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ORIGINAL RESEARCH

Perspectives on Using Fast-Dissolving Paracetamol for Mild-to-Moderate Pain Management in Elderly or Diabetic Patients with Delayed Gastric Emptying Rates: An Exploratory Study

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Purpose: Pain is considered a major clinical and socioeconomic problem worldwide. Delayed gastric emptying rates allegedly influence the suitability of pain-relief medications in patient populations such as the elderly and individuals with diabetes. Faster pain relief was reportedly achieved by using a fast-dissolving paracetamol (FD-APAP) formulation. This study aims to gain insights to healthcare professionals' (HCPs) perspectives towards using FD-APAP in addressing barriers of pain relief in patient populations susceptible to delayed gastric emptying rates.

Patients and Methods: A two-step modified Delphi consensus study was conducted among a panel of 10 general practitioners (GPs) and four endocrinologists. The first step comprises in-depth discussions around evidence relevant to FD-APAP for pain management in patient populations with delayed gastric emptying rates (elderly/diabetics). The second step (a survey) was based on the summarized input from the first step. Consensus was accepted upon ≥70% agreement. Perspectives on pain management by FD-APAP for elderly patients were explored among GPs, while those for diabetic patients were explored among GPs and endocrinologists.

Results: Consensus was achieved, whereby all panel members found FD-APAP to be favorable and relevant for pain management in the elderly and the diabetic patient populations. GPs additionally raised the consensus on the importance of considering comorbidities associated with diabetes while having minimal complications during pain management.

Conclusion: The panel found the faster disintegration and absorption of FD-APAP relevant and useful for patients with delayed gastric emptying, wherein, pain in the elderly and those with diabetes could be treated effectively with limited side-effects.

Keywords: fast-dissolving paracetamol, consensus, delayed gastric emptying, pain relief, elderly, diabetics

Introduction

Pain is considered a major clinical, social, and economic problem in communities around the world.[1] Approximately 20% of the adults suffer from pain globally and 10% are newly diagnosed with chronic pain each year.[2] Pain management could involve pharmacological therapeutics (eg, oral or topical analgesics, opioids, tricyclic antidepressants [TCAs] for neuropathic pain) as well non-pharmacological therapeutics (eg, physical exercise, lifestyle management, and behavioral therapy).[3,4]

Pharmacologic therapeutics such as non-prescription oral analgesics are available over the counter for patients to self-manage their pain symptoms.[5] Paracetamol (APAP) and nonsteroidal anti-inflammatory drugs (NSAIDs) have been considered as the front-line pharmacologic agents for the symptomatic treatment of mild-to-moderate pain.[6] The

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suitability of these medications depends on the type of pain and patient risk factors (eg, age, presence of comorbidities related to metabolism, gastrointestinal [GI] or cardiovascular).[7]

Paracetamol is rapidly absorbed from the small intestine,[8] while absorption from the stomach is negligible. Thus, the absorption rate of oral APAP from the GI tract is directly dependent upon gastric emptying rate whereby reduced gastric emptying rates may result in delayed absorption of APAP into the system.[9,10] Drug metabolism in patients of advancing age or with diabetes have been associated with physiological changes in gastric emptying.[11–13] Studies had reported impaired APAP absorption in aging patients, wherein aging was found to be associated with modest slowing of gastric emptying.[14,15] The effects of aging on gastric emptying are of relevance to the absorption kinetics of oral medications and post-meal glucose levels which are critical in those with diabetes.[14] These events in turn could impede effective pain relief in the elderly or diabetics.

Pain relief may be achieved by faster disintegration and absorption[16,17] which could potentially aid population with slow gastric emptying rates, eg, the elderly or diabetic individuals. The development of a fast-dissolving APAP (FD-APAP) formulation was reported to increase the gastric emptying rate leading to faster absorption of APAP in the GI tract.[16,18,19] The FD-APAP formulation contains a disintegrant system of alginic acid, calcium carbonate, and crospovidone which increases the rate of tablet dissolution.[16,18,19] Alginic acid and calcium-carbonate result in rapid disintegration of APAP into a uniform suspension of fine APAP particles, while crospovidone promotes the dissolution in water. This increases the surface area of APAP leading to early absorption of the active ingredient by the body than standard APAP, thereby improving the bioavailability for pain management by paracetamol.[16,19]

Herein, this study aimed to qualitatively explore and understand the perspectives of a panel of healthcare professionals comprising general practitioners (GPs) and endocrinologists towards innovative treatment options like FD-APAP in addressing barriers of pain relief in patient populations of the elderly or diabetics who are susceptible to delayed gastric emptying through evidence-based sharing.

Materials and Methods

Study Design and Setting

This study was conducted in a two-phase modified Delphi method of consensus among a panel of ten general practitioners (GPs) and four endocrinologists across Australia, Colombia, India, Malaysia, Saudi Arabia, and Sweden (Figure 1). The Delphi method[20,21] comprises of a two-step system. The study participants were anonymized and blinded towards each other and the study's sponsor. All responses collected from the study participants were deidentified.

In the first step of the Delphi methodology, in-depth interviews were conducted with each panel member with discussions around pre-shared evidence-based materials; in the second step, summary of the key findings from the interviews were shared with the respondents, and a consensus was obtained. A consensus was obtained based on a Likert Scale of 1–5, with 1 being "strongly disagree" and 5 being "strongly agree". Consensus was established when there was ≥70% unanimity (agreement or disagreement) within the panel, ie, at least seven GPs and three endocrinologists).[21]

This study involved one-on-one 60-minute virtual interviews with GPs and endocrinologists at two different stages, wherein stage one interviews were conducted between March and May 2020 among a panel of 10 GPs from Australia, Colombia, Saudi Arabia, Malaysia, and Sweden (n=2 from each country), while stage two interviews were conducted between October and November 2020 among a panel of four endocrinologists from Australia (n=1), India (n=1), and Malaysia (n=2).

