

# PHARMACOTHERAPY REVIEW COMPARES AND CONTRASTS BETWEEN THE TWO STRATEGIES SUCH AS CARBOHYDRATE COUNTING AND FIX DOSING WITH REGARDS TO EFFICACY AND SAFETY.

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## I. INSULIN

A hormone produced by beta cells, in the pancreas. After we take food insulin is released in blood and it helps to uptake glucose from food and used as a form of energy. It also provides storage of excess glucose in liver.

Insulin has been used in all types of diabetic patients. Insulin needs predominantly depends on the balance of insulin secretion and insulin resistance. Patients with type 1 diabetes requires insulin throughout their life, unless they have an islet or they have done pancreas transplant where as patient with type 2 diabetes require insulin due to the destruction of beta cell function over time.<sup>6</sup>

## II. CARBOHYDRATE COUNTING:

A meal approach places emphasis on the total amount of carbohydrate consumed. People with diabetes can use carbohydrate counting as a meal planning option. Carbohydrate counting gives a precise method for comparing food and meal time insulin creating potential for improved blood glucose control.

The goal of diabetes management is absolute normalization of blood glucose level, although reducing glycemic variability is an important factor in reducing long term complications. So it is very important for correct determination of an individual insulin to carbohydrate ratio to encounter such type of strategy.<sup>5</sup>

## III. INSULIN TO CARBOHYDRATE RATIO:

The amount of carbohydrate in grams (In a meal) covered by 1 unit of insulin. The ratio is not fixed and it is determined by many factors like time of day, level of physical activity, physical stress.

Dosing titration schema varies among clinicians but general patterns exist for adjusting prandial insulins, fixed dosing algorithms strategies are, at times, used. A different strategy that is sometimes used for the same purpose is carbohydrate counting with individualized insulin-to-carbohydrate ration.

An evidence-based pharmacotherapy review will be done in my following studies that compares and contrasts between the two strategies indicated above with regards to efficacy and safety.

### Primary literature Review

	<b>Study 1 (carbohydrate counting method)</b>	<b>Study 2 (fixed dosing algorithm)</b>	<b>Study 3 (comparison between the carbohydrates counting method and the simple algorithm method)</b>
Design	61 patients with type 1 diabetes treated with continuous subcutaneous insulin infusion are assigned randomly to either carbohydrate counting method (as an intervention) or premeal insulin dose estimation in the usual empirical way (as a control). At baseline and twelve and twenty four weeks, A1c, FBG, BMI, waist circumference, daily insulin dose, and capillary glucose data, and Diabetes-Specific Quality-of-Life Scale (DSQOLS) questionnaire. <sup>1</sup>	11 patients with type 1 diabetes, on continuous subcutaneous insulin infusion are recruited. Basal infusion rates are optimized. Lunch carbohydrate content was pre-calculated according to weight-maintenance diet. Over 2–4 days, patients perform SMBG according to the protocol of the algorithm. Insulin dose was titrated downward until PPBG was (180–250 mg/dl [10–14 mmol/l]) starting with the usual insulin-to-carbohydrate ratio. Accordingly, endocrinologists set bolus insulin recommendations to normalize PPBG concentrations. <sup>2</sup>	24 weeks randomized multicenter controlled study compared two algorithms for adjusting mealtime (glulisine) insulin along with a standard algorithm for adjusting background (glargine) insulin. 273 patients with type 2 diabetes mellitus were recruited. Glargine and glulisine were weekly adjusted in the 2 groups based on SMBG from the previous week. The simple algorithm group (control) was given glulisine before each meal. The carbohydrate counting (intervention) group was given insulin to carbohydrate ratio to utilize for each meal and adjusted their dose of glulisine based on the amount of carbohydrate consumed at each meal. <sup>3</sup>

Results	According to DSQOLS scores, BMI reduction and waist circumference, the intervention group showed a statistically significant improvement than the control group. HbA1c of the intervention group was -0.35% lower than control. The rate of hypoglycemic incidences was lower in	The correlation between the clinically determined dose adjustments and those of the algorithm is $R^2 = 0.95$ , $P < 1e - 18$ . <sup>2</sup>	Glycated hemoglobin levels at week 24 was A1c=6.70% (simple algorithm) and A1c=6.54% (carb count). The reduction of HbA1c was -1.46 and -1.59%. The target A1C <7.0% was achieved by 73.2% of the patients (simple algorithm) and by 69.2% of the patients (carb count). Respective values for A1C <6.5% were 44.3 and 49.5%. The total daily dose of insulin was lower, and there was a trend toward less weight gain in carb
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	the test group as well. <sup>1</sup>		count group patients. Severe hypoglycemia rates were low and equal in the two groups. <sup>3</sup>
<b>Conclusion</b>	Adult patients with type 1 diabetes mellitus treated with continuous subcutaneous insulin infusion are better benefited if the intensification and dose calculation was based on carbohydrate counting method rather than a fixed dose algorithm in regards to improved quality of life, reduce waist circumference, BMI and Glycated Hemoglobin percentage. <sup>1</sup>	The proposed algorithm has the potential of drastically simplifying the determination of correct insulin-to-carbohydrate ratios and correctly administering and intensifying the insulin therapy. <sup>2</sup>	Simple algorithm showed a higher reduction of mean glycated hemoglobin. The simple algorithm based patients achieved 7.0% A1c by the rate of 73.2% while 69.2% of patients on carb. counting achieved the 7.0%A1c. In contrast, 44.3% of simple algorithm patients only achieved 6.5%A1c while 49.5% of patients achieved the same percentage. Carb count group had less rates of weight gain. And <b>severe hypoglycemia</b> rates were low and statistically insignificant between both groups. <sup>3</sup>

