Diabetes Ther
https://doi.org/10.1007/s13300-024-01568-9

REVIEW

Barriers to the Use of Insulin Therapy and Potential Solutions: A Narrative Review of Perspectives from the Asia–Pacific Region

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Received: December 4, 2023 / Accepted: March 14, 2024

ABSTRACT

The rising prevalence of type 2 diabetes (T2D) is posing major challenges for the healthcare systems of many countries, particularly in the Asia–Pacific Region, in which T2D can present at younger ages and lower body mass index when compared with Western nations. There is an important role for insulin therapy in the management of T2D in these nations, but available evidence suggests that insulin is under-utilized and often delayed, to the detriment of patient prognosis. The authors of this article gathered as an advisory panel (representative of some of the larger Asia–Pacific nations) to identify their local barriers to insulin use in T2D, and to discuss ways in which to address these barriers, with their outputs summarized herein. Many of the key barriers identified are well-documented issues of global significance, including a lack of healthcare resources or of an

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Published online: 16 April 2024

integrated structure, insufficient patient education, and patient misconceptions about insulin therapy. Barriers identified as more innate to Asian countries included local inabilities of patients to afford or gain access to insulin therapy, a tendency for some patients to be more influenced by social media and local traditions than by the medical profession, and a willingness to switch care providers and seek alternative therapies. Strategies to address some of these barriers are provided, with hypothetical illustrative case histories.

Keywords: Asia–Pacific region; Barriers; Insulin therapy; Type 2 diabetes; Patient education

Key Summary Points

The prevalence of type 2 diabetes (T2D) in the Asia–Pacific region is increasing, with the proportion of undiagnosed diabetes in the Western Pacific and South East Asia estimated to be ~50%.

Global barriers to initiation of insulin therapy include poor healthcare infrastructure, insufficient patient education and patient misconceptions, and socioeconomic factors including access to and cost of medication.

Barriers specific to the Asia–Pacific region include skepticism about Western medicine, and greater influence of parochial traditions, peers, and unverified social media reports.

Strategies to address these barriers include education and support of both physicians and patients, raising awareness of diabetes and the benefits of insulin, improving the diversity of HCPs and clinical care teams, and improving access to new-generation insulin analogues and insulin delivery devices

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INTRODUCTION

The worldwide prevalence of diabetes, especially type 2 diabetes (T2D), is increasing, particularly throughout the Asia–Pacific region. In the 38 countries and territories in the Western Pacific Region (as defined by the International Diabetes Federation [IDF]), the prevalence of diabetes is predicted to increase from an estimated 11.9% in 2021 to 14.4% by 2045 [1]. Simultaneously, the prevalence of diabetes in the IDF South East Asia Region is estimated to increase from 8.7% to 11.3% by 2045 [1]. The recent ICMR-INDIAB study reports that there are 101 million individuals with diabetes in India alone [2]. Meanwhile, Pakistan (which is part of the World Health Organization [WHO] Eastern Mediterranean Region, but geographically located in South East Asia) is estimated to be the country with the highest age-adjusted prevalence of diabetes (30.8% in 2021) in the world [1]. Furthermore, as the proportion of undiagnosed diabetes in the Western Pacific and South East Asia regions is estimated to be ~50%, these figures are likely to be under-estimations [1].

The increase in prevalence of T2D across the Asia–Pacific region can be attributed to a multitude of factors, including rapid socio-economic growth and urbanization, which have resulted in changes in lifestyle behaviors, such as the increased consumption of energy-dense food and drinks. In many countries, foods high in sugar, fat, and carbohydrates are popular at social gatherings and religious festivals, and refined staple carbohydrates dominate many diets in the region [3]. Along with reductions in physical activity levels, particularly incidental activity, these dietary changes are contributing

to a rise in the prevalence of overweight and obesity, and the increased risk of T2D.

Regional differences in genetic/ethnic predisposition and susceptibility are also important factors to consider. Compared with other ethnic groups, people from South Asia with T2D tend to develop the disease at a younger age and lower body mass index, and more often manifest with dysglycemia, dyslipidemia, and cardiovascular diseases compared with other ethnic groups [4]. Furthermore, given the heightened risk of premature development of cardiorenal complications in early onset T2D, early and intensive risk factor management is merited [5].

As β-cell dysfunction progresses over time, many people with T2D treated with oral glucose-lowering drugs become unable to achieve or maintain adequate glycemic control and will require insulin therapy [6]. There will also be a minority of people newly diagnosed with T2D who will benefit from early or immediate insulin introduction, such as those with considerable weight loss, ketosis, severe symptoms of hyperglycemia, or steroid-induced hyperglycemia [7, 8]. It is also reported that the T2D subtype of severe insulin-deficient diabetes (SIDD), which often requires earlier initiation of insulin, is very common in South Asia [9–11]. Timely insulin initiation in all patients is necessary to achieve optimal glycemic control and to reduce diabetes-related complications [6].

The earlier onset of T2D, and more rapid decline in β-cell function and insulin secretion, among many populations in the Asia–Pacific region makes insulin one of the major treatment strategies to minimize the burden of diabetes-associated morbidity and mortality. However, despite the proven benefits and existing guidelines for the initiation of insulin therapy [12, 13], insulin utilization and glycemic control remain suboptimal. For example, in Bangladesh, patients were shown to experience delayed diabetes treatment initiation of around 1.79 ± 3.26 years in an analysis of data collected in 2019 [14]. Furthermore, the 11-country First Basal Insulin Evaluation (FINE) Asia study, conducted using people enrolled in a registry between 2006 and 2008, demonstrated that insulin initiation was being delayed by ~9 years among people with inadequately controlled T2D, with HbA1c at time of initiation (10.5%) highest in patients from South East Asia [16, 17]. With regards to glycemic control, poor target achievement has been reported in several countries. The 2019 annual report of the Australian National Diabetes Audit indicated that the mean HbA1c for ~4140 patients with T2D being treated at participating centers was 8.1%, which is above the general target of ≤ 7.0% recommended by the Australian Diabetes Society [18]. In India, the A_1chieve study reported that the mean HbA1c in patients with T2D was 9.2% at the time of insulin initiation, and the prevalence of both macrovascular and microvascular complications was high [15]. In Iran, only 13.2% of patients with diabetes were achieving glycemic targets in 2016 [19].