The suitability of using FD-APAP for pain management among elderly patients was discussed with the GPs, while the insights of managing pain with FD-APAP in diabetic patients were discussed with both GPs and endocrinologists. These insights were obtained after the respondents review the evidence shared with during the interviews. Each respondent would rate the evidence based on its credibility, impact, and clarity. The perspectives from the GPs and endocrinologists were respectively consolidated and shared, and the consensus was correspondingly obtained during the second round.[21]

Panel Recruitment

The GPs and endocrinologists were invited to participate in the study if they have ≥10 years of clinical experience and ≥60% of their time spent in direct patient care. The additional inclusion criteria of GPs were if they had ≥60 patients/

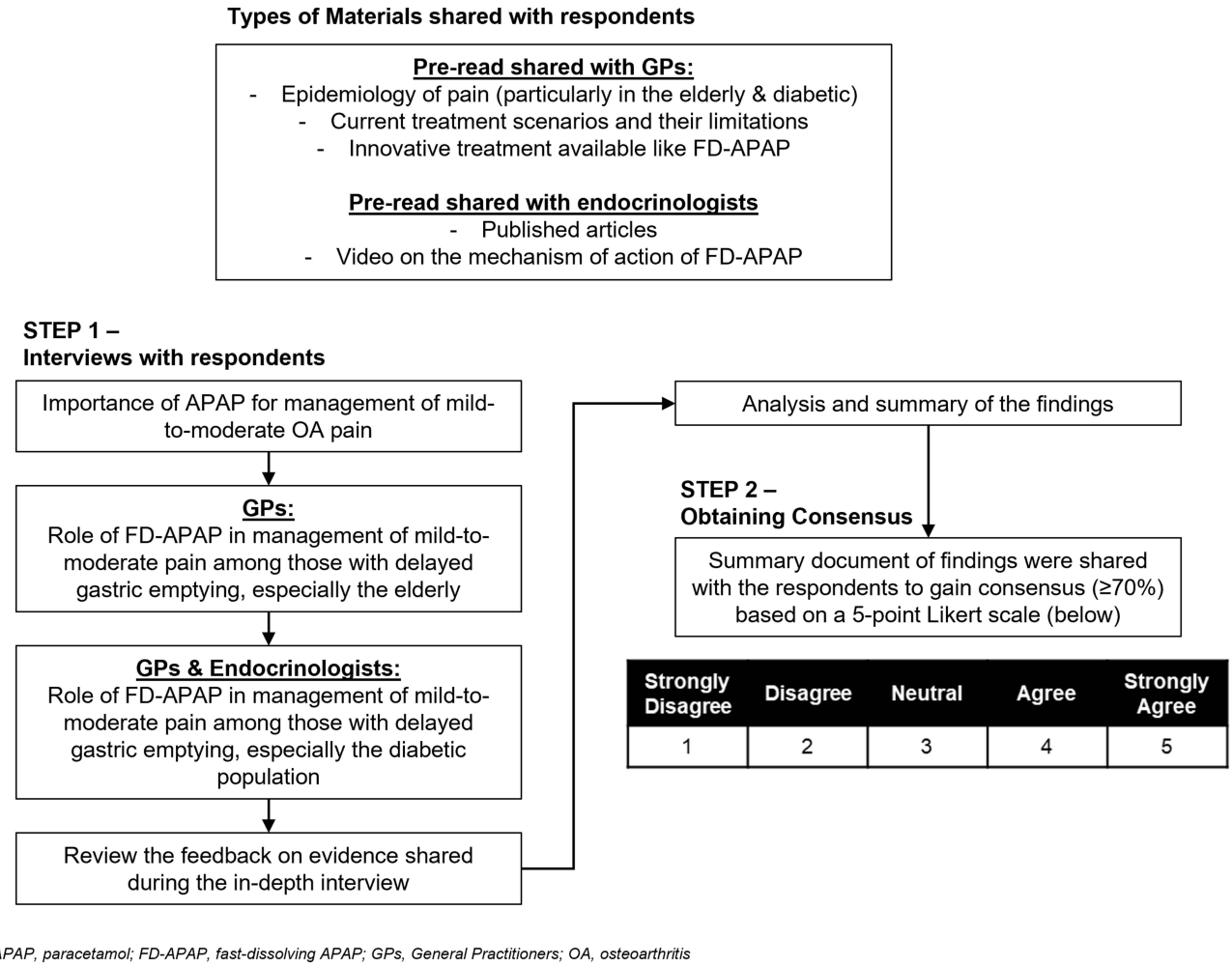


Figure 1 Schematic of the discussion flow and review of evidence.

month suffering from mild-to-moderate pain, ≥30% of the patients with mild-to-moderate pain were 60 years or older, and if they had treated ≥30% of the patients with mild-to-moderate pain with APAP, whereas the additional inclusion criteria of endocrinologists were if they had seen ≥30 diabetic patients/month who suffered from mild-to-moderate pain and had treated ≥30% of the patients with mild-to-moderate pain with APAP.

