):e817–20.
2. Mitre E, Susi A, Kropp LE, Schwartz DJ, Gorman GH, Nylund CM. Association between use of acid-suppressive medications and antibiotics during infancy and allergic diseases in early childhood. JAMA Pediatr 2018;172(6):e180315.
3. Trikha A, Baillargeon JG, Kuo YF, Tan A, Pierson K, Sharma G, et al. Development of food allergies in patients with gastroesophageal reflux disease treated with gastric acid suppressive medications. Pediatr Allergy Immunol 2013;24(6):582–8.
4. Centers for Medicare & Medicaid Services. Proton pump inhibitors: use in adults. CMS; 2013. www.cms.gov/Medicare-Medicaid-Coordination/Fraud-Prevention/Medicaid-Integrity-Education/Pharmacy-Education-Materials/Downloads/ppi-adult-factsheet.pdf (accessed Dec 2017).
5. Tenni P, Dunbabin D. A guide to deprescribing proton pump inhibitors. Hobart: Primary Health Tasmania; 2016. https://www.primaryhealthtas.com.au/wp-content/uploads/2018/09/A-Guide-to-Deprescribing-Proton-Pump-Inhibitors.pdf (accessed Jul 2018).
6. Bell JC, Schneuer FJ, Harrison C, Trevena L, Hiscock H, Elshaug AG, et al. Acid suppressants for managing gastro-oesophageal reflux and gastro-oesophageal reflux disease in infants: a national survey. Arch Dis Child 2018;103(7):660–4.
7. Kirby CN, Segal AY, Hinds R, Jones KM, Piterman L. Infant gastro-oesophageal reflux disease (GORD): Australian GP attitudes and practices. J Paediatr Child Health 2016;52(1):47–53.
8. van der Pol RJ, Smits MJ, van Wijk MP, Omari TI, Tabbers MM, Benninga MA. Efficacy of proton-pump inhibitors in children with gastroesophageal reflux disease: a systematic review. Pediatrics 2011;127(5):925–35.
9. Vandenplas Y, Rudolph CD, Di Lorenzo C, Hassall E, Liptak G, Mazur L, 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). J Pediatr Gastroenterol Nutr 2009;49(4):498–547.
10. Gieruszczak-Białek D, Konarska Z, Skórka A, Vandenplas Y, Szajewska H. No effect of proton pump inhibitors on crying and irritability in infants: systematic review of randomized controlled trials. J Pediatr 2015;166(3):767–70.e3.
11. Royal Australian College of Physicians. Paediatrics and Child Health Division: top 5 low-value practices and interventions. EVOLVE recommendation 4 [Internet]. Sydney: RACP; 2016 [cited 2018 Apr 12]. Available from: https://evolve.edu.au/published-lists/paediatrics-and-child-health-division
12. National Institute for Health and Care Excellence. Gastro-oesophageal reflux disease in children and young people: diagnosis and management. London: NICE; 2015. www.nice.org.uk/guidance/ng1/resources/gastrooesophageal-reflux-disease-in-children-and-young-people-diagnosis-and-management-51035086789 (accessed Jul 2018).
13. Royal Children's Hospital Melbourne. Gastrooesophageal reflux in infants [Internet]. Melbourne: RCH [cited 2018 Apr 12]. Available from: www.rch.org.au/clinicalguide/guideline_index/Gastrooesophageal_reflux_in_infants
14. Therapeutic guidelines: gastrointestinal. Version 6. Melbourne: Therapeutic Guidelines Limited; 2016.
15. Braithwaite J, Hibbert PD, Jaffe A, White L, Cowell CT, Harris MF, et al. Quality of health care for children in Australia, 2012–2013. JAMA 2018;319(11):1113–24.
16. Freedberg DE, Kim LS, Yang YX. The risks and benefits of long-term use of proton pump inhibitors: expert review and best practice advice from the American Gastroenterological Association. Gastroenterology 2017;152(4):706–15.
17. Gracie DJ, Ford AC. The possible risks of proton pump inhibitors. Med J Aust 2016;205(7):202–3.
18. Pharmaceutical Benefits Advisory Committee. March 2018 PBAC outcomes: other matters. Canberra: Australian Government Department of Health; 2018. www.pbs.gov.au/industry/listing/elements/pbac-meetings/pbac-outcomes/2018-03/other-matters-03-2018.pdf (accessed Apr 2018).
19. Quitadamo P, Miele E, Alongi A, Brunese FP, Di Cosimo ME, Ferrara D, et al. Italian survey on general pediatricians' approach to children with gastroesophageal reflux symptoms. Eur J Pediatr 2015;174(1):91–6.
20. Hassall E. Over-prescription of acid-suppressing medications in infants: how it came about, why it's wrong, and what to do about it. J Pediatr 2012;160(2):193–8.
21. Dahlen HG, Foster JP, Psaila K, Spence K, Badawi N, Fowler C, et al. Gastro-oesophageal reflux: a mixed methods study of infants admitted to hospital in the first 12 months following birth in NSW (2000–2011). BMC Pediatr 2018;18(1):30.
22. Slaughter JL, Stenger MR, Reagan PB, Jadcherla SR. Neonatal histamine-2 receptor antagonist and proton pump inhibitor treatment at United States children's hospitals. J Pediatr 2016;174:63–70 e3.
23. Safe M, Chan WH, Leach ST, Sutton L, Lui K, Krishnan U. Widespread use of gastric acid inhibitors in infants: are they needed? are they safe? World J Gastrointest Pharmacol Ther 2016;7(4):531–9.
24. Long HA, Solski L, Rebuck JA, Bridgeman C. Infantile gastroesophageal reflux: adherence to treatment guidelines in the hospital setting. J Pediatr Pharmacol Ther 2018;23(1):41–7.
25. Ahrens D, Behrens G, Himmel W, Kochen MM, Chenot JF. Appropriateness of proton pump inhibitor recommendations at hospital discharge and continuation in primary care. Int J Clin Pract 2012;66(8):767–73.
26. Angelidou A, Bell K, Gupta M, Tropea Leeman K, Hansen A. Implementation of a guideline to decrease use of acid-suppressing medications in the NICU. Pediatrics 2017;140(6):e20171715.
27. Royal Children's Hospital Melbourne, Emergency, Gastroenterology and Clinical Nutrition departments. Reflux (GOR) amd GORD [Internet]. Melbourne: RCH; 2018 [updated 2018 May; cited 2018 Jul]. Available from: www.rch.org.au/kidsinfo/fact_sheets/Reflux_GOR
28. NSW Health Office of Kids and Families. Infants and children: acute management of the unsettled and crying infant. Sydney: NSW Ministry of Health; 2016.
29. Tasmanian HeathPathways. Gastro-oesophageal reflux in children [Internet]. Available from: https://tasmania.healthpathways.org.au.