Cum Laude

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Deprescribing proton pump inhibitors: Addressing prolonged and unnecessary use in paediatric hospitalised children

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Background: Proton pump inhibitors (PPIs) are approved for shorth-term (≤ 12 weeks) use in children older than one month. Long-term PPI therapy has been associated with increased risk of gastrointestinal and respiratory infections, fractures and micronutrient deficiencies. This study will be the first to describe paediatric PPI use in hospitalised paediatric patients in South Africa in relation to Hospital Level Paediatric Standard Treatment Guidelines (STG)-recommendations of PPI therapy.

Methods: A retrospective cross-sectional study was conducted across two tertiary public hospitals in South Africa (01 February 2023–31 January 2024). Data from medical records of paediatric hospitalised patients (< 18 years) who received a PPI prescription within the study period were evaluated. Data analysed included demographic data, in-hospital and discharge PPI prescription particulars. Descriptive statistics were used to present the analysed data.

Results: Among 400 patients, only 28% of prescriptions aligned with STG-recommended indications, while 48% of prescriptions were prescribed for non-recommended indications. The median duration of PPI therapy was 31 days and only 7% of prescriptions complied with STG-recommended durations. Long-term use (> 12 weeks) occurred in 17.5% of patients. Deprescribing strategies of PPI prescriptions was employed in 23.8% of cases, predominantly intravenous (IV)-to-oral de-escalation.

Conclusion: The findings highlight STG prescribing deviations and infrequent attempts of PPI deprescribing. Structured PPI prescription review processes, clear STG recommendations and proactive deprescribing strategies are required to promote rational PPI use.

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Background

Proton pump inhibitors (PPIs) are approved for short-term (≤ 12 weeks) use in children older than one month.[19-22] Indications include gastro-oesophageal reflux disease (GORD), eosinophilic oesophageal oesophagitis (EOE), eradication of *H. pylori* infection or peptic-ulcer disease (PUD), bleeding of oesophageal varices, gastrointestinal bleeding, or erosions, nausea and vomiting and stress-ulcer prophylaxis (SUP).[14] However, treatment durations are poorly defined in both local and international guidelines. The duration of PPI use in the treatment of GORD, *H. pylori* and bleeding of oesophageal varices is most explicitly described in the literature, with the longest recommended treatment duration between eight- and 12-weeks.[4,6,9,11,13-15]

Long-term PPI use is associated with increased risk of gastrointestinal and lower respiratory tract infections, bone fractures and allergies.[3] It is recommended that a PPI should be prescribed for validated short-term use (≤ 12 weeks) to ensure safe and rational medicine use.[5,7]

Some studies define long-term PPI use in the paediatric population as use exceeding 12 weeks.[5,18] While the STG currently limit PPI use to a maximum of four to eight weeks of therapy.[14] The package inserts of PPIs evaluated in this study generally associate adverse events with PPI use beyond 12 weeks. Additionally, from package inserts of PPIs evaluated in this study, the risk of bone fractures is increased with use beyond one year and vitamin B12 deficiency with use beyond three years.[19-22]

Methods

A retrospective, cross-sectional analysis was conducted at two tertiary public health facilities in South Africa. This study included hospitalised paediatric patients (aged < 18 years) who received at least one PPI prescription during their admission within the study period (01 February 2023–31 January 2024). Data was collected from physical medical records and included demographic information and PPI prescription details. Descriptive statistics summarised PPI use,

Table I: Indications of PPI prescriptions not according to STG recommendations across age groups

	0 –28 days	> 28 days–12 months	> 12–24 months	> 24 months–12 years	> 12–< 18 years	Total
Indications not according to STG n (%)						
Age group	36 (9)	111 (27.8)	46 (11.5)	169 (42.3)	38 (9.5)	400
SUP: mechanical ventilation	14 (60.9)	22 (37.9)	6 (25)	21 (30.4)	5 (27.8)	68
Feeding intolerance	5 (21.7)	15 (27.3)	7 (30.4)	6 (8.2)	2 (11.1)	35
GI issues (vomiting, GI discomfort, diarrhoea)	3 (13)	12 (21.8)	3 (13)	11 (15.1)	3 (16.7)	32
Chemotherapy, corticosteroid, or anticoagulant use	0	0	4 (17.4)	11 (15.1)	3 (16.7)	18
*Other	0	1 (1.8)	0	11 (15.1)	3 (16.7)	13
*GI anomalies	0	4 (7.3)	1 (4.3)	4 (5.5)	1 (5.6)	10
*Signs of bleeding unrelated to GIB	1 (4.3)	1 (1.8)	2 (8.7)	3 (4.1)	2 (11.1)	9
Cerebral palsy without feeding intolerance or GORD	0	0	0	4 (5.5)	1 (5.6)	5
Ingestion of corrosive substance	0	0	0	1 (1.4)	0	1
Total	23	58	24	69	18	192

Percentages are based on total patients within a column.

*Other: SUP: trauma, SUP: cancer, SUP: surgery, otitis media, gastric pull-up

*GI anomalies: Biliary -, duodenal -, oesophageal atresia, laryngomalacia,

*Signs of bleeding unrelated to GIB: bleeding of gums, haemolytic anaemia, haematuria, epistaxis, INR high, low platelets

Gastrointestinal (GI), stress ulcer prophylaxis (SUP), Gastrointestinal bleed (GIB)

appropriate of prescriptions and frequency of deprescribing strategies. Ethical approval was obtained from University of the Western Cape (UWC) Biomedical Research and Ethics Committee (BMREC) and the National Health Research Database under the Western Cape Government Health Department (WC202401_001).