Materials Shared with Respondents

Both GPs and endocrinologists were provided with pre-read summarizing evidence that have been deidentified, wherein any identifying information of the manufacturer of the drug FD-APAP have been removed prior to sharing with the panel.

The anonymized pre-read evidence included topics on

- Pain epidemiology,[1,22,23] especially in the elderly and diabetic.[24–28]
- Current treatment scenarios and limitations.[29–37]
- Evidence on the relevance and benefits of innovative treatments like FD-APAP (Panadol with OPTIZORB®) in the targeted patient population subsections[16,17] were additionally shared with GPs, while a video on FD-APAP's mechanism of action was shared with the endocrinologists.

The following anonymized evidence were shared with GPs and endocrinologists during the interview:

GPs

- Data on FD-APAP versus standard APAP pertaining to faster pain relief[17] (Unpublished data from the study sponsor).
- GI changes associated with aging and/or diabetes.[38–42]
- Relevance and applications of innovative treatments like GI suitability, disintegration, absorption and bioavailability in patient population with slow gastric emptying compared to standard APAP (Unpublished data from the study sponsor).[9,16,43–50]
- Evidence specific to the needs of diabetics and the impact on their GI needs, and relevance of FD-APAP compared to standard APAP (Unpublished data from the study sponsor).[36,37,51]

Endocrinologists

- FD-APAP pharmacokinetics, particularly its faster disintegration, absorption, bioavailability, and ability to provide faster pain relief than standard APAP.[16,17]
- The impact of diabetes on the GI tract and its influence on gastric emptying.[36,37,51]
- Patient variability between FD-APAP and standard APAP (Unpublished data from the study sponsor).
- Gastric dysmotility in diabetic patients (Unpublished data from the study sponsor).

Results

Characteristics of the GPs and Endocrinologists

The GPs had clinical experience between 10 and 44 years in private (n=9) or public (n=1) clinics and spent ≥65% of their time in direct patient care. The GPs saw 75–2000 patients/month and 20–93% of these patients suffered from mild-to-moderate pain. About 30–90% of GPs' patients suffering from mild-to-moderate pain were elderly. Among them, 5–70% had an underlying diabetes condition. For all the patients complaining of pain, 30–100% had been treated with APAP (Table 1).

The endocrinologists had clinical practice experience between 10 and 22 years in private (n=3) or public (n=1) hospitals and spent ≥95% of their time in direct patient care. These endocrinologists saw 40–250 diabetic patients/month and 10–50% of their patients suffered from mild-to-moderate pain. Among all endocrinologists' patients complaining of pain, 30–80% were treated with APAP (Table 2).

Table 1 Characteristics of General Practitioners (GPs) and Endocrinologists

General Practitioners (GPs)										
	Australia (n=2)		**Colombia (n=2)**		**Malaysia (n=2)**		**Saudi Arabia (n=2)**		**Sweden (n=2)**	
Years of practice	44	22	25	10	25	15	11	10	20	17
Practice setting (Clinic)	Private	Private	Private	Public	Private	Private	Private	Private	Private	Private
Proportion of time in direct patient care (%)	90	95	100	68	100	100	100	100	100	99
Number of patients seen in a month	1000	600	150	75	2000	1000	800	800	150	300
Number of patients suffering from mild-to-moderate pain, such as headaches	200	120	130	65–70	400	200	560	640	50	200
Proportion of patients of the following demographics (%)										
Aged ≥60 years	50	70	60	70	30	30	60–70	50	90	65
Aged ≥60 years with diabetes	5	20	5	18	15	10	60–70	40	10	15
Treated with paracetamol	100	50	40	60–70	30	30	80–90	60–70	50	100

Table 2 Characteristics of Endocrinologists

Endocrinologists				
	Australia (n=1)	**India (n=1)**	**Malaysia (n=2)**	
Years of practice	22	20	20	10
Practice setting	Private clinic	Private hospital	Private hospital	Public/government hospital
Proportion of time in direct patient care (%)	95	95	100	100
Number of diabetic patients seen in a month	320	500	300	400
Number of patients suffering from mild-to-moderate pain, such as headaches	60	250	100	40
Proportion of patients treated with paracetamol (%)	80	70	>30	50

GPs' Perspectives

Standard APAP versus FD-APAP for Pain Management

Most GPs deemed the evidence regarding FD-APAP's rapid onset of action, and its advantages compared to standard APAP as good/excellent in terms of credibility (n=7), clarity (n=6), and impact (n=9) (Table 3). The evidence on relieving pain in 15 minutes had appealed to the GPs across the countries. A Colombian GP cited

Table 3 General Practitioners' (GPs) (n=10) Rating on Credibility, Clarity, and Impact of Evidence in the Study, the Rating Scale Used Was 1 to 5, with 1= Poor and 5= Excellent

