Brief Communication

Choice of Insulin in Type 2 Diabetes: A Southeast Asian Perspective

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Abstract

Southeast Asia faces a diabetes epidemic, which has created significant challenges for health care. The unique Asian diabetes phenotype, coupled with peculiar lifestyle, diet, and healthcare-seeking behavior, makes it imperative to develop clinical pathways and guidelines which address local needs and requirements. From an insulin-centric viewpoint, the preparations prescribed in such pathways should be effective, safe, well tolerated, nonintrusive, and suitable for the use in multiple clinical situations including initiation and intensification. This brief communication describes the utility of premixed or dual action insulin in such clinical pathways and guidelines.

Keywords: Asia, basal insulin, biphasic aspart, biphasic lispro, diabetes, dual action insulin, patient-centered care, postprandial glycemia, premixed insulin

Diabetes in Southeast Asia

Southeast Asia is one of the hot spots of the diabetes pandemic and bears more than its fair burden of the disease. Belonging to the Western Pacific Region of the International Diabetes Federation, the zone reports a diabetes prevalence of 9.3% and a large number of deaths, most of which occur in individuals below the age of 60.[1]

An earlier onset of diabetes, rapid development of complications, and longer life expectancy have led to an increase in the burden of diabetes and diabetes complications. This strains the existing health-care system, which finds it challenging to handle the twin burden of communicable and noncommunicable disease which Southeast Asian nations face.

Importance of Clinical Pathways

The role of clinical pathways and clinical recommendations is of utmost importance in such a scenario. Well-crafted pathways and algorithms, based on evidence, help in providing much-needed guidance to physicians and other health-care providers who deal with diabetes. Such documents are expected to offer a comprehensive management strategy, which includes screening and diagnostic tools, as well as nonpharmacologic and pharmacological interventions. They empower general physicians to tackle diabetes in peripheral clinical setups and encourage timely management of the disease, thus reducing preventable complications.

Detailed suggestions are available from professional bodies such as the American Diabetes Association, European Association for Study of Diabetes, American Association of Clinical Endocrinologists, and International Diabetes Federation.[2-4] There is criticism, however, regarding the actual patient centeredness of these publications and their pan-ethnic appropriateness.[5,6] The techniques of diagnosis, thresholds for intervention, targets of management, and tools

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used to achieve them (the four T's) must be pragmatic, realistic, and concordant with dietary and lifestyle patterns. In view of this, many Asian countries have developed their own national guidelines, relevant to their local needs.[7] This is in tune with the national list of essential medicines that each country develops: the subtle differences in these lists reflect the peculiar needs and requirements of each country.[8]

Need for Southeast Asia Specific Clinical Pathways

In diabetes care, we often tend to follow a Western-oriented management strategy. Data and recommendations from the Western world are usually extrapolated directly to Southeast Asia, without realizing that unique anthropometry, lifestyle, and glucophenol type of Southeast Asia modulate responses to pharmacotherapy. It should also be recognized that many Southeast Asian countries, especially the more urbanized and multiracial ones, are experiencing increasing rates of obesity and diabetes

The Asian type 2 diabetes phenotype is well known.[9] Southeast Asians have a relatively lower body mass index, and insulin secretory defect plays a more important role in the pathogenesis of diabetes. Caucasians, on the other hand, present with predominant insulin resistance. Thus, insulin replacement, both prandial and basal, is needed at an earlier stage in Asians with diabetes. There is a unique Asian lifestyle, "diet type," and health care-seeking behavior, which is prevalent across most of the continent. In many countries of Southeast Asia, persons present to the health-care system at a relatively later stage, with significant glucotoxicity and lipotoxicity. Reversal of this toxicity may entail the administration of adequate amounts of both prandial and basal insulin.

Animal studies have proven that malnutrition during pregnancy can lead to decreased β-cell function and mass in newborns. Mothers who had suffered the Dutch Famine gave birth to children who developed impaired glucose tolerance and type 2 diabetes in later life.[10] The Great Chinese Famine sufferers experienced an increase in the risk of hyperglycemia during adulthood. This association appears to be exacerbated by a nutritionally rich environment in later life.[11] While most countries in Asia have experienced chronic food shortages in the past and this pathophysiologic pathway may have contributed to diabetes in elder generations, food sufficiency has been achieved now.

Rice forms the staple diet of all of Southeast Asian countries, and the high carbohydrate load requires prandial insulin coverage in persons with diabetes. The Southeast Asian diet pattern is also peculiar. Many persons take two heavy meals in a day and find it difficult to adjust to a 3 + 3 meal pattern which is an essential correlate of a basal-bolus regimen.

The high postprandial glucose levels, observed in Asian populations, are due to the intake of high carbohydrate meals in large quantity, a relatively higher glycemic index of food staffs in this ethnic group,[12] delayed presentation of the patient, and acceptance of insulin therapy. The prescription and use of insulin therapy must correctly and appropriately address the Asian pathophysiology and lifestyle habits.