#### V. GUIDE LINE REVIEW:

#### IV. DISCUSSION

Fixed dosing algorithm seemed a simpler way to initiate insulin. It is also a more efficient way to achieve the target A1c=7.0% to a higher probability than carbohydrate counting. But if our target was to achieve A1c=6.5%, carbohydrate counting is a way much more method of achieving it. 49.5% of patients will achieve this strict goal by using carbohydrate counting while only 44.3% of patients using the simple fixed dosing algorithm would be able to achieve it. On the other hand, carbohydrate counting method is a more complex way of calculating the insulin dose and it is a slightly safer method with little significant percentage of developing hypoglycemia comparing the fixed dose algorithm. The body mass index is increased more with the fixed dosing algorithm. So in brief, fixed dosing algorithm is more efficient for most of the patients while the carbohydrate counting dosing method is a safer method in regards to hypoglycemia. And it causes a smaller BMI increase than the fixed dosing method. The waist circumference reduction is more with carbohydrates counting method. Type 2 diabetic patients on carbohydrates counting method are proved to have a better quality of life scores than patients on fixed dosing algorithms. So choosing the method will depend on the baseline BMI of the patient and on the target HbA1c that is already preset before initiating the therapy as well as the individualized tolerance of hypoglycemia.

According to the ADA/ AACE guidelines, Patients that do not meet their glycemic goals on OADs can start with basal insulin alone if the glycated hemoglobin levels is below 10%. should start with insulin glargine or detemir 10 units at the morning or NPH 5-10 units at bedtime. Usually 0.2 units/kg is used and increased by 1 unit every morning until FBG is below 110 mg/dl while OADs are not stopped. Multi-dose insulin can be started later on including basal dose at the evening and premeal correction dose scale of bolus dose usually 2 units for 151 to 200 mg/dl and 4 units for 201 to 250 mg/dl and 6 units for 251 to 300 mg/dl and 8 units for 301 to 350 mg/dl and 10 units for 351-400 mg/dl or start detemir or glargine at evening then single dose bolus insulin at the largest meal started 5 units/meal or 1/3 of basal dose per meal, usually which dose is less is chosen for the patient. Patients with glycated hemoglobin above 10% or RBG above 250 mg/dl require basal/bolus plan. Firstly TDD should be calculated by  $\text{kg} \times 0.4$  and 50% of the dose is given as basal and the other 50% is divided equally between meals. Dose can be increased by 1 unit at breakfast or dinner every day until pre-prandial of FBG is below 110 mg/dl.

#### VI. CONCLUSION

In conclusion, there are two methods of initiation, dosing and intensifying insulin. The simple fixed dose algorithm and the carbohydrate counting method. the main reason in choosing

either of them is the correct assessment of patient and individualization by several means. First, HbA1c goal of therapy, if the patient's glycated hemoglobin goal is 7% there is a higher probability of achieving it by using the fixed dose algorithm rather than the carbohydrate counting method. In contrast, if the patient's goal is 6.5% then the carbohydrate counting method is more crucial in this scenario. Second, the patient's tolerance of the hypoglycemia by the insulin used is essential in choosing the method of dosing. It's been found that fixed dose algorithm is associated with higher incidences of hypoglycemia comparing to the carbohydrate counting method. So if the patient is developing more hypoglycemia episodes due to many reasons, the carbohydrate counting method is a better choice here. Moreover, if the patient's therapeutic plan includes insulins that are more susceptible of causing hypoglycemia such as NPH, the patient would be better using the carbohydrate counting method. Thirdly, the patient's weight plays an important role. The fixed dose algorithm has showed to be increasing the weight more than the carbohydrate counting method of the same type of insulin used in both. So if the patient's BMI is already very high it would be more wise to use the carbohydrate counting method. On the other hand, carbohydrate counting method is a more sophisticated method and it involves more counseling time and it is not practical for certain populations such as elderly patients. In brief, the key in choosing the method of dosing is individualization of the patients.

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