Data from the WHO also indicate that insulin therapy is significantly underutilized in Asia compared with other regions. While ~75% of people with diabetes live outside of Europe and the United States, the WHO region of the Americas, the WHO European region, and the WHO Western Pacific region account for more than 60% of global revenue generated from insulin products, suggesting that the market in the WHO South-East Asia region is being significantly underserved [20]. The results of a 2021 analysis of insulin imports in 82 countries, including nine in Asia, indicate that there is a gap in many countries in Asia between the assumed insulin "need" and the actual number of patients who receive treatment, with an estimated supply:need ratio of 0.36 in the Asia region in 2018 (interquartile range [IQR]: 0.21–0.99) [21].

This author panel gathered for an advisory board meeting to explore and provide perspectives on the topic of barriers to insulin initiation in the Asia–Pacific region and to discuss potential solutions. This article summarizes the collective opinions of the authors, with hypothetical case studies included to illustrate how barriers to insulin initiation can be overcome. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

What are the Reasons for Delayed Initiation of Insulin Therapy?

Many of the reasons behind the inappropriate delay in the initiation of insulin therapy apply globally and are well documented [22–27] (see Fig. 1 for a summary [22–30]). The reasons are complex, and barriers exist at the patient, physician, and healthcare system level, and often overlap. Many of the negative attitudes among both healthcare professionals (HCPs) and patients with T2D toward starting insulin therapy and gaps in healthcare service provision were highlighted in the global DAWN (2001) and DAWN2 studies (2012), and are still prevalent today [28, 30, 31].

What are the Barriers to Insulin Initiation in the Asia–Pacific Region?

Broadly, the barriers to insulin initiation identified above also apply to the highly heterogenous Asia–Pacific region. However, the prevalence and relevance of each barrier may vary depending on the region or population and their characteristics. Moreover, some barriers may be specific to a region, country, or population within a country, reflecting the unique socioeconomic, cultural, or healthcare system particularities of that region/population. An overview of key WHO Global Health Observatory indicators related to diabetes and diabetes management strategies is provided for a subset of countries within the Asia–Pacific region in Table 1, highlighting the heterogeneity in population and healthcare circumstances across the region [32].

Suboptimal patient understanding and health education is a critical barrier to insulin initiation encountered across all of the Asia–Pacific countries represented by the author panel. Low levels of health education (or health literacy) can drive patient unawareness not only of the benefits of starting insulin therapy but also of diabetes in general and its progression. For example, a study of attitudes and beliefs in 33 Thai patients with T2D found that 18 patients had an incorrect understanding of the causes of T2D and five patients had no understanding of the causes at all [33]. Five patients mentioned that they wanted to control their T2D to avoid having to inject themselves with insulin [33]. Patients may view the use of insulin (and accompanying glucose monitoring) as an inconvenient lifelong sentence of drug dependence and complex regimens, which, if they are unable to master, can

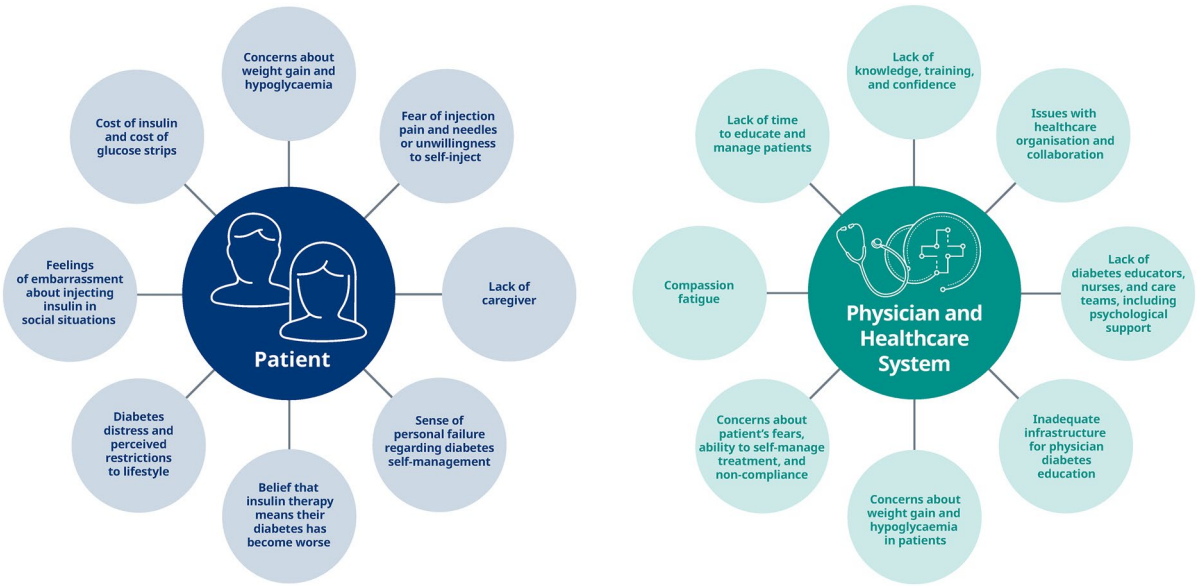

Fig. 1 Common barriers to insulin initiation in people with T2D [22–30]. *T2D* type 2 diabetes

