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Dotting the I's and Crossing the T's of Insulin Therapy in India

The discovery of insulin over a century ago stands as one of modern medicine's most significant milestones, enduring through time. Yet, in India, we continue to confront fundamental challenges associated with insulin therapy.

Insulin is crucial for the survival of individuals with type 1 diabetes (T1D). It's also the preferred treatment for managing hyperglycemia during pregnancy, in hospital settings, and for patients with multiple comorbidities, where its use is extensively prevalent in India. However, in the context of type 2 diabetes (T2D), the adoption of insulin therapy is frequently deferred, a notable concern in the Asian Indian healthcare landscape [1]. There are several reasons for this delay all of which have been explained in detail in the review by Wangnoo et al. [2]

Viewing the world through an economist's lens often reveals hidden incentives driving actions. In India, the decision to initiate insulin therapy in patients with T2D is frequently influenced by such skewed incentives. From a physician's standpoint, starting a patient on insulin is more time-consuming than prescribing an oral medication. Medical practice in India is predominantly volume-based, where physicians, due to lower payment per patient, see a higher number of patients daily to maintain their income. According to a study published in the British medical journal, primary physicians in India spend on an average 2 minutes per patient [3]. Therefore, time, alongside money, becomes a crucial factor. The additional time needed to explain to a pa-

tient the need to commence insulin therapy is often subconsciously balanced against the time it takes to prescribe a pill. For patients, adding insulin introduces an extra layer of complexity and expense in a population largely paying for healthcare out-of-pocket. This is compounded by prevalent myths and misconceptions about insulin use, adding to the hesitation in its adoption.

Physicians initiating insulin therapy in patients with T2D generally choose between basal insulin and premixed insulin. The IMPACT India survey by Mohan et al. [4] revealed that premixed insulin is often favored for initial insulin therapy in these patients. With the introduction of biosimilar basal insulin, an increase in the preference for basal insulin can be expected. The initiation and titration of insulin in T2D has been discussed in detail in the article titled "A Practical Approach to the Initiation, Titration and Intensification of Insulin Therapy in Adults with Diabetes in the Indian Context: Recommendations by Association of Clinical Endocrinologists Consensus Group" published in the current edition of the journal [5].

The article by Erukulapati et al. recommends initiating basal insulin in insulin naïve patients at a dose of 6–10 units per day, based on the initial HbA1c levels. However, from my perspective, the starting dose of basal insulin for Asian Indian patients should be higher than the recommendation in the aforementioned article. Our published retrospective study examined the optimal final dose of insulin glargine needed to achieve targeted fasting capillary glucose levels in hospitalized patients, as well as the variables influencing this final dose. Our findings indicated that the average final dose of basal insulin was 25 units (0.33 units/kg). The most significant variable affecting the final basal insulin dose was found to be the HbA1c value [6]. While the utilizing this data, we proposed a formula to calculate the appropriate basal insulin dose: Basal insulin dose (in units/kg) = 0.064 + 0.030 × HbA1c [7]. A study conducted in a hospital setting might not directly translate to out-

patient scenarios. However, the crucial takeaway is that determining the initial dose of basal insulin needed to reach ideal target levels warrants further investigation and research.

Asian Indian patients frequently present with 'glucotoxicity' and signs of relative or absolute insulin deficiency at the onset of insulin therapy. A significant proportion of these patients exhibit clinical symptoms of diabetes in adulthood, akin to the condition historically termed 'Flatbush' diabetes [8]. This similarity often results in a considerably higher initial insulin requirement. Failure to meet this demand in both the initiation and titration phases can lead to persistent glucotoxicity and hinder achieving optimal glycemic control.

The technique of insulin administration remains a significant challenge for Asian Indian patients. In a study by Kalra et al. [9], substantial deficiencies were identified in the insulin injection practices among this group. A prevalent issue is the repeated use of insulin syringe or pen needle that leads to inadequate and improper insulin delivery. Additionally, the occurrence of lipohypertrophy is common among both T1D and T2D patients [10]. These problems are likely a result of the insufficient number of diabetes educators within the healthcare system. Moreover, physicians often lack the time to thoroughly instruct patients on proper insulin techniques. Patient compliance also poses a challenge, with many skipping their insulin doses for various reasons. The critical matter of correct insulin injection techniques is comprehensively addressed in the article by Erukulapati et al. [5].

The storage of insulin in India poses distinct challenges due to the country's tropical climate, which subjects insulin to higher temperatures during storage and transportation. Furthermore, in India, insulin vials are more commonly used than Insulin pens. The inconsistent 24-hour electricity supply in several regions makes refrigeration difficult. Notably, Pendsey et al.'s study highlights an innovative solution: storing insulin in earthen clay pots, which effectively substitutes for refrigeration. This finding is particularly valuable for tropical environments like India, offering a practical approach to maintaining insulin efficacy [11]. Insulin management in patients receiving glucocorticoids presents a significant challenge. This became particularly evident during the recent COVID-19 pandemic, when glucocorticoid use was widespread, leading to frequent cases of hyperglycemia. We conducted a randomized, open-label trial comparing the standard basal-bolus insulin approach with a novel algorithm for managing glucocorticoid-induced hyperglycemia in hospitalized patients. This algorithm took into account various factors, including the type and dose of glucocorticoid and the patient's baseline diabetes status prior to glucocorticoid administration. A key feature of the algorithm was the alignment of insulin action with the glucocorticoid profile. Our new approach demonstrated superior performance in terms of glycemic control and variability compared to the standard of care [12].

Following the publication of this algorithm, particularly during the COVID-19 pandemic, we recognized the significance of another variable: the patient's baseline status of the hypothalamic-pituitary-adrenal (HPA) axis. Patients with long-term use of systemic or inhaled glucocorticoids often exhibit a suppressed HPA axis, which increases the risk of early morning hypoglycemia when using long-acting insulin [13]. We have since refined our algorithm to incorporate this variable and are currently conducting a study to further explore its implications.

Technology offers promising solutions for addressing the challenges associated with insulin initiation and proper usage in the Asian Indian context. Previously, we developed the "Centurion insulin app", specifically designed to assist physicians in timely initiating insulin therapy for patients with T2D. We are committed to making this technology widely accessible; hence, we've made the app's code open-source and published it on GitHub, inviting other developers to contribute and enhance its functionality [14]. Additionally, Singla et al. [15] are working on a machine learning algorithm tailored for insulin dosing in T1D patients, addressing a critical and complex issue. Furthermore, social media can be a powerful tool to debunk myths surrounding insulin use, while also promoting correct insulin techniques, usage, and storage practices.

In summary, administering insulin therapy within the Asian Indian healthcare framework presents distinct challenges. Therefore, the publication of specialized guidelines for adult insulin therapy in India by Erukulapati et al. [5], as featured in this journal, represents a significant advancement. Additionally, it is anticipated that this article will inspire young researchers to further explore and address the existing knowledge gaps in the application of insulin therapy.

Conflict of interest
The author declare no conflict of interest.

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