Insulin for Type 2 Diabetes in Southeast Asia

Such control can be achieved by various regimens including basal, premixed, basal bolus, basal plus, and different delivery devices, namely, vials/syringes and disposable/reusable pens, can be utilized this purpose. The choice of regimens, preparation, and delivery devices should be made in a patient-centered manner,[13] following the spirit of informed and shared decision-making.

In a national clinical pathway or algorithm, however, preference should be given to therapeutic options which have the potential to provide maximum benefit to the maximum number of intended beneficiaries. Choosing an inappropriate insulin may delay control, worsen complications, and negatively impact the patient's (and community's) trust in the health-care system. On the other hand, initiating an insulin which provides effective, safe, well-tolerated, convenient, and nonintrusive glucose control helps improve both biomedical and psychosocial outcomes.

Clinical pathways and algorithms designed for Southeast Asia should be based on pathophysiological abnormalities, dietary content, dietary pattern, lifestyle, and healthcare-seeking behavior. Thus, it is especially important with respect to guidance related to the choice of insulin for initiation. Asian evidence which proves the need for greater prandial insulin coverage,[14] and the advantages of specific insulin preparations should be taken into consideration.[15]

Most persons request for insulin therapy which does not interfere with, or intrude into, their lifestyle. In an overstretched health-care system, it also makes sense to use stock and dispense a minimum number of pharmaceutical preparations. Thus, an insulin which can be used both for initiation and intensification should take precedence over preparations which are limited to the use in only specific clinical settings.

Premixed Insulin for Southeast Asia

In the Southeast Asian content, this option seems to be premixed insulin. This class of insulin provides comprehensive glucose control, including both fasting and postprandial euglycemia, with a lesser number of injections. Premixed analogs, such as biphasic aspart and biphasic lispro (lispro mix), have the advantage of lower hypoglycemia, lower levels of postprandial glucose excursions, better adherence, improved quality of life, and higher patient satisfaction with treatment. The dual action coformulation, insulin degludec aspart, which is an improvement over existing insulin preparations, has added advantages of even lower hypoglycemia, nocturnal hypoglycemia, and greater flexibility.[16]

Premixed or dual action insulin is the insulin of choice across most of the Asian and African countries.[17] This is borne out

by statistics which reveal that premixed insulin is the most popular type of insulin used in the Southeast Asian Region.[18] The A1chieve observational study also showed that premixed insulin analogs were the preferred mode of insulin use in Indonesia.[19]

Premixed insulin can be used once daily, twice daily, or thrice daily, depending on the clinical situation. It can be used for initiation as well as intensification and lends itself to easy self-titration by the user and to physician-led dose titration. Various regimens, such as high-mix, hetero-mix, and reverse hetero-mix regimens,[20] allow for control of difficult-to-control or refractory diabetes.

Premixed insulin is included as an insulin of choice for initiation as well as intensification in guidelines from the International Diabetes Federation,[3] Australasia,[21] Cambodia,[22] India,[7] Japan,[23] Myanmar,[24] South Africa,[25] and Vietnam.[26] This reinforces the utility of this preparation in diabetes care. Premixed insulin is also mentioned in the national lists of essential medicines of various Southeast Asian countries[8] including Cambodia,[27] Myanmar,[28] and Vietnam.[29] The comprehensive Laotian formulary of essential medicines[30] also mentions "insulin zinc (mixed)" as an essential drug. This preparation therefore seems optimal for inclusion in various national clinical pathways and guidelines across Southeast Asia.

Data from DiabCare Asia suggest that conventional strategies and practices are ineffective in achieving good glycemic control. In Malaysia, for example, only 41% of participants achieved a target HbA1c <7.0%, with a mean HbA1c of 7.8 ± 2.2%.[31] Indonesia reported a mean HbA1c of 8.2 ± 2.0%, with 32.1% participants achieving target.[32] Results from Bangladesh showed a mean HbA1c of 8.6 ± 2.0%, with only 23.1% of the patients achieving the target of <7%.[33] Surveys in Thailand show similar trends, with 29.7%–41.3% participants reaching HbA1c goal in various studies.[34] These figures suggest that we need to enhance efforts for timely initiation of insulin, with preparations that are effective in controlling both fasting and postprandial glucose.

Southeast Asian Leadership

Southeast Asia is recognized as a global leader in the provision of essential medicines for chronic disease, with best practices from Vietnam being highlighted by the World Health Organization website.[35]

It seems natural, therefore, for Southeast Asian nations to continue their proactive and patient-centered approach toward the management of diabetes. This is accomplished by ensuring publication and adoption of updated national clinical pathways and guidelines, which reflect and respond to the lifestyle, dietary patterns, and biomedical as well as psychosocial needs of their citizens.

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Conflicts of interest

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