Table 1 Key WHO Global Health Observatory indicators related to diabetes and diabetes management strategies

	AUS	BGD	CHN	IND	IDN	IRN	KOR	MYS	PAK	PHL	THA
Domestic general government health expenditure as percentage of current health expenditure* (%)	76.0	16.9	54.1	34.3	59.4	55.2	61.0	56.2	29.0	39.3	70.4
Out-of-pocket expenditure as percentage of current health expenditure* (%)	13.8	73.0	34.4	49.8	27.5	34.5	29.1	32.1	57.5	44.6	9.0
Prevalence of overweight in adults† (%) [95% CI]	64.5 [60.9–68.0]	20.0 [16.5–23.9]	32.3 [28.7–36.2]	19.7 [16.9–22.8]	28.2 [24.2–32.3]	61.6 [58.0–65.2]	30.3 [27.2–33.4]	42.5 [38.1–47.0]	28.4 [24.1–33.2]	27.6 [23.6–32.0]	32.6 [28.2 – 37.1]
Prevalence of obesity in adults† (%) [95% CI]	29.0 [25.3–32.9]	3.6 [2.4–5.1]	6.2 [4.7–7.9]	3.9 [3.0–5.0]	6.9 [5.0–9.0]	25.8 [22.6–29.3]	4.7 [3.6–5.9]	15.6 [12.5–19.0]	8.6 [6.3–11.3]	6.4 [4.6–8.7]	10.0 [7.4 – 13.1]
Prevalence of insufficient physical activity in adults† (%) [95% CI]	30.4 [23.7–37.9]	27.8 [16.4–39.1]	14.1 [10.1–19.4]	34.0 [22.3–47.7]	22.6 [16.0–30.9]	33.2 [25.9–41.4]	35.4 [20.9–52.9]	38.8 [29.7–48.6]	33.7 [20.3–47.0]	39.7 [31.3–48.6]	24.6 [18.2 – 32.3]
Existence of operational policy/strategy/action plan for diabetes‡ (Y/N)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Existence of evidence-based national guidelines/protocols/standards for the management of: (Y/N)											
Diabetes*	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Physical inactivity*	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Overweight/obesity*	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Existence of tax on foods high in fat, sugars, or salt* (Y/N)	No	Yes	No	Yes	No	No	No	No	No	No	No
Implementation of a nutrition public awareness program in the past 2 years* (Y/N)	Yes	Yes	Yes	Yes	Yes	Yes	NR	Yes	No	Yes	Yes
General availability of diabetes testing at the primary healthcare level* (by HbA1c, Y/N)	Yes	No	DK	Yes	No	Yes	NR	Yes	No	Yes	Yes

Table 1 continued

	AUS	BGD	CHN	IND	IDN	IRN	KOR	MYS	PAK	PHL	THA
General availability of diabetes testing at the primary healthcare level* (by blood glucose measurement, OGTT, Y/N)	Yes	Yes	Yes	Yes	Yes	Yes	NR	Yes	Yes	Yes	Yes
General availability of insulin in the public health sector* (Y/N)	Yes	No	No	Yes	No	Yes	NR	Yes	No	Yes	Yes
General availability of metformin in the public health sector* (Y/N)	Yes	Yes	Yes	Yes	Yes	Yes	NR	Yes	No	Yes	Yes

Data represent the most recent values for each indicator as of January 16, 2024. Full details of collection and/or calculation of data, as well as relevant definitions, are available at the WHO Global Health Observatory website here: https://www.who.int/data/gho/data/indicators

AUS Australia, *BGD* Bangladesh, *CHN* China, *CI* confidence intervals, *DK* don't know, *HbA1c* glycated hemoglobin, *IND* India, *IDN* Indonesia, *IRN* Iran, *KOR* Republic of Korea, *MYS* Malaysia, *NR* no response, *OGTT* oral glucose tolerance test, *PAK* Pakistan, *PHL* Philippines, *THA* Thailand, *WHO* World Health Organization

*As of 2021. †As of 2016, age-standardized estimate

result in adverse outcomes and a decline in quality of life. Education levels in some regions also fail to dispel myths around the use of insulin. Patient miseducation on social media platforms is also a challenge, as it can embed a negative perception of the physician's motivations and their relationships with the pharmaceutical industry. This may also drive a preference for alternative medicine or traditional 'cures' and raise doubts that insulin can prevent future complications or death. Preference for alternative medicine over modern 'western' medicine may also be rooted in tradition and cultural beliefs, as is often the case in India, China, and Bangladesh.

Barriers to insulin may also originate at a physician or healthcare system level. The growing complexities in international and locally recommended management pathways for people with T2D have delayed or stopped insulin initiation in favor of newer therapies, such as glucagon-like peptide-1 (GLP-1) receptor agonists and sodium-glucose co-transporter-2 (SGLT-2) inhibitors, in patients who are in need of treatment intensification and would benefit from insulin [34].

Primary care physicians initiate insulin in many countries in the Asia–Pacific region, although many lack confidence and the support of allied HCPs. In Indonesia, insulin is initiated by internal medicine specialists in the government healthcare service, although it can be prescribed by primary care physicians in private practice. In many regions including Iran and China, appropriate infrastructure for the delivery of diabetes education is not sufficient, as is an integrative multidisciplinary approach to diabetes care. Currently, a lack of a centralized healthcare system or fragmentation of care across discrete or siloed teams, long delays in referrals for insulin therapy, and suboptimal transfer of patient information between entities are important institutional-level challenges that need to be addressed.