Results

Among 400 paediatric patients, 200 per facility, omeprazole was the most frequently prescribed PPI (79.3%, *n* = 317). Only 28% of prescriptions corresponded to STG-recommended indications, while 48% (*n* = 192) were for indications not according to STG-recommendations. Indications of PPI prescriptions not according to STG recommendations are seen below (*Table I*). Among these, the most frequently prescribed indication was for SUP related to mechanical ventilation at 35.4% (*n* = 68). Additionally, the most frequent indication for all PPI prescription throughout the patient cohort was SUP for mechanical ventilation (17%, *n* = 68). The remaining 24% (*n* = 96) of patients lacked a documented indication, underscoring one of the challenges of retrospective data collection.

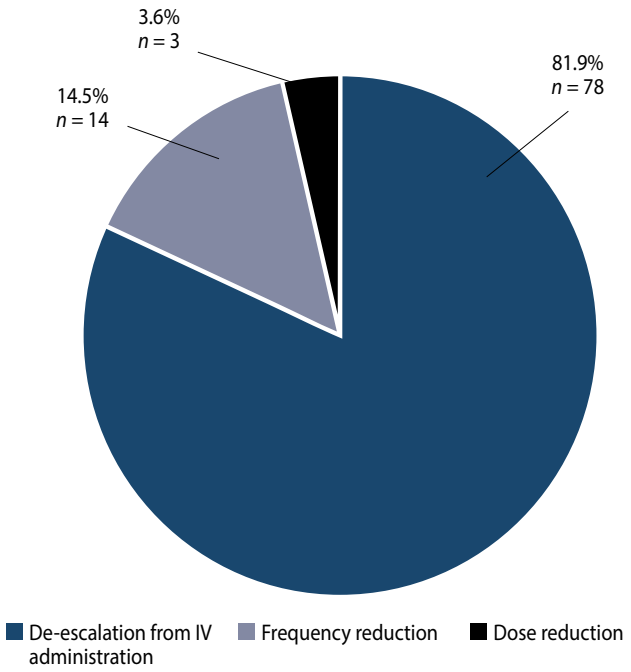

Figure 1: Deprescribing strategies

The median duration of PPI prescriptions use was 31 days (range: 1–251 days). Only 7% (*n* = 28) of prescriptions aligned with STG-recommended duration for the stated indication. Furthermore, 20.8% of patients received a PPI prescription at least a third time during their current hospitalisation. Long-term PPI use (> 12 weeks) was observed in 17.5% (*n* = 70) of patients. The majority (*n* = 228, 57%) of the patients was discharged with a PPI prescription. Omeprazole was the most frequently prescribed PPI (*n* = 194, 85.1%) upon discharge.

PPI prescription deprescribing strategies were employed in 23.8% (*n* = 95) of patients, most commonly de-escalation from IV to oral therapy (81.9%, *n* = 78) *(Figure 1)*.

Notably, 46.3% (*n* = 36) of the patients in whom PPI prescription IV de-escalation was employed were between the ages of 0 days and 12 months. This finding suggests inappropriate initial PPI use according to patients' age. Since pantoprazole is the primary IV PPI available in the public health care setting, however, lacks validation for use in children < 12 months.

Discussion

The findings of this study highlight deviations from STG-recommended PPI prescribing practices in paediatric hospital care. The absence of explicit treatment duration recommendations within the national STG may contribute to unnecessary prolonged PPI therapy. Prescribers

may initiate PPIs for acute conditions, however, fail to discontinue therapy due to the lack of structured medication review processes, clear documentation of initial indication and clear evidence-based recommendations. However, prolonged PPI use (> 12 weeks) may contribute to adverse events such as increased risk of infections,[1,2,7] bone fractures[23] and nutrient malabsorption,[5,12,18] ultimately contributing to polypharmacy. It is imperative for clinicians to navigate the balance between the risk of discontinuing PPI therapy as opposed to the benefit it proposes in reducing the risk of potential adverse events and reducing potential unnecessary medication use.

Three consensus guidelines from India, Canada and the United States offer similar approaches on deprescribing PPI therapy.[8,16-17] Firstly, the importance of systematically re-evaluating the necessity of PPI therapy, especially after the predetermined period of use has passed with symptom improvement (e.g. four weeks of PPI therapy for GORD). Then, deprescribing can be implemented either by abruptly discontinuing PPI therapy or via a tapering regimen, stepping down to alternative acid-suppression therapy (histamine-2-receptor antagonists), intermittent use for a shorth predetermined period, on-demand use or through dose reduction.[8,16-17] There are currently no studies that directly compare different deprescribing strategies and therefore no definitive optimal approach exists.[16] Lastly, all patients without a documented indication or need for PPI therapy should be reviewed and considered for PPI discontinuation.[8,16-17] No PPI deprescribing guidance specific to paediatric patients exists.

Recommendations for practice based on the findings of this study:

1. Evidence-based guidelines should provide explicit recommendations on the duration of PPI therapy for each recommended indication.
2. Evidence-based guidelines should integrate deprescribing protocols of PPI therapy specific to the paediatric population.
3. Pharmacists should play an active role in the review of PPI prescriptions to determine the need for acute use as opposed to continued use, to ensure safe and rational use.

Conclusion

This study highlights discrepancies between PPI prescribing practices and national guideline recommendations in the hospitalised paediatric population. Prolonged and unnecessary therapy remains common, posing avoidable risks to paediatric patients. Clear STG guidance, structured medication review processes and proactive deprescribing strategies are vital to optimise care.

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