Comparative Study Between Multiple Insulin Doses Regimen Versus Twice Daily Regimen in Children and Teenagers with Type One Diabetes in Mosul City

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ORIGINAL STUDY

Comparative Study Between Multiple Insulin Doses Regimen Versus Twice Daily Regimen in Children and Teenagers with Type One Diabetes in Mosul City

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ABSTRACT

Objectives: To evaluate the glycemic control and to identify the possible side effects of multiple insulin regimen versus twice daily regimen among diabetic patients whom visited the endocrine unit at Al Khansa'a Teaching Hospital in Mosul from the 1st of January 2023 to the end of December 2023.

Methods: This is a cohort descriptive study. Patients case sheets were reviewed to acquire the mandatory information. The questionnaire was composed of two sections, first section included demographic information while the second covered specific diabetes Mellitus information.

Results: Sixty-nine children with type 1 diabetes were included in the study, with (52%) males and (48%) females. About two thirds of the studied sample were on multiple daily injections of insulin and one third was on twice daily dosing. HbA1c mean was dropped from 10.8 ± 1.7 at baseline to 8.5 ± 1.5 ($p < 0.001$) among BID group, while it dropped from 11.3 ± 1.7 at baseline to 8.1 ± 1.0 ($p < 0.001$) among MDI group. There was no significant difference in reported hypoglycaemia between the two groups: which was 29 out of 43 (67%) among MDI group compared to 16 out of 26 (62%) among BID group.

Conclusion and Recommendation: It has been demonstrated that multiple insulin regimen can improve teenagers' glycemic control with less episodes of hypoglycemia. Providing Rapid-acting insulin (lispro) and long-acting insulin (glargine) in hospital and centers dealing with diabetes is beneficial as their prices are not affordable to all patients' families.

1. Introduction

Type 1 diabetes mellitus (T1DM) previously known as insulin-dependent diabetes, is an illness that often manifests itself throughout childhood and adolescence. The condition is characterized by a lack of insulin production as a result of pancreatic beta cell destruction in a condition which necessitates lifelong insulin treatment necessary for survival (Kakleas et al., 2015). It is one of the most common chronic diseases that has a major burden to the patient and family (Sav et al., 2015). International study groups and systematic reviews have been demonstrated that the annual worldwide incidence of type 1 diabetes mellitus is estimated to be 79,000 and the prevalence to be 500,000 among children younger than 14 year of age (Patterson et al., 2014). No recent study documenting clear Insulin-dependent diabetes incidence in Iraqi children.

Strict glycemic control is essential to postpone the start and reduce the development of complications associated with diabetes (Davidson, 2004; Vasudevan, Burns and Fonseca, 2006; Hahr and Molitch, 2015), that's why intensive insulin treatment is advised to attain this management (DAFNE Study Group, 2002; Griesdale et al., 2009; Ilkova et al., 1997). Dietary attentiveness, frequent blood glucose testing, and numerous insulin injections are required for successful diabetes management (American Diabetes Association, 2015). Aggressive management of insulin dependent diabetes can be achieved by using many injections of rapid-acting insulin plus basal dose of long-acting insulin to mimic endogenous insulin secretion, which is characterized by continuous basal insulin production and meal-related peaks (Rajaraman). Insulin glargine (Lantus; Aventis Pharmaceuticals, US) is a clear basal insulin analogue produced by recombinant DNA technology with duration of action of approximately 24 hours and fewer adverse effects (Vajo, Fawcett and Duckworth, 2001; McKeage and Goa, 2001).

In pediatric age patients, due to their increased weight, height, and caloric demands as they go through normal growth and development, children with insulin dependent diabetes mellitus have distinct insulin needs (Davis and Alonso, 2004). There is continuous need to create more rapid-acting insulin formulations similar to endogenous insulin secretion to provide efficient glycemic regulation without the risk of hypoglycemia and hyperglycemia (Davis and Alonso, 2004).

Several studies have been conducted to evaluate the use of multi-doses of insulin, there has been no guarantee evidence of its effect on glycemic control (Hoogma et al., 2006). Several reports demonstrated improvement with this regimen at the onset of diabetes or after switching from a twice daily to a multi-doses of insulin therapy regimen. Other studies, showed that switching to multi-doses either had no effect at all or made glycemic control worse (Kaiserman et al., 2017).

Wars influenced health services in Iraq generally and Mosul specifically, disrupting the healthcare system and compromising the glycemic control of children with diabetes (Odhaib et al., 2022). Even though multi-dose insulin regimens are widely regarded as the best way to manage insulin dependent patients (Rosnser and Roman-Urrestarazu, 2019). Its implementation in insulin dependent children in Iraq is not yet universal. In order to assess the effectiveness of each insulin regimen and determine any potential adverse effects, this study was carried out.

2. Materials & methods

This is retrospective cohort study included children and adolescents with insulin dependent who attended follow-up appointments at the Endocrinology unit, of Al Khansa'a Teaching Hospital in Mosul/Iraq, between April 2023 and December 2023. The clinic's records were used to identify every patient with insulin dependent diabetes mellitus.

All children and teenagers with insulin dependent diabetes mellitus had their current insulin regimen assessed. According to what their treating physician decided and discussed with their parents, the patients included were either on twice daily insulin or multiple doses of insulin. Short acting insulin and intermediate acting insulin (also known as neutral protamine Hagedorn, or NPH) were administered twice a day, once in the morning and once in the evening prior to meals. The multi-dose therapy included three daily doses of aspart, a rapid-acting insulin administered before meals, and one daily dose of long-acting insulin (glargine) after bedtime. While some patients receiving multiple doses started on a regimen at the time of diagnosis, others started on a twice-daily schedule and transitioned to multiple doses based on the doctor's suggestion and their parents' consent.