Regarding the cost of insulin, in many countries in the Asia–Pacific region, including India, Pakistan, and Bangladesh, most expenditure associated with insulin and blood glucose monitoring is borne out-of-pocket by people with T2D. For example, middle-income individuals

in India, who comprise 70–80% of the overall population, have to pay for their insulin [35] and, in Bangladesh, the average annual cost for medicines for people with T2D in 2019 was USD 474.5 [36]. In China, all diabetes drugs are included in the National Reimbursement Drug List (NRDL) but needles for insulin injection are not included, and most patients do not follow the guidance of changing needles for each injection. In Bangladesh, China and Malaysia, blood glucose monitors and strips are an out-of-pocket expense for patients, which can result in a lack of insulin titration, while, in Iran, there is variable reimbursement to cover the cost of new-generation insulins. Financial pressures can also be a concern for physicians. In some countries, including Bangladesh, India, and South Korea, physicians in private practice can be reluctant to start insulin therapy or switch to newer insulin analogues due to concerns that patients will switch physicians.

Specific barriers to insulin initiation highlighted by members of the author panel in the different subregions within the Asia–Pacific region are summarized in Table 2.

How Can Barriers to Insulin Initiation Be Overcome in the Asia–Pacific Region?

Potential solutions to the barriers to insulin initiation in the Asia–Pacific region include patient, physician, and healthcare system initiatives, as well as access to new-generation insulin analogues and insulin delivery devices. Patient communication, education, and support are obligatory. Multidisciplinary teams can be key to initiating and titrating insulin, and overcoming physicians' time constraints. These teams can include diabetes educators, diabetes specialist nurses, dieticians, and educated peer-support workers.

Inclusion of HCPs and team members with different ethnic backgrounds may help to overcome barriers in culture or language when communicating with patients [37]. For example, in Australia, which has a large migrant and culturally diverse population and many Australian-born indigenous populations, more than 300 languages are estimated to be spoken in the home and patients can experience language issues and require culturally appropriate care [38, 39]. Patients from different cultures may also hold traditional beliefs regarding diabetes and insulin, and these should also be considered when providing care. Physicians from other medical specialties also need to be involved in educating patients about the benefits of insulin, for example cardiologists and ophthalmologists.

Patient education and training can be delivered via education programs run by medical societies, government departments, and pharmaceutical companies. For example, the Diabetic Association of Bangladesh runs a large network of healthcare centers across the country, and, along with providing care for patients with diabetes, organizes education programs and produces education materials for diabetes educators and other health professionals. The association also produces films to raise patient awareness. Diabetes Australia has extensive online resources related to living with diabetes, as well as live and virtual events. There may be the potential for a specific module on insulin therapy to be developed.

Raising awareness of diabetes and the benefits of insulin among the general population can also help to battle misconceptions and increase patient acceptance. Public campaigns on social media or local television are powerful channels of communicating with patients, as is the use of patient 'influencers' such as celebrities or trusted community leaders. One such initiative in Pakistan, run in collaboration with the local government and sponsored by the pharmaceutical industry, includes a video of a well-known cricketer with diabetes sharing the message that a healthy life without complications is possible. In Thailand, a program to recruit village health volunteers to support self-management in individuals with a high risk of T2D development has been found to increase scores on knowledge and self-efficacy for T2D prevention in both health volunteers and high-risk individuals in the community after 12 weeks. The authors suggest that the possibility of similar programs should also be explored in other countries in the Asia–Pacific region [40].

Physician education and support are also key to improving the use of insulin. Treating physicians

Table 2 Key barriers to insulin initiation in the Asia–Pacific region

South Asia	Western Asia	East/South East Asia	Australasia
Patient			
Belief in alternative medicine or traditional cures; lack of trust in physician; cost of insulin and glucose monitoring	Reluctance to start a new treatment; belief that insulin is an 'end-of-the-road' treatment; cost of glucose monitoring	Perceived complexity of treatment; low education levels; belief in alternative medicine or traditional cures; cost of needles and glucose monitoring	Fears that insulin is 'the last resort'; belief in traditional cures
Physician			
Lack of time and resources	Difficulties understanding the complexities in treatment options; lack of time to educate and manage patients	Lack of confidence in initiation and titration of insulin; insufficient number of trained specialist and support staff for treating diabetes	Complex guidelines that recommend newer therapies ahead of insulin such as SGLT-2 inhibitors and GLP-1 RAs. Insulin may be regarded as a later option
Healthcare system			
Free insulin not always available for those who cannot afford to pay	Inadequate infrastructure for diabetes education	Non-systematic availability and delivery of diabetes education; very low number of diabetes nurses and educators	Inadequate resources for diabetes education in the public and private systems

Barriers discussed by members of the author panel from South Asia (India, Pakistan, and Bangladesh), Western Asia (Iran), East Asia (China and South Korea), South East Asia (Indonesia, Malaysia, Philippines, and Thailand), and Australasia (Australia)

GLP-1 RA glucagon-like peptide-1 receptor agonist, *SGLT-2* sodium-glucose co-transporter-2

need to understand the complex and heterogeneous nature of T2D to individualize treatment based on diverse and heterogeneous lifestyles, and taking into account phenotype, cultural, and economic factors [41]. Clear national guidelines emphasizing the role of insulin are key to providing this guidance.

As well as governmental health authorities, non-governmental organizations, medical associations, and the pharmaceutical industry can all play a role in the provision of continuing medical education and financial support. The use of novel types of educational tools, including interactive virtual patient simulation scenarios, electronic guidelines, and decision-support apps can all assist in training initiatives.

