Understanding Australian Pharmacists' Perceptions on the Utilisation of Oral 5-HT3Antagonists as Pharmacist-Only Anti-Emetics in Comparison to Oral D2 Antagonists

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Abstract

Objectives: To investigate the perception of community pharmacists on the down-scheduling of 5-HT3 antagonists to pharmacist-only-medicine for treatment of acute nausea and/or vomiting in Australia. Methods: A nationwide anonymous survey targeting Australian community pharmacists was conducted from April to May 2023. Responses were collected and analysed quantitively or qualitatively, where appropriate. Key findings: Participants reported that 5-HT3 antagonists were effective at treating nausea and/or vomiting and would likely recommend their use. Training is required to manage supply due to concerns related to their side effects. Conclusion: Participants supported down-scheduling of 5-HT3 antagonists for the treatment of nausea and/or vomiting in Australia. A pilot study on the provision of 5-HT3 antagonists by pharmacists is recommended as is the development of guidelines for pharmacist-only supply before down-scheduling is considered.

Keywords

community pharmacists, schedule 3 medicines, nausea and/or vomiting, 5-HT3 antagonists, D2 antagonists

Introduction

Community pharmacists in Australia play an integral role in diagnosing and providing symptomatic relief of nausea and/or vomiting (N/V).[1] Supply of anti-emetics by pharmacists is currently limited by scheduling of medications by the Ther- apeutic Goods Administration (TGA). In Australia, serotonin (5-HT3) antagonists, such as ondansetron (administered orally or via injection) and granisetron (administered orally or via injection) are prescription-only-medications (Schedule 4, S4).[2,3] Dopamine (D2) antagonists, such as prochlorperazine (administered orally) are pharmacist-only-medications (Schedule 3, S3) and may be supplied over the counter (OTC) specifically for the treatment of nausea associated with migraine[2] (Supplementary material S1).

Down-scheduling 5-HT3 antagonists to S3 pharmacist- only-medications may provide additional options for pharma-cists to consider when treating N/V. Presently, the perceptions of pharmacists on the down-scheduling of 5-HT3 antagonists is limited. This study aimed to gather community pharmacists' perceptions on the down-scheduling of oral 5-HT3 antagonists to S3, specifically regarding their opinions on their efficacy and safety and to determine if they possess the knowledge and training to safely provide them.

Methods

An anonymous survey (developed using Qualtrics and ac-cessible via QR code) was disseminated via social media and the research team's personal network (including direct email to 51 pharmacies in South Australia) during April and May of 2023. Participants were required to be (i) at least 18 years old,
(ii) a pharmacist registered with the Australian Health Prac- titioner Regulation Agency, and (iii) practicing as a com- munity pharmacist.

Participants responded to short-answer and Likert scale multiple-choice questions regarding the safety and efficacy of

D2 antagonists and 5-HT3 antagonists. The pharmacists' level of training and their clinical skills in providing these medi- cations safely were also explored. Results were exported to
Microsoft Excel for analysis. Short answer questions were thematically analysed using Delve 2023. The study was ap- proved by the UniSA Human Research Ethics Committee (ID205449).

Results

A total of 190 participants took part, however only 98 participants practicing in a primary health care setting fully completed the survey. More than half of the participants (53%) were early career pharmacists with less than 5 years of practice experience, whereas 8% reported to have at least 16 or moreyears of practice experience (Table 1).

The majority of participants (*n* = 84, 86%) had supplied an oral D2 antagonist for an OTC N/V request. A significant number (*n* = 96, 98%) perceived oral D2 antagonists to be effective in managing N/V as compared to oral 5-HT3 antagonists. The remaining 2% (*n* = 2) perceived oral D2 antagonists not to be effective compared to 5-HT3 antagonists. When asked how often patients reported experiencing side effects whilst taking oral
D2 antagonists, 5% (*n* = 5) reported 'regularly', 63% (*n* = 62) reported 'occasionally' and the remaining 32% (*n* = 31) reported 'patients had never reported side effects'. In comparison, 3% (*n* = 3) reported patients taking 5-HT3 antagonists would ex- perience side effects 'regularly', 39% (*n* = 38) 'occasionally' and the remaining 58% (*n* = 57) reported 'patients have never re-ported side effects'.

There were 87 participants (89%) who believed that oral 5-
HT3 antagonists should be down-scheduled to S3 while 11%(*n* = 11) said they should not. When asked if pharmacists could
safely supply oral 5-HT3 antagonists as OTC, 92% believed they could whilst 8% believed they could ommended to prevent patient harm.

Demographics

Postcode
n = 98

not.

Discussion

A significant number of community pharmacists (n = 87, 89%) supported the down-scheduling of oral 5-HT3 antagonists toS3 for acute treatment of N/V (Table 2). This aligns with the evidence which suggests that pharmacist-led anti-emetic in- terventions are safe and effective.[5]

Participants (*n* = 83, 85%) believed that oral 5-HT3 antagonists cause less harm than oral D2 antagonists (Supplementary material S2). Prior literature has suggested that both classes of anti-emetics are equally tolerable.[6] Despite acceptable tolerability, D2 antagonists can cause extrapyramidal side effects[7] and 5-HT3 antagonists may harm the foetus during first trimester of pregnancy.[8] Pharmacists did show concern regarding 5-HT3 antago-
nists and pregnancy, mentioning "pregnancy is an area that should be overseen by a medical practitioner" and that down-scheduling could "decrease general practitioner in- volvement in pregnancy-induced nausea". Concerns re- garding constipation were raised with 5-HT3 antagonists, as one pharmacist mentioned "side effects such as constipation are common" and another mentioned there would be an "increased need for medications to treat constipation". Pharmacists also raised concerns about QTc prolongation
with 5-HT3 antagonists. This was part of the reason why the TGA decided to not down-schedule ondansetron in 2020.[4] While 5-HT3 antagonists have been reported to cause QTc prolongation, this adverse effect is mainly associated with high dose and intravenous administration in patients with risk factors for Torsades de Pointes.[9] In a primary health care setting, patients would be treated with an orally ad- ministered 5-HT3 antagonist. Furthermore, when used short term in patients without such risk factors, there is minimal risk for QTc prolongation.[9] Appropriate counselling of such risks when supplying 5-HT3 antagonists is therefore rec-

Pharmacists were most concerned about masking theunderlying cause of N/V (Supplementary material S3).