Every three months, each candidate was assessed. The study excluded participants who had a history of non-compliance, did not receive regular follow-up, or moved from twice to multi-insulin doses in less than three months. Notably, the dosage of insulin was adjusted or increased in people who attained puberty based on their glycemic state.

The hospital information system was used to retrieve clinical data, such as age, gender, height and weight measurements, and daily insulin dosage per kilogram of body weight. Records of individuals with co- occurring autoimmune disorders were obtained; they included autoimmune thyroid disease and celiac disease; two conditions linked to diabetes. The National Glycohemoglobin Standardization Program states that glycated hemoglobin levels (HbA1c) were determined using high-performance liquid chromatography and reported as HbA1c %.

HbA_{1c} levels were monitored routinely every three-four month for three successive reading. The mean was calculated for each patient to estimate the baseline HbA_{1c} and used for comparison. A target HbA_{1c} was set as less than 8 before puberty and fewer than 7.5 after puberty (Kharode, Coppedge and Antal, 2019).

The Nineveh Health Directorate provided ethical approval. Personal identifiers were not included in

the data. Additionally, participation was voluntary and responses were kept private.

The data was analyzed using SPSS, version 20. The number (percentage) and mean $\pm$ standard deviation (SD) was calculated for demographic data, and for HbA_{1c} values. The differences between categorical variables were assessed. A p value of <0.05 was considered as statistically significant.

3. Results

Sixty-nine children with type 1 diabetes were included in the study, with 36 (52%) males and 33 (48%) females. Age distribution included 29 (42%) as 10–15 years of age, 30 (44%) as 5–10 years of age, and 10 (14%) as <5 years of age. Out of 69 children, 43 (62%) were on multiple daily injections of insulin, while 26 (38%) were on twice daily dosing. There was significant drop in the HbA1c mean $\pm$ SD from baseline to follow up level in both groups: MDI group had HbA1c drop from 11.3 ± 1.7 at baseline to 8.1 ± 1.0 (p < 0.001), while BID group had HbA1c drop from 10.8 ± 1.7 at baseline to 8.5 ± 1.5 (p < 0.001). The drop in HbA1c was more evident in MDI group (drop of 3.2 ± 1.8 in MDI group compared to 2.3 ± 1.9) with a trend toward statistical significance, p value $= 0.069$.

There was no significant difference in reported hypoglycemia between the two groups: MDI group reported hypoglycemia in 29 out of 43 (67%) compared to 16 out of 26 (62%) in BID group, p $= 0.618$. Reported frequent hypoglycemia was also not significant between the two groups.

4. Discussion

Our study examines the differences in glycemic control between the BID insulin regimen and MDI regimen in children and adolescents with T1DM at one hospital in Mosul city, Iraq.

While MDI regimen is often regarded as the preferred option for treating pediatric T1DM patients [20] a lot of patients in Iraq and many other countries are not using this regimen yet [21].

Most of the patients attending our hospital had bad initial HbA1C level to begin with but within three months after the treatment plan was initiated, there was good improvement in overall control. As expected, this improvement was not as noticeable in the six-and nine-months follow-up. A potential reason could be that the initial treatment regimen starts with cause a sufficient satisfaction that the patient control. As expected, this improvement was not as noticeable in the six- and nine-months follow-up. A

potential reason could be that the initial treatment regimen starts with cause a sufficient satisfaction that the patient did his best, which then led to a decrease in compliance, as a result it's reflected in the improvement of the mean HbA1c at these two time points. Numerous studies have shown that multiple insulin therapy (as opposed to traditional twice-daily insulin therapy) improves glycemic control [22-26]. We found that patients on an MDI insulin regimen had a more frequent history of hypoglycemic episodes, however this difference was not statistically significant. Because of the small number of patients in the study and the history of hypoglycemia was not immediately detected via blood sugar monitoring; rather, it was only obtained from patient records. Also, there is more than one doctor in our consultation unit who follow, counsel and document the records. That's why these results might not apply to the whole population. Other studies have found that taking MDI results in more consistent glucose control and fewer hypoglycemic episodes [27]. This can be explained by the fact that glargine insulin has a fewer relative risk of hypoglycemia due to its flat profile of plasma insulin levels and lack of a noticeable peak of activity [28]. The benefits of the MDI insulin regimen have been discussed, however more frequent injections of insulin and blood glucose monitoring are still required. Consequently, in order to have better results, it is essential to properly educate the patient and their family. It is important to note that patients on an MDI regimen were taking their blood glucose levels about four times a day. However, because our study was retrospective in nature, complete records were not available, therefore this information was not directly evaluated. The main limitation on our results is the fact that this was an uncontrolled, retrospective, non-randomized study. Furthermore, it was not possible to evaluate compliance directly, which may have had an impact on the metabolic control that was being evaluated after beginning the MDI regimen. While daily carbohydrate consumption and dietary habits are significant factors to take into account when evaluating the impact of changing an insulin regimen, our study did not directly evaluate these variables.

5. Conclusion and recommendation

In summary, compared to a BID regimen, MDI regimen has favorable effects on the overall control of children and adolescents with T1DM, but to have more positive results, the MDI insulin regimen needs greater cooperation and understanding from patients and their families on this commitment to higher insulin injections and more frequent blood

glucose monitoring. Furthermore, MDI patients experienced fewer hypoglycemic episodes, however this was not statistically significant. Sadly, rapid-acting insulin (Aspart) and long-acting insulin (glargine) are not always available in hospital and centers dealing with diabetes as its price is not affordable to all patients' families, we recommend ministry of health provide more care and medications to these group of patients.

Conflict of interest

The authors report no conflict of interest concerning this study.

Acknowledgement

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