Some barriers to patient and physician acceptance of insulin may be removed with greater access to new-generation insulin analogues and improved insulin delivery devices. New-generation insulins demonstrate improved pharmacology, safety, and dosing time flexibility versus human insulin, along with simpler titration algorithms. Insulin delivery devices are easier to use, less painful, faster to teach compared with a vial and syringe, and are becoming smaller and more discrete to use. The latest insulin pumps are also moving towards a fully automated artificial pancreas closed-loop system, which will increase convenience for patients. While cost or variable insurance reimbursement remains a barrier, cost of insulin can be overcome in some regions if patients understand the benefits [42].

CONCLUSIONS

The Asia–Pacific region faces a huge healthcare challenge from the rising prevalence of T2D. Moreover, T2D can have a relatively early onset in many patients in this region, hence aggressive glycemic control is vital to limit the burden of diabetic complications, and insulin therapy is therefore likely to be widely beneficial. Many healthcare systems in the region are ill prepared to meet this challenge, however, due to being under-resourced, or from national healthcare policies that make insulin therapy widely unaffordable by excluding the reimbursement of insulin, or of insulin administration equipment, glucose monitors, test strips etc. Even where insulin is easily available, there are significant barriers to its timely use. These include a lack of time and confidence on the part of physicians, lack of integrated care, lack of patient education, and widespread misconceptions about the risks and difficulties of insulin use, and what the decision to start insulin therapy signifies about disease progression and life expectancy. These barriers are reported globally but there are others that are more intrinsic to the Asia–Pacific region, such as skepticism about 'Western' medicine, and a tendency for perceptions to be guided from parochial traditions, peer groups, and unverified (and often untrue) reports on social media. Meeting these challenges is a vitally important goal in the years ahead. In the long term, it will require HCPs to organize and lobby for increased patient education, systems of integrated care and resources, and patient access to insulin. In the shorter term, we must be alert to the indications for initiating insulin in individual patients, the barriers that we might need to be overcome to gain patient acceptance, and individualized tactics that might help to achieve this.

Illustrative Case Histories

Please note, the case histories included on the following pages are purely hypothetical and intended to illustrate the barriers discussed in the main text, with some suggested approaches to overcome these.

Case 1: Dae-Seong, Busan, South Korea: Common fears and misconceptions about insulin

Dae-Seong is a 54-year-old technician with type 2 diabetes of 6 years' duration. He is married with two sons in secondary school and has a sedentary lifestyle. His oral glucose-lowering drugs have been slowly increased since diagnosis to attempt to achieve glucose control. Dae-Seong is currently on metformin 2000 mg daily, gliclazide 80 mg twice daily, linagliptin 5 mg daily, and atorvastatin 40 mg daily. He is not hypertensive and has no history of diabetes-related chronic complications. He has a body mass index of 25.3 kg/m^2, with fasting glucose

of 168 mg/dl (9.3 mmol/l), HbA1c 8.6%, and serum creatinine of 0.8 mg/dl (0.04 mmol/l).

Due to the fact that Dae-Seong is taking multiple glucose-lowering drugs but remains poorly controlled, it is suggested that his gliclazide should be substituted for basal insulin. Dae-Seong expresses a reluctance to start insulin and becomes visibly upset. On questioning, he reveals that he is concerned about injections and hypoglycemia, and he feels he has failed to manage his diabetes and asks how long he can expect to live.

Dae-Seong is reassured when the following points are explained to him:

- There is no evidence of diabetic complications yet, so he can expect many years of good-quality life.
- Insulin is used by patients with type 1 diabetes for an entire lifetime, and its role is to prevent complications and maintain health. Many patients with type 2 diabetes who begin insulin wish they had done so years earlier.
- Modern basal insulins carry a very low risk of hypoglycemia, and impending hypoglycemia can be recognized and addressed. A regimen will be designed that introduces insulin at a low dose and builds slowly and simply until an appropriate dose is reached.

A meeting can be arranged with a specialist nurse who will demonstrate how easy and painless it is to administer insulin via a modern injector device.

Case 2: Pranav, Bangalore, India: Urgent need to initiate insulin earlier than guidelines appear to recommend, and risk of loss to follow-up

Pranav is a 32-year-old single man who works as a software development engineer. Six months ago, he was routinely assessed and found to have a body mass index of 30.2 kg/m^2 and HbA1c 7.8%. He was diagnosed with type 2 diabetes (T2D) and started on metformin 1000 mg per day along with sitagliptin 100 mg per day. Pranav recently returned to his surgery complaining of balanoposthitis and symptoms of lethargy, and questioning revealed that he also had signs of polyuria and polydipsia, and recent weight loss. Blood tests revealed his fasting blood glucose to be 280 mg/dl (15.5 mmol/l), his postprandial blood glucose to be 412 mg/dl (22.9 mmol/l), and his HbA1c to be 11.4%.

It is explained to Pranav that he really needs to begin insulin therapy immediately due to symptoms of gluco- and lipotoxicity. However, Pranav has read widely about T2D since being diagnosed because he has a family history of this disease. He is aware of guideline recommendations and understands insulin to be a 'last-resort' therapy. He argues that he could try other drugs such as glucagon-like peptide-1 receptor agonists, and sodium-glucose co-transporter-2 inhibitors, which could delay the need for insulin. He makes veiled suggestions about seeking a second opinion from another physician.

Pranav is reassured, however, when the following points are explained:

- Guideline recommendations cover the broad T2D population and provide scope for individualization. His clinical course is atypical and likely to be linked to his family history.
- Insulin is, in fact, *not recommended as a treatment of last resort*; other, less potent, therapies are included as alternatives in early stage T2D only because traditional insulin products carried a risk of hypoglycemia and were considered more 'invasive'. In fact, modern insulins carry a low risk of hypoglycemia, and impending hypoglycemia can be recognized and addressed.
- People with type 1 diabetes (T1D) have no other options than insulin, and use it successfully for their entire lifetime to prevent complications and maintain health. Pranav's presentation of T2D is similar to that of T1D.
- In fact, Pranav has decompensated diabetes that could potentially be corrected by a temporary course of insulin. It is important for his health to get his glucose levels controlled, and then modifications of therapy can be considered, including withdrawal of insulin.