	Australia (n=2)		**Malaysia (n=2)**		**Saudi Arabia (n=2)**		**Colombia (n=2)**		**Sweden (n=2)**	
Physicians rating on evidence about FD-APAP's rapid onset of action and its advantages compared to standard APAP.										
Credibility	Neutral	Fair	Good	Good	Excellent	Good	Good	Good	Fair	Excellent
Clarity	Fair	Good	Excellent	Fair	Fair	Excellent	Excellent	Excellent	Fair	Excellent
Impact	Good	Good	Good	Good	Excellent	Excellent	Excellent	Good	Fair	Excellent
Physicians rating on evidence shared to demonstrate that "FD-APAP dissolves/disintegrates faster."										
Credibility	Excellent	Good	Excellent	Good	Excellent	Excellent	Excellent	Excellent	Good	Excellent
Clarity	Good	Good	Excellent	Excellent	Fair	Excellent	Excellent	Good	Good	Excellent
Impact	Good	Fair	Excellent	Good	Excellent	Excellent	Excellent	Excellent	Fair	Excellent
Physicians rating on evidence shared to demonstrate that "FD-APAP has faster absorption."										
Credibility	Excellent	Good	Good	Good	Excellent	Excellent	Excellent	Excellent	Good	Excellent
Clarity	Good	Good	Excellent	Excellent	Good	Excellent	Excellent	Excellent	Good	Excellent
Impact	Excellent	Good	Excellent	Good	Excellent	Excellent	Excellent	Excellent	Fair	Excellent
Physicians rating on evidence shared to demonstrate that "FD-APAP has better bioavailability."										
Credibility	Excellent	Good	Good	Good	Excellent	Excellent	Excellent	Excellent	Fair	Excellent
Clarity	Excellent	Good	Excellent	Excellent	Good	Excellent	Excellent	Excellent	Good	Excellent
Impact	Excellent	Good	Excellent	Good	Excellent	Excellent	Excellent	Excellent	Good	Excellent
Physicians rating on evidence about FD-APAP's relevance among the diabetic population										
Credibility	Fair	Fair	Good	Good	Excellent	Excellent	Excellent	Excellent	Neutral	Excellent
Clarity	Neutral	Neutral	Excellent	Good	Good	Excellent	Good	Excellent	Good	Excellent
Impact	Neutral	Good	Excellent	Excellent	Good	Fair	Excellent	Excellent	Neutral	Excellent

> … a molecule that allows better absorption and a quick perceptible relief of pain … that only 15 minutes after ingesting the pill orally … I find that very attractive.

An Australian GP mentioned "it will improve compliance because it will work faster and be another arrow in the quiver for controlling pain - so people will be more open to taking it.", and a GP in Malaysia shared "the faster we can relieve the pain, the better it is."

Comparatively, the GPs who rated the same evidence as fair/neutral (credibility: n=3; clarity: n=4; impact: n=1) cited the need for i) more details (eg, study period, selection criteria, pain measure assessment, etc), ii) more independent studies on FD-APAP besides those done by the manufacturer, and iii) studies in generalizable populations to improve the credibility. An Australian GP said, "would have liked to see … when they were conducted … the number of people in the studies, the entrance criteria and how they assessed the pain." A Colombian GP shared

> it would be necessary that other types of studies from other scientific communities…which could be vouching for these results … to give … absolute and impartial credibility.

A GP in Sweden stated, "The population is dental pain population, I would like to have other population that are more like the patients … at my clinic."

Relevance and GI Suitability of FD-APAP Vs Standard APAP for Pain Management in the Elderly Population

There was a shared perspective that the elderly had disordered gastric emptying. A GP from Australia said, "(the elderly) have delayed gastric acting time, lesser pH, changes in gastric mucosa. You can't give strong painkillers to them."

All evidence regarding innovative treatment options such as FD-APAP was considered credible, impactful, and clear when considering its ability to address needs for those with slower gastric emptying rates or other GI changes. A Colombian GP said,

> We want to assess pain management of the elderly patient, products that give…a real effectiveness in pain management and can provide us with real absorption that allow the elderly patient, to manage pain properly.

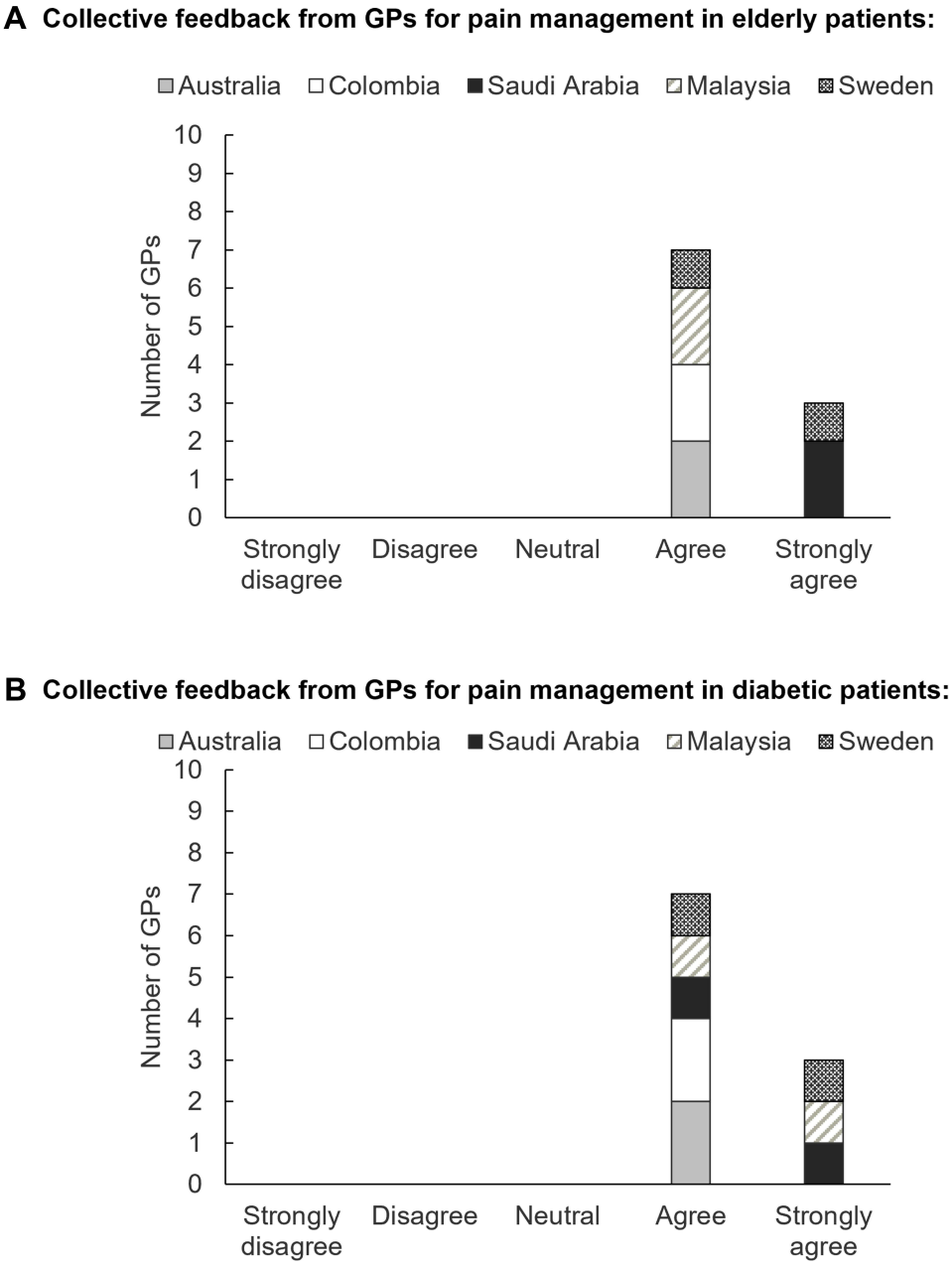
On the other hand, the GPs who rated fair/neutral (n=3) perceived the lack of clarity on the mechanism of action. A GP from Saudi Arabia shared "The study is easy to understand, but the clarity of the reasons behind the mechanism isn't clear".