New South Wales	18 (18.4)
Australian Capital Territory	12 (12.2)
Victoria	9 (9.2)
Queensland	19 (19.4)
South Australia	24 (24.5)
Western Australia	15 (15.3)
Tasmania	1 (1.0)
Northern Territory	0 (0)
Practice experience	
1 to 5 years	52 (53.1)
6 to 10 years	24 (24.5)
11 to 15 years	14 (14.3)
16 to 20 years	2 (2.0)
More than 20 years	6 (6.1)

Several pharmacists (*n* = 21, 21%) said that down-scheduling could lead to patients not seeking appropriate medical advice. If oral 5-HT3 antagonists were to be down- scheduled, guidelines for pharmacists to diagnose the specific type of N/V and supply the medication must be developed and implemented. A perceived lack of training (*n* = 63, 63%) was the most commonly reported barrier to down-scheduling of 5-HT3 antagonists (Supplementary material S3), reinforcing the need for guidelines and ap- propriate training to ensure safe supply of 5-HT3 antago- nists as OTC medicine. Training may include assessment of skills related to diagnosis and treatment of N/V, profes- sional collaboration with medical practitioners through partnered prescribing. Moreover, development and

Table 2. Pharmacists' Responses.Questions and Responses

	Total (%) *n = 98*
1. Have you ever supplied an oral D2 antagonist for an OTC nausea and vomiting request?	
Yes	84 (85.7%)
No	14 (14.3%)
2. In your experience practicing in your role, how effective do you perceive oral D2 antagonists to be at treating nausea and vomiting as opposed to 5-HT3 antagonists?	
Extremely effective	0 (.0%)
Very effective	11 (11.2%)
Effective	29 (29.6%)
Somewhat effective	56 (57.1%)
Not effective at all	2 (2.0%)
3. In your experience, how often do patients report experiencing unwanted/harmful side effects whilst taking oral D2 antagonists?	
Regularly	5 (5.1%)
Sometimes	62 (63.3%)
Never	31 (31.6%)
4. Do you believe that oral 5-HT3 antagonists should be made available as a schedule 3 medicine?	
Yes	87 (88.8%)
No	11 (11.2%)
5. How likely would you be to supply an oral 5-HT3 antagonist as a schedule 3 medication for the treatment of acute nausea and vomiting over the counter?	
Regularly	53 (54.1%)
Sometimes	40 (40.8%)
Never	5 (5.1%)
6. In your experience practicing in your role, how effective are oral 5-HT3 antagonists at treating nausea and vomiting?	
Extremely effective	28 (28.6%)
Very effective	54 (55.1%)
Effective	14 (14.3%)
Somewhat effective	1 (1.0%)
Not effective at all	0 (.0%)

7.

8. Comparing the oral 5-HT3 and D2 antagonists currently available in Australia, do you perceive 5-HT3 antagonists to cause less harm than D2 antagonists?
   Yes 83 (84.7%)
   No 15 (15.3%)
9. Have you received any formal/semi-formal post-graduate training regarding the use of 5-HT3 antagonists? (For example, CPD, conferences, engaged with other educational materials)
   Yes 36 (36.7%)
   No 62 (63.3%)
10. Do you believe pharmacists could safely supply 5-HT3 antagonists over the counter?
   Yes 90 (91.8%)
   No 8 (8.2%)

completion of continuing education modules that include real-life case studies would assist pharmacists to analyse cases and determine treatment approaches.

There are several limitations to consider. Firstly, this study included 98 participants who were mostly recruited from social media and the majority (n = 52, 53%) were early career pharmacists. This sample of pharmacists may not represent the diversity of opinions of all pharmacists as there are an estimated 21,000 community pharmacists in Australia. The study had a high exclusion rate as 48% (n = 60) of participants did not complete the entire survey. A pilot study of pharmacist-diagnosed N/V and supply of 5-HT3 antagonists as S2 medicines is required to determine safety of down- scheduling and provision of these medicines by pharmacists before another submission to amend the scheduling of 5-HT3antagonists is made in Australia.

Conclusion

This is the first study to investigate pharmacists' perceptions upon the down-scheduling of 5-HT3 antagonists in Australia. Pharmacists perceive 5-HT3 antagonists as safe, effective and superior compared to D2 antagonists; supporting the down- scheduling of oral 5-HT3 antagonists to S3 medications to treat acute nausea and vomiting in the community.

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Author Contributions

AH formulated the survey questions, promoted the survey, data interpretation and wrote the article; JLJ designed the study, formu- lated the survey questions, promoted the survey, data interpretation and wrote the article, WCC designed the study, formulated the survey questions, promoted the survey, data interpretation and wrote the article.

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Data Access Statement

The data are stored as de-identified, password protected files within the University of South Australia: Clinical and Health Sciences networkdrive.

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Data Availability Statement

The data will be shared on reasonable request with the correspondingauthor

Supplemental Material

Supplemental material for this article is available online.

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