However, due to his young age, Pranav will live with diabetes for many years, so is at risk of developing complications. It is therefore illogical to delay the most effective therapy of all just because other T2D therapies are available; it is

better to achieve good glycemic control now and maintain that for life.

Case 3: Inaya, Lahore, Pakistan: Peer-driven skepticism about insulin and modern medicine

Inaya is a 48-year-old mother of six who works part-time in a bakery. She has been diagnosed with type 2 diabetes for 4 years and, at a recent health check, she was found to have a body mass index of 27.7 kg/m^2 and HbA1c of 9.2%. Since Inaya has shown little interest in her diabetes, she has been prescribed a very simple regimen of two tablets per day of a metformin + dapagliflozin combination product. Due to worsening HbA1c, an attempt was made to prescribe liraglutide 18 months ago, but this was unsuccessful after she was initially resistant to injections and then complained of nausea.

Eye examinations show early signs of diabetic retinopathy, although Inaya does not perceive any loss of visual acuity.

It is suggested to Inaya that she should add basal insulin to her therapy to improve her glycemia, halt the progression of retinopathy, and prevent other potential complications. However, Inaya counters that she feels perfectly well and does not understand why she needs medicine at all, especially insulin. On further questioning, she reveals that she has read on social media that insulin is a dangerous drug that is overhyped by 'the establishment' and pharmaceutical industry. Her mother has also persuaded her that such medicines were never needed by her generation, so she would rather not take any new drugs. Notes made by the team nurse who attempted to train Inaya in the use of liraglutide reveal, however, that she and Inaya share a love of cricket.

These case notes were then used to change the conversation towards subjects about which Inaya felt more positive. Inaya was persuaded to attend a further educational session with a diabetes nurse to learn more about her diabetes and insulin where she was told that:

- Former Pakistan cricket captain Wasim Akram has insulin-treated diabetes.
- This hero of hers has produced short educational films encouraging people like her to take their diabetes seriously, as they themselves had done.
- Inaya is not alone in being influenced by social media platforms and non-expert peer groups, but she owes it to herself and to her children to seek out other perspectives on matters related to her health.
- In this regard, her cricket hero and healthcare providers have her best interests at heart.

The nurse would provide Inaya with an opportunity to watch the videos made by her cricket heroes and to access other patient education assets with no obligation on her part.

Case 4: Aranya, Bangkok, Thailand: Difficulty affording insulin therapy due to lack of reimbursement

Aranya is a 62-year-old grandmother whose type 2 diabetes was no longer being controlled with metformin plus sulphonylurea (HbA1c of 8.6%). It was therefore suggested to her that basal insulin should be added, but the choice of agent was driven by cost, as Aranya is from a lower socio-economic background and universal health coverage provides only basic insulin products (neutral protamine Hagedorn, regular and premix) free of charge. However, twice-daily neutral protamine Hagedorn insulin resulted in a few mild hypoglycemia episodes (fasting blood glucose or overnight glucose of >56 mg/dl to <70 mg/dl [>3.1 mmol/l to <3.9 mmol/l]) not requiring assistance, and, as insulin titration progressed, these episodes became more frequent, but not severe. To reduce hypoglycemia, the sulphonylurea was discontinued and insulin re-titrated. With very careful meal management, Aranya was able to achieve her glycemic goal.

Nevertheless, Aranya developed negative feelings towards insulin because of the hypoglycemia. It was explained to Aranya that 'second-generation' insulins reduce the risk of hypoglycemic episodes, but Aranya remained reluctant to consider these, as they are not covered by universal health coverage.

In Thailand, cost can be a major issue, especially for underprivileged individuals. The universal health coverage, which covers approximately 80% of the Thai population, provides only basic insulins for people with diabetes free of charge, and glucose strips are not covered for patients with type 2 diabetes. Therefore, many insulin-treated patients have suboptimal

glycemic control due to lack of adequate glucose monitoring and suboptimal insulin regimens.

The hospital diabetes care team and diabetes educators worked with Aranya to assess her willingness to pay to switch to a newer basal insulin once she was informed of the following:

- Poor glycemic control leads to an increase in micro- and macrovascular complications.
- Prevention of complications and glycemic control are well-recognized ways to effectively manage diabetes treatment costs.
- The newer insulins reduce the occurrence of hypoglycemic episodes.

Well-managed diabetes can benefit a patient's quality of life.

Case 5: Jirayu, Phuket, Thailand: Overcoming systemic difficulties through education of GPs

Jirayu is a 43-year-old IT specialist who works in Bangkok and has a body mass index of 32.6. He has been self-administering insulin for several months, with the advice and support from the diabetes care team from the hospital. Jirayu is due to move to a new area where face-to-face contact with a diabetes specialist will not initially be possible. Although Jirayu has been self-administering insulin successfully until now, he is concerned that healthcare professionals (HCPs) at the clinic near his new home will not be able to manage his diabetes treatment effectively and his condition will worsen.

Telehealth has been implemented in many hospitals in Thailand, and provides an alternative option for HCPs to keep in regular contact with their patients or patient caregivers. This system also allows HCPs to counsel on titration or adjustment of insulin dosage in patients who are not easily able to see a diabetes specialist. Jirayu decided to discuss with his new general practitioner (GP) about continuing keeping in contact with his diabetes care team via a teleconference app. His GP agreed upon this and suggested that treatment be based on shared decision-making. With this strategy, Jirayu's diabetic condition could be well managed without regular face-to-face visits with a diabetes specialist.