All GPs agreed/strongly agreed with their peers that i) the evidence shared on FD-APAP for pain management was credible, clear, and impactful, particularly when considering its ability to address needs such as slower gastric emptying rates or other GI changes and ii) considered FD-APAP to be a better alternative to NSAIDs, since NSAIDs were much more damaging towards the GI system in the elderly population, which was a key consideration when prescribing treatment for mild-to-moderate pain (Figure 2A).

Relevance and GI Suitability of FD-APAP Vs Standard APAP for the Diabetic Population

In addition to the elderly population, the GPs were concerned about the under-treatment of pain among the diabetic population and the need for a drug which effectively addressed the pain with minimal GI impact and with considerations for diabetes-associated comorbidities. A GP from Malaysia shared "Instead of giving more potent painkillers (NSAIDs or Cox-2 inhibitors) for nerve pain, which have GI side-effects, it will be good to have another option", while a GP from Australia stated being "more worried about anti-inflammatories staying in the gut for longer, causing things like ulcers or bleeding."

The evidence on FD-APAP's relevance in the diabetic population was rated good/excellent by the GPs in terms of credibility (n=8), clarity (n=8), and impact (n=7) (Table 3), based on the reasons that the evidence had demonstrated the importance of this innovative technology, and its relevance in the diabetic population with regards to slower gastric emptying rates. A Malaysian GP said, "Compared to normal (APAP), absorption of (FD-APAP) is faster. Figures are credible." A GP from Colombia also shared, "it is a study…which shows the power of advanced (ibuprofen) with (FD-APAP) over standard (APAP), which I think is striking and significant …."



APAP, paracetamol; FD-APAP, fast-dissolving APAP; GI, gastrointestinal; GPs, General Practitioners

Figure 2 Consensus among GPs pertaining to the relevance of FD-APAP for pain management in the elderly and diabetic patient populations based on the feedback of their peers. Collective feedback from GPs for pain management in (**A**) elderly patients towards FD-APAP evidence credibility and impact, suitability of FD-APAP as a better alternative to NSAIDs, and key advantages of FD-APAP pertained to the faster disintegration and absorption of FD-APAP technology (OPTIZORB®) and (**B**) diabetic patients in terms of the relevance of FD-APAP and being able to address the need in patients with slower gastric emptying rate or GI changes, and the need to consider the complications or comorbidities associated with diabetes, while at the same time having minimal complications.

The GPs from Australia, Saudi Arabia, and Sweden had rated fair/neutral in terms of the credibility (n=3), clarity (n=2), and impact (n=3) of the evidence pertaining to FD-APAP's relevance in the diabetic population (Table 3). While the evidence was convincing for the diabetic population, they were still inclined to prescribe FD-APAP to the elderly without comorbidities of diabetes. An Australian GP mentioned, "I'd rather just consider it more for the elderly rather than diabetics in particular because I think it's hard to just think about that group." There was a desire to see more data based on comparative studies in diabetics versus non-diabetics with associated comorbidities/complications, or elderly non-diabetic individuals versus elderly diabetic individuals and their gastric emptying rates.

An Australian GP shared, "… interesting to see the data for elderly non-diabetics versus elderly diabetics and their gastric emptying rates." Additionally, respondents also wanted to learn more about the mechanism of action. The GP from Saudi Arabia said, "The study is easy to understand, but the clarity of the reasons behind the mechanism isn't clear."

