

The KgA1c Paradox: Widening the spectrum

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Abstract

The term KgA1c paradox is used to describe the unwanted rise in weight that occurs when HbA1c is controlled using conventional therapy. We highlight facets of pathophysiology, prevention, pharmacology, person centred care, and epidemiology, which correspond to the concept of KgA1c paradox. We suggest a novel index, KgA1c product [(BMI) x (HbA1c)], which can be used to evaluate efficacy of drugs, and assess metabolic control in persons with diabetes,

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The term KgA1c paradox is used to describe the unwanted rise in weight that occurs when HbA1c is controlled using conventional therapy.¹ This term is used frequently to highlight the need for therapies that can reduce body weight and glucose at the same time. In this opinion piece, we suggest other uses for the KgA1c paradox.

The Paradox of Pathophysiology

One of the cardinal symptoms of uncontrolled diabetes is weight loss.² It is expected, therefore, that individuals with high HbA1c should have a low body mass index (BMI), and vice versa. This, however, is not always true. Overweight and obese persons, with insulin and leptin resistance, are more likely to have high glucose levels. This may be termed as a KgA1c paradox, where body weight and glucose control are inversely related to each other. On the other hand, persons with relatively high levels of insulin resistance and glucose may have a normal BMI as well. This may also be termed as normal weight obesity.³ This correlation helps justify the higher prevalence of diabetes in populations with mildly raised BMI.

The Paradox of Prevention

Obesity and diabetes are closely linked with each other, as

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the portmanteau diabetes suggests.⁴ Both are significant clinical as well as public health challenges, and need to be prevented. Which of these should be focussed on first is an enigma for policy makers and planners. This is a KgA1c paradox, too, as we debate which the primary target of preventive interventions should be.

The Paradox of Pharmacology

In recent years, the glucagon-like peptide 1 receptor agonists (GLP1RA) have developed as tools for the management of both diabetes and obesity. Examples include liraglutide and semaglutide. Dual peptide agonists, of both GLP1 and glucose-dependent insulinotropic polypeptide (GIP), such as tirzepatide, also have approval for both type 2 diabetes and obesity treatment.⁵

While these drugs reduce both glucose and body weight at lower doses, a KgA1c paradox comes into play with the use of higher doses. Higher doses of GLP1RA and GIP+GLP1RA are able to do so without causing hypoglycaemia or a fall in glucose. This may be due to enhanced glucagon sensitivity, which acts as a bulwark against hypoglycaemia. Such a situation does not seem to arise with triple agonists such as retatrutide, which acts at the glucagon receptor as well.⁶

The Paradox of Person-Centred Care

The oft-used term person-centred care,⁷ is touted as a panacea for optimal delivery of, and satisfaction with, diabetes care. At the same time, existing guidelines, which focus on weight reduction in diabetes, do not take personal preferences, wishes and needs, into account. It is possible that an individual may desire to gain or maintain weight, for professional or personal reasons.

This is also a KgA1c paradox, where a particular person living with diabetes may request for medication which increases weight. This is common in culture where a heavy built is associated with a perception of being 'macho', well-to-do and healthy. A truly person-centric approach should take this into mind while crafting a prescription for glucose control.

The Paradox of Plenty

The last few decades have witnessed a rapid increase in the number of medications and other therapies for both obesity and diabetes. Prevalence rates of both syndromes,

unfortunately have shown an equally steep rise.⁸ This is another KgA1c paradox: in spite of enhanced ability to manage both 'Kg' and 'A1c,' there is minimal benefit observed in our communities and countries. Many hypotheses have been put forward to justify this situation. Change in lifestyle and dietary patterns, poor motivation on part of patients and public, and clinical inertia displayed by physicians are some reasons. Irrespective of these, we must work, as responsible health care professionals, to achieve optimal KgA1c control in persons living with diabetes.

The KgA1c Product

We suggest the use of a novel index, the KgA1c product, to determine the status of comprehensive metabolic care in a particular individual.

$\text{KgA1c product} = (\text{BMI}) \times (\text{HbA1c})$

Normal KgA1c

$< 23 \times 5.7 = 131.1$ for Asian Indians

$< 25 \times 7.0 = 142.5$ for Caucasians

Acceptable KgA1c

$< 25 \times 5.7 = 175$ for Asian Indians

$< 27 \times 7.0 = 189$ for Caucasians

It is well known that weight and glucose are relatively difficult to control, as compared to blood pressure and lipids. Using weight and glucose together, in a single index, helps assess overall metabolic health more comprehensively. It also motivates both the person living with diabetes and his/her health care team to pay equal attention to non-glycaemic parameters of health. The ethno-specific nature of the index allows the KgA1c product to be used in a personalized manner.

Summary

We highlight various paradoxes of modern diabetes praxis, all of which can be termed as the KgA1c paradox. We share a practical and pragmatic suggestion, converting KgA1c from a paradoxical challenge to a pragmatic solution.

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