To increase the number of diabetes educators in Thailand, the Thai Association of Diabetes Educators, among others, has provided regular training courses and a curriculum for HCPs or other medical personnel who are interested in diabetes care. This is a good opportunity for GPs who have to take care of patients with diabetes and want to improve their knowledge of and skills in diabetes management. They can also send their nurses or other medical personnel to attend the curriculum to better manage patients with diabetes. This is a practical strategy to improve diabetes care, including insulin management, in hospitals where there are no diabetes specialists.

Case 6: Peter, Sydney, Australia: Overcoming systemic difficulties through establishment of a multidisciplinary team

Peter is a 68-year-old retired man with an 8-year history of type 2 diabetes. He was admitted to the emergency department following a fall from a ladder. Medications on admission included metformin 1 g twice daily, empagliflozin 25 mg once daily, and linagliptin 5 mg once daily. He had previously trialed a glucagon-like peptide-1 receptor agonist but did not persist on this treatment due to gastrointestinal side effects. He had not consulted his family doctor for several years. Peter's HbA1c on admission was 12%, his estimated glomerular filtration rate was 65 ml/min/1.73 m^2, and his lipid levels were at target. He was not known to have any diabetes-related complications. He was assessed by the diabetes team, then discharged on twice-daily insulin. Due to hospital restrictions, a review was organized for 3 months. Peter was uncertain how to titrate his insulin or how long he should persist with the injections and what monitoring he needed. He was referred by his family doctor to an endocrinologist and diabetes educator. Management consisted of revision of injection technique, change of insulin needle length to 4 mm, advice regarding rotation of injection sites, and monitoring of his glucose levels prior to the injections prior to breakfast and dinner, as well as education regarding prevention and treatment of hypoglycemia.

A management plan was made in conjunction with the family doctor, including guidelines as to how to titrate the insulin and what glucose targets were appropriate. The family doctor continued to review Peter every few weeks, with the

endocrinologist seeing Peter at 3- then 6-month intervals. The key factors in management were:

- Communication between all healthcare professionals in a timely manner after discharge.
- Guidelines delivered by the endocrinologist to the family doctor, with insulin adjustment algorithm based on self-monitoring of glucose.
- A diabetes educator ensuring that insulin injections were appropriate with revision of sick day management.
- Oversight by the endocrinologist.

Case 7: Dr. Thomas, Chennai, India: Reluctance to start insulin due to lack of confidence and clinical support

Dr. Thomas is a successful 35-year-old physician practicing in Chennai. However, he is often overwhelmed by the number of patients he has to see in a day. Although he has a special interest in diabetes care, he runs a solo practice with no dedicated dietician or diabetes educator, and has found it difficult to educate his patients regarding diabetes. He admits that he often sees patients with severe uncontrolled diabetes who are already taking 3–4 oral antidiabetic drugs, yet many continue to have a HbA1c value greater than 9%. While he is aware that he needs to consider initiating insulin, he is reluctant to do so because it would mean an extra 20–30 min of his time. Due to the long list of patients waiting outside his consultation room on any given day, he does not feel he can spare this time to initiate insulin.

When one of his patients develops a severe diabetic foot problem, Dr. Thomas decides that it is time he changes his daily practices. He joins a certificated course, which vastly improves his overall knowledge of treating diabetes. He also starts attending various diabetes meetings, where he learns the value of avoiding clinical inertia and the need for starting insulin early if multiple oral antidiabetic drugs are not effective. He begins to employ a dietician, whom he enrolls in a program to gain certification as a diabetes educator. The dietitian learns how to administer insulin, and how to teach patients about blood glucose and continuous glucose monitoring. She also prescribes healthy diets and increasing physical activity for patients. Together, Dr. Thomas and the dietitian develop specialized educational materials for patients with diabetes.

Dr. Thomas finds that, with the addition of the dietitian/diabetes educator to his clinic, his own time is freed up and he is under less pressure. Moreover, his patients benefit considerably from the extra attention that is given to them by the diabetes educator. Over time, Dr. Thomas finds that the general level of diabetes control in his patients improves considerably. Moreover, as he now starts seeing more patients with diabetes, he focuses his practice on diabetes and its associated comorbid conditions.

The lessons Dr. Thomas learns are as follows:

- It is difficult for an individual physician to spend enough time to educate people with diabetes.
- Addition of a dietitian/diabetes educator greatly enhanced his practice and improved the control of diabetes in his clinic.
- His own self-improvement in knowledge of diabetes gave him the confidence to treat even difficult cases of diabetes.

Dr. Thomas does not hesitate anymore to use insulin whenever indicated. In fact, he has even started using a short course of insulin early in the treatment of those who present with infectious ketonemia, grossly elevated HbA1c, weight loss, or other symptoms of uncontrolled diabetes.

Case 8: Mrs. Karim, Ashulia, Bangladesh: Overcoming sudden stoppage of insulin

Mrs. Karim is a 45-year-old woman. Two years ago, she was experiencing typical symptoms such as polyuria and polydipsia. Mrs. Karim's OGTT revealed her fasting blood glucose to be 14 mmol/l and her postprandial blood glucose to be 26 mmol/l. Regular pre-mixed insulin was initiated, as well as the introduction of dietary modifications and exercise.

As advised by a local village physician, Mrs. Karim stopped taking insulin after she experienced nocturnal hypoglycemia. Three months later, she developed the same symptoms of hyperglycemia that she experienced 2 years prior at the initial diabetes detection. Mrs.

Karim then began to omit her nightly dose of insulin, taking it only in the morning.