All GPs agreed/strongly agreed with the feedback from their peers that i) FD-APAP is considered favorable and relevant for pain management in diabetic patients and believed in its ability to address the need of slower gastric emptying rates or other gastrointestinal changes was important, and ii) there were greater underlying needs in these patients to manage complications or comorbidities associated with diabetes, while having minimal GI complications when managing pain (Figure 2B).

Endocrinologist's Perspectives

Pain Management in the Diabetic Population

Overall, endocrinologists expressed concerns over the sensitivity of the GI tract when managing mild-to-moderate pain and it corroborated the evidence shared on the impact of GI changes in the diabetic population. An endocrinologist from Australia stated,

> most of us think about impaired gastric motility more of the patients with Type I diabetes. Type II patients they've got so many intercurrent problems that … we're not really alert to it … maybe these patients really aren't absorbing it.

Endocrinologists also highlighted therapeutic options such as opioids and NSAIDs provided limited support to diabetic patients, particularly those with gastritis or other GI complications, given the possibility of delay gastric emptying rates. An endocrinologist from India shared

> the choices of treatment that we can offer are very limited when you have gastritis or reflux disease, so I cannot use NSAIDs and Cox-2 inhibitors. Constipation is a huge problem any opioid sort of medicines I cannot use ….

Role of FD-APAP in Management of Mild-to-Moderate Pain Among the Diabetic Population

Majority of the endocrinologists regarded the evidence pertaining to the faster disintegration, faster absorption rate, and better bioavailability (in the first 30 minutes) of FD-APAP as credible, clear, and impactful (Table 4).

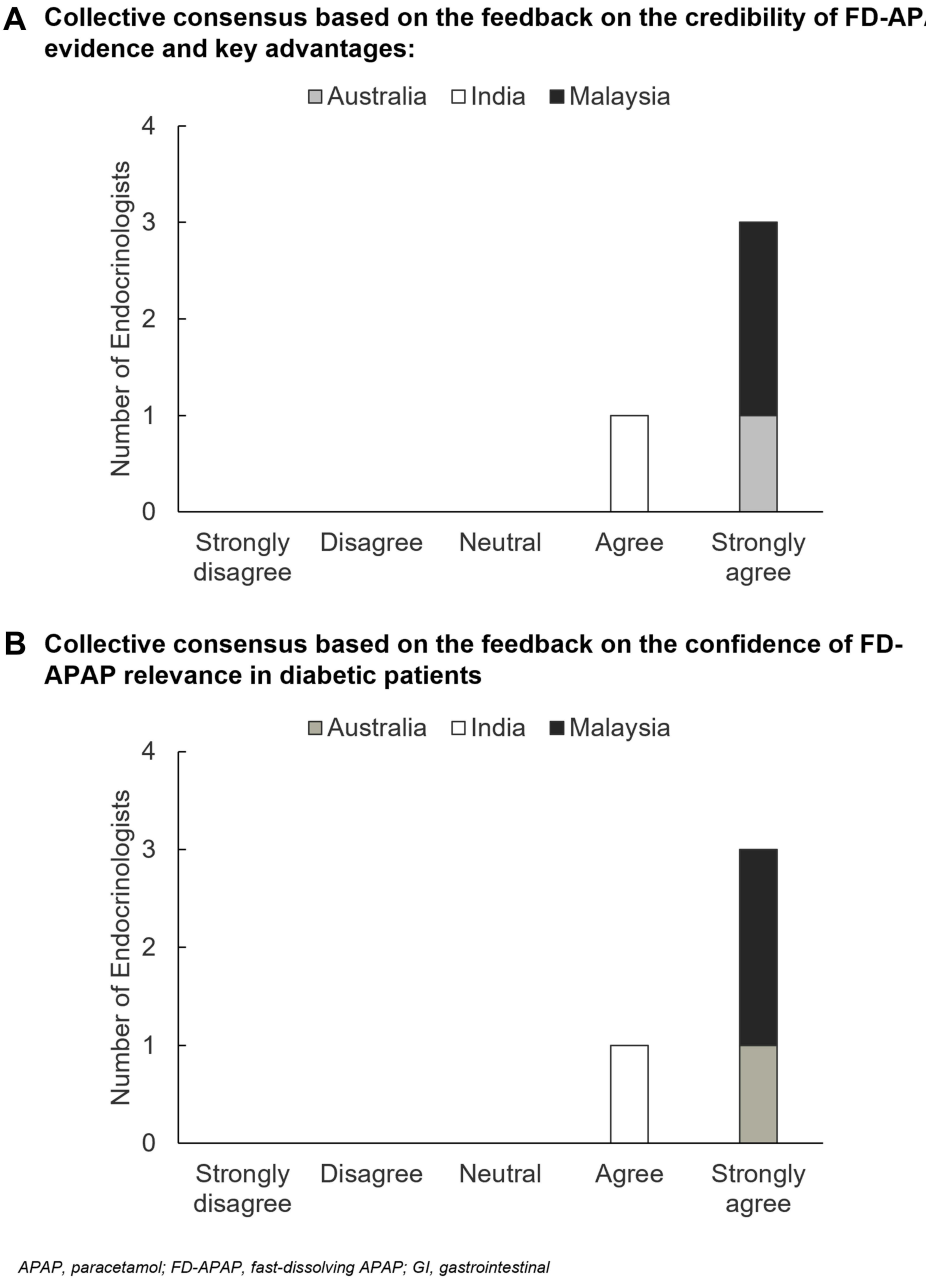
Three of four endocrinologists were confident FD-APAP would be able to address the needs of diabetic patients (Table 4), based on the low variability and faster absorption which might provide faster pain relief. A Malaysian endocrinologist reported that the evidence was "Quite impactful because can see the variability in the standard (APAP) is

Table 4 Endocrinologists' Rating on the Credibility, Clarity and Impact of the Evidence Shared for the Following Statements

	Australia (n=1)	India (n=1)	Malaysia (n=2)	
Physicians rating on evidence about FD-APAP's rapid onset of action and its advantages compared to standard APAP.				
Credibility	Good	Excellent	Neutral	Good
Clarity	Good	Excellent	Good	Good
Impact	Good	Excellent	Good	Good
Physicians rating on evidence shared to demonstrate that "FD-APAP dissolves/disintegrates faster."				
Credibility	Good	Excellent	Good	Good
Clarity	Good	Excellent	Good	Neutral
Impact	Good	Excellent	Good	Good
Physicians rating on evidence shared to demonstrate that "FD-APAP has faster absorption."				
Credibility	Good	Excellent	Good	Good
Clarity	Good	Excellent	Good	Good
Impact	Good	Excellent	Good	Good

double that of FD-APAP." On the contrary, another Malaysian endocrinologist was neutral (Table 4), citing a need for future studies with a larger sample size, "need a larger sample size and bigger population taking into account the general population."

Consensus was achieved among four endocrinologists who considered the evidence shared on FD-APAP to be credible, clear, and impactful, given its faster disintegration and absorption (Figure 3A). All endocrinologists agreed/strongly agreed on the relevance of FD-APAP for mild-to-moderate pain management among diabetic patients and being able to address the unmet need of slower gastric emptying rates or other GI changes (Figure 3B).



APAP, paracetamol; FD-APAP, fast-dissolving APAP; GI, gastrointestinal

Figure 3 Consensus among endocrinologists pertaining to the relevance of FD-APAP for mild-to-moderate pain management in the diabetic patient population based on the feedback of their peers. Collective consensus on (**A**) the evidence on FD-APAP relevance in diabetic population is credible, believable, and impactful; key advantages of FD-APAP pertained to the faster disintegration and absorption of FD-APAP technology (OPTIZORB®) and (**B**) There is good confidence around the relevance of FD-APAP for mild-to-moderate pain management, and being able to address the slower gastric emptying rates or GI changes in diabetic patients.

Discussion

Pain is considered as one of the most common problems globally. Despite the availability of treatment options for pain management, there are limitations in management of individuals with delayed gastric emptying rates, including but not limited, to the elderly and diabetic population.[52] Herein, the panel of GPs and endocrinologists found the evidence demonstrating FD-APAP's rapid onset of pain relief, disintegration, absorption, and bioavailability in the elderly or diabetics to be relevant for managing pain among these patient populations who are susceptible to delayed gastric emptying. The insights from this study suggest the plausible inclusion of FD-APAP to list of suitable therapeutics for managing pain in patients of older age or diabetics with thorough appraisal of each patient's circumstances.

Both APAP and NSAIDs are considered as first-line pharmacologic agents for self-managing pain.[53–55] However, NSAIDs are typically avoided due to possible GI, renal and cardiovascular-related adverse effects in the elderly and patients with comorbidities (ie, diabetics).[32,56] Paracetamol remains a first-choice analgesic for most adults to manage mild-to-moderate pain, wherein the recommended dose of ≤4g/day was typically well-tolerated in healthy adults.[43,57] Delayed gastric emptying due to aging- or comorbidities-associated physiological changes has been reported to influence the pharmacokinetics and pharmacodynamics of drugs.[10,12,13] However, there is a paucity of large-scale randomized clinical trials demonstrating the efficacy or dosing suitability of APAP among patients advancing age or comorbidities, thereby suggesting a potential need to rely on clinician expertise and observations of the real-world clinical settings to understand the relevance of an innovative formulation for managing pain.[57–59]

Based on the evidence shared, FD-APAP was shown to have better GI suitability, disintegration and absorption, and was able to provide faster pain relief compared to standard APAP with no differences in the side-effects.[9,16,43,44] Alternatively, opioid analgesics have also become a more prevalent treatment for chronic pain.[60,61] However, opioid-related management of chronic pain often leads to increasing doses,[62] which has been associated with higher rates of opioid-related adverse events like drug overdose and death.[63] In Australia, inappropriate prescription of strong opioids was more prevalent in older patients.[64] Similarly, a study examining opioid analgesics in patients with diabetes reported that opioid therapy negatively affected the patients' outcomes.[65] As FD-APAP has been reported to effectively manage mild-to-moderate pain,[16,17] it could potentially reduce possible abuse of opiates, especially in patients with chronic pain.

The use of opioid analgesics has also been associated with an increased delay in gastric emptying rate,[66,67] which could cause a higher potency and longer duration of action in the patient populations of older age or with diabetes. In this study, the panel of HCPs perceived FD-APAP to be a better alternative in addressing the needs of patients with slower gastric emptying rates or other GI changes when prescribing treatment for mild-to-moderate pain.

Peripheral diabetic neuropathy (PDN) afflicts more than 50% of the diabetic patients with an estimate of 16–34% presenting to clinical care with painful neuropathic symptoms.[68,69] Clinical guidelines recommend TCAs, gabapentinoids, serotonin-norepinephrine reuptake inhibitors (SNRIs) and/or sodium-channel blocked for managing PDN pain.[70] However, most of these pharmacological agents are prescription-based which could impact the ease of access to pain relief measures for diabetic patients. In this study, both GPs and endocrinologists consented to the relevance of FD-APAP for pain management in diabetic patients and its capacity to address the implications of slower gastric emptying rates or other gastrointestinal changes associated with diabetes. This suggests a possible alternative therapeutic for relieving pain in diabetic patients.