Mrs. Karim experienced a recent non-healing ulcer on her left toe following a trauma. She was referred to BIRDEM, a tertiary care hospital. Mrs. Karim's HbA1c levels were 11.3% with normal renal function.

The management plan for Mrs. Karim consisted of a split-mixed regimen, antibiotic prescription, and diabetes education. As patients may sometimes feel more comfortable with local physicians, education on future diabetic management, including insulin management, was provided to Mrs. Karim's local physician.

The key features of the management plan were:

- Split-mixed insulin regime of short-acting postprandial insulin, to keep postprandial blood glucose between 8 and 10 mmol/l and intermediate-acting insulin to keep pre-prandial blood glucose between 6 and 7 mmol/l.
- Diabetes education including advice on self-adjustment of insulin and hypoglycemia.
- Education on self-empowerment in Mrs. Karim's diabetes management.
- Dietary advice and adjustment, as well as frequent home monitoring.
- Communication with Mrs. Karim's local physician.

ACKNOWLEDGEMENTS

Medical Writing and Editorial Assistance Support for the development of this manuscript, under the direction of the authors, was provided by Edward Potts and Helen Marshall, of Ashfield MedComms, an Inizio company, and funded by Novo Nordisk. Drafts of the article were prepared by a medical writer, funded by the sponsor, and were circulated to all authors for review. The sponsor reviewed the final draft of the article for medical accuracy, with no input on the content of the article at any stage.

Author Contributions. The concept for this review article was agreed on by all authors (Roger Chen, Azizul Hasan Aamir, Mohammod Feroz Amin, Pongamorn Bunnag, Siew Pheng Chan, Lixin Guo, Mohammad E. Khamseh, Viswanathan Mohan, Nemencio Nicodemus Jr., Anthony Roberts, Tri Juli Edi Tarigan, Kyu-Chang Won, and Roopa Mehta) and the sponsor. All authors (Roger Chen, Azizul Hasan Aamir, Mohammod Feroz Amin, Pongamorn Bunnag, Siew Pheng Chan, Lixin Guo, Mohammad E. Khamseh, Viswanathan Mohan, Nemencio Nicodemus Jr., Anthony Roberts, Tri Juli Edi Tarigan, Kyu-Chang Won, and Roopa Mehta) critically reviewed the article and approved the final version for submission.

Funding. Sponsorship for this narrative review article and the Rapid Service Fee were funded by Novo Nordisk.

Declarations

Conflicts of Interest. Roger Chen: was a speaker and/or attendee of advisory boards and has received research funding from: Abbott, Astra Zeneca, Boehringer Ingelheim, Eli Lilly and Novo Nordisk; Azizul Hasan Aamir: is a member of the speaker bureau for Sanofi, Novo Nordisk, Getz Pharma, Hilton Pharma and CCL Pharma; Mohammod Feroz Amin: has been a speaker and/or on advisory boards or a recipient of research funding for Eli Lilly, Novo Nordisk, Synovia (Sanofi), ACI, Beximco and Incepta Pharmaceuticals Bangladesh; Pongamorn Bunnag: has acted as a speaker or advisor/consultant for AstraZeneca, Boehringer Ingelheim, Zuellig Pharma, Novo Nordisk, Sanofi, Abbott, LG Lifesciences, Bayer and Celltrion; Siew Pheng Chan: has received honoraria as speaker and advisory board member from: Abbott, AstraZeneca, Boerhinger-Ingelheim, Merck, Novo Nordisk, Servier, Zuellig Pharma Therapeutics; Lixin Guo: has participated as an advisory board member/consultant for Abbott, AstraZeneca, Bayer, Boehringer-Ingelheim, Dreisamtech, Dongbao, Eli Lilly, Gan & Lee, Hansoh, Hengrui, Huadong Medicine, Hua Medicine, Innovent, Janssen, Novartis, Novo Nordisk, Merck,

Pfizer, Sanofi, Synapsor, Takeda, Zense and 3sbio, and has received research funding or grants from the National Natural Science Foundation of China, the Beijing Natural Science Foundation, Abbott, AstraZeneca, Bayer, Dreisamtech, Eli Lilly, Hansoh, Hengrui, Huadong Medicine, Hua Medicine, Innovent, Meitekanger tech, Novo Nordisk, Salubris, Sanofi, Synapsor and Zense; Mohammad E. Khamseh: has received honoraria and research grants from Novo Nordisk, Roche, Sanofi and Merck; Viswanathan Mohan: has received honoraria and research grants from Novo Nordisk, Eli Lilly, Sanofi, Boehringer Ingelheim and several Indian Pharma companies; Nemencio Nicodemus Jr.: has received speaker honoraria from Novo Nordisk and Sanofi; Anthony Roberts: has received research funding or honorarium from Eli Lilly, AstraZeneca, Novo Nordisk, MSD, Boehringer Ingelheim, Janssen, Novartis, Lexicon Pharmaceuticals and Inc., Sanofi; Tri Juli Edi Tarigan: has received honorarium as speaker/consultant, support for research/clinical trial/attendance at educational meetings from AstraZeneca, Sanofi, Novo Nordisk, Boehringer Ingelheim, Servier, Kalbe Pharma, Sanbe, ZP Pharma and more; Kyu-Chang Won: has received research grants and speaker honoraria from Novo Nordisk, Eli Lilly, and Sanofi; Roopa Mehta: has acted as a speaker or advisor/consultant for Abbott, Amgen, AstraZeneca, Boehringer Ingelheim, Eli Lilly, Novo Nordisk, Sanofi and Silanes. Mohammad E. Khamseh is an Editorial Board member of Diabetes Therapy. Mohammad E. Khamseh was not involved in the selection of peer reviewers for the manuscript nor any of the subsequent editorial decisions.

Ethical Approval. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

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