Interestingly, there was limited awareness among the doctors on the gastric emptying rates in the diabetic population, since the primary focus of treatment had always been on comorbidities associated with diabetes. The evidence shared had prompted the doctors to reconsider their pain management approach, having conceded that gastric emptying rates in diabetic patients could impact upon both the effectiveness of their pain treatment and diabetes. There is a need to conduct randomized clinical trials on the use of FD-APAP in the diabetic population to better understand the suitability and dosing recommendations of FD-APAP.

Overall Implications of FD-APAP

The panel of HCPs found the evidence for FD-APAP convincing and considered FD-APAP as a favorable treatment alternative for managing mild-to-moderate pain among patients with slower gastric emptying rates. However, some

physicians had perceived a lack of clarity in the mechanism of action on how the innovative technology of FD-APAP can address delayed gastric emptying during mild-to-moderate pain management among elderly and diabetic population. As such, impactful and resonating communications pertaining to the key advantages and mechanism of action of the innovative technology could potentially boost the awareness and confidence of alternative treatment options among physicians. Notably, there was limited awareness about different kinds of pain and the presence of slow gastric emptying, especially among the diabetic population. This further suggests a need to also educate the doctors about any additional studies done using innovative technologies for pain management in this patient population.

During the interviews, the physicians shared that the key advantages of FD-APAP, ie, its faster onset of action, could increase patient compliance. Factors such as the duration of treatment period, disease symptoms and severity have been associated with therapeutic compliance,[71] wherein the effectiveness of the pain-relief medication, ie, how fast can patients experience relief and for which degree of pain severity, could influence the patients' reception towards a certain treatment option. Furthermore, patients with chronic diseases (eg, hypertension, diabetes) may be less compliant with their treatment.[71] Hence, physicians' awareness of an effective and innovative pain-relief medication like FD-APAP could potentially address the barriers in effectively managing mild-to-moderate pain among their patients with delayed gastric emptying rates such as in the elderly and the diabetic populations.

Study Strengths

This study had included the perspectives of both GPs and endocrinologists with clinical experience in providing pain-relief treatments for patient populations susceptible to delayed gastric emptying rates in the elderly or individuals with diabetes. Furthermore, this study was conducted across six countries to which a consensus was reached and had served as a preliminary insight to the relevance of FD-APAP for pain management in the region. The collective perspectives of both GPs and endocrinologists across the countries provided insights into the potential of FD-APAP in overcoming barriers in managing pain in these patient populations with special consideration of comorbidities in the diabetic patient population needed.

Study Limitations

This study has some limitations. One limitation of this study is that the small sample size of GPs and endocrinologists recruited to the panel and screening criteria and majority of the HCPs in the panel were practicing in a private healthcare setting. As such, the profiles of the HCP panel may not be representative of the clinician population in each country and cannot be generalized. Therefore, future studies with a larger sample size of GPs and endocrinologists from both private and public or government healthcare institutions are warranted. As the materials and evidence shared with the respondents were specific to the elderly and/or those with diabetes, the findings may limit the perspectives of FD-APAP application in the general population. Another limitation of the study is the potential bias associated with the evidence shared with the respondents, whereby majority were from the manufacturer and did not have a large sample size or compared the efficacy of FD-APAP with other types of pain management agents. Further studies conducted independently, with a larger patient sample size inclusive of the general population and comparisons with other pain relief therapeutics are needed.

Conclusion

The findings revealed that the panel of GPs and endocrinologists in this study would prefer a product that provided faster disintegration, absorption, and pain relief with limited side-effects. The panel found FD-APAP to be relevant and useful in patients with delayed gastric emptying, wherein, pain in the elderly and those with diabetes could be managed effectively. However, there is a need for additional studies involving treating pain and managing complications associated with diabetes while concurrently reducing GI issues. Larger, independent studies, including the general population, would increase the credibility and impact of the innovative technology used in treating pain. Furthermore, further studies involving a larger sample size of HCPs in each region are crucial to validate the relevance of FD-APAP as a possible alternative for managing pain among patients with delayed gastric emptying rates.

Data Sharing Statement

The authors confirm that the data supporting the findings of this study are available within the article.

Ethics Approval and Declaration

The study was performed in accordance with the guidelines of the Declaration of Helsinki.[72] No clients or patients were involved in this study. The research team invited experts to participate in the research. All participants voluntarily participated in the research without coercion or reward. Only experts who had provided informed consent to participate in this study were included to complete the Delphi interviews and questionnaire. As agreed with the experts, the data were analyzed anonymously while respecting confidentiality and privacy and has not been shared with other parties. The content of the interview questions and questionnaire do not concern medical scientific research, and there is no infringement of the participant's physical and/or psychological integrity of the subject. This research sought to understand the perspectives of healthcare professionals towards the use of a fast-dissolving APAP formulation for managing pain relief and was reviewed to be a market research study using survey-based methodology (Global Compliance and Quality, Cerner Enviza, and Oracle Company). The Market Research Codes of conduct states that opinion-based market research studies do not require institutional review board or ethics committee approval. See reference here – British Healthcare Business Intelligence Association (BHBIA) https://www.bhbia.org.uk/ and the European Pharmaceutical Market Research Association (EphMRA) Code of Conduct https://www.ephmra.org/ (section 1.1–1.3).

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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