SJIF Impact Factor: 6.711

WORLD JOURNAL OF ADVANCE HEALTHCARE RESEARCH

ISSN: 2457-0400
Volume: 8.
Issue: 10
Page N. 172-176
Year: 2024

Original Article www.wjahr.com

COMPARATIVE STUDY BETWEEN BASAL BOLUS INSULIN REGIMEN VERSUS TWICE DAILY REGIMEN IN CHILDREN AND TEENAGERS WITH TYPE ONE DIABETES IN MOSUL CITY

Raghad T. Aziz, Nourhan T. Younis[2], Sarmad O. Rashid[3], Zakaria A. Kassim[4]* and Sharef W. Mulaabed[5]

[1]Pediatric Specialist, Al Khansa'a Hospital, Endocrine Consultation Unit, Mosul, Iraq.
[2]Paediatric Specialist, Al Khansa'a Hospital, Endocrine Consultation Unit, Mosul, Iraq.
[3]Paediatric Specialist, Al Khansa'a Hospital, Pediatric Consultation Unit, Mosul, Iraq.
[4]Family Medicine Specialist, Emergency Department Manager, Al Khansa'a Hospital, Mosul, Iraq.
[5]Paediatric Specialist, Arnold Palmer Hospital for Children, Orlando, Florida, United States.

Article Received date: 21 August 2024 **Article Revised date:** 11 Sept. 2024 **Article Accepted date:** 01 October 2024

***Corresponding Author: Zakaria A. Kassim**

Family Medicine Specialist, Emergency department manager, Al Khansa'a Hospital, Mosul, Iraq.

ABSTRACT

Objectives: To evaluate the glycemic control and to identify the possible side effects of multiple insulin regimen versus twice daily regimen among patients visited to endocrine consultation unit at Al Khansa'a Teaching Hospital in Mosul during 1st of January 2023 to the end of December 2023. **Methods:** this is a cohort comparative study. Patients' case sheets were reviewed to acquire the mandatory information. The questionnaire was composed of two parts, the first included demographic information of the patients and 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. Two third of the studied sample were on multiple daily injections of insulin and one third were on twice daily dosing. HbA1c mean was dropped from 10.8 ± 1.7 at baseline to 8.5 ± 1.5 ($p < 0.001$) in BID group, while it dropped from 11.3 ± 1.7 at baseline to 8.1 ± 1.0 ($p < 0.001$) in MDI group, which make MDI regimen had trend toward statistical significance in comparison to BID. 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. **Conclusion:** It has been demonstrated that multiple insulin regimen improves children and teenager's glycemic control, we recommend ministry of health to provide rapid-acting insulin (Aspart) and long-acting insulin (glargine) in hospital and centers dealing with diabetes as its price is not affordable to all patients' families.

KEYWORDS: Diabetes Mellitus, Pediatrics, Mosul city.

INTRODUCTION

Insulin-dependent diabetes, is a disease that frequently appears during childhood and adolescence. Because of pancreatic beta breakdown, the illness is characterized by a lack of insulin synthesis, making lifelong insulin therapy necessary for survival.[1] It is one of the prevalent chronic diseases that has a major burden to the patient and family.[2] International studies and systematic reviews have been demonstrated that the prevalence of type 1 diabetes mellitus among children under the age of 14 is estimated to be 500,000, and the yearly incidence is predicted to be 79,000 worldwide.[3] no recent study documenting clear Insulin-dependent diabetes incidence in Iraqi children.

Maintaining strict glycemic control is essential to postpone the start and reduce the development of complications associated with diabetes[4-6], that's why intensive insulin treatment is advised to attain this management.[7-9] Dietary attentiveness, frequent blood glucose testing, and numerous insulin injections required for successful diabetes management and to decrease the disease burden on patients and families.[10] 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.[11] Insulin glargine, a recombinant DNA-produced as a basal insulin analogue, with less side effects and a roughly 24-hour half-life of activity.[12-13]

In pediatric age patients, due to their increased weight, height, and caloric demands as they go through normal growth and development, children and adolescent with insulin dependent diabetes mellitus have distinct insulin needs.[14] There is continuous need to create more rapid-acting insulin formulations similar to endogenous insulin secretion to provide efficient glycemic regulation without the danger of hypoglycemia and hyperglycemia.[14]

Despite the fact that 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.[15] Numerous studies showed that this regimen improved outcomes when diabetes first appeared or when moving 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.[16]

Wars influenced health services in Iraq generally and Mosul specifically, disrupting the healthcare system and compromising the glycemic control of children with diabetes.[17] Even though muti-doses insulin regimens are widely regarded as the best ways to manage insulin dependent patients.[18] In order to assess the effectiveness of each insulin regimen and determine any potential adverse effects, this study was carried out.

MATERIALS AND METHODS

Children and adolescents with insulin dependent diabetes mellitus who attended follow-up appointments at the endocrinology consultation unit at Al Khansa'a Teaching Hospital in Mosul, Iraq, between January 2023 and December 2023 were included in this cohort comparative study. 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 %.

HbA1c levels were consistently checked for three consecutive months at intervals of three to four months. To determine the baseline HbA1c for each patient, the mean was computed and utilized as a benchmark. According to the clinical practice guidelines of the Nelson Textbook of Pediatrics, a goal HbA1c was set at less than 8 before puberty and fewer than 7.5 after puberty.[19]

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 26. The number (percentage) and mean ± standard deviation (SD) was calculated for demographic data, and for HbA_{1c} values. The differences between categorical variables were assessed by Chi–squared ($\chi 2$) test. A p value of < 0.05 was considered as statistically significant.

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 +/- 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.

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 (more than 10) but within three months after the treatment plan was initiated, there was significant 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 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.

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.

ACKNOWLEDGEMENT

We appreciate the assistance offered by the medical staff at Al Khansa'a Teaching Hospital and the thorough attention the Nineveh Directorate of Health gave to our study project. Without the help of each of these individuals, this study would not have been feasible.

Conflict of Interest

The authors report no conflict of interest concerning this study.

REFERENCES

1. Kakleas K, Soldatou A, Karachaliou F, Karavanaki K. Associated autoimmune diseases in children and adolescents with type 1 diabetes mellitus (T1DM). Autoimmunity reviews, 2015 Sep 1; 14(9): 781-97.
2. Sav A, King MA, Whitty JA, Kendall E, McMillan SS, Kelly F, Hunter B, Wheeler AJ. Burden of treatment for chronic illness: a concept analysis and review of the literature. Health Expectations, 2015 Jun; 18(3): 312-24.
3. Patterson C, Guariguata L, Dahlquist G, Soltész G, Ogle G, Silink M. Diabetes in the young–a global view and worldwide estimates of numbers of children with type 1 diabetes. Diabetes research and clinical practice, 2014 Feb 1; 103(2): 161-75.
4. Davidson JA. Treatment of the patient with diabetes: importance of maintaining target HbA1c levels. Current medical research and opinion, 2004 Dec 1; 20(12): 1919-27.
5. Vasudevan AR, Burns A, Fonseca VA. The effectiveness of intensive glycemic control for the prevention of vascular complications in diabetes

mellitus. Treatments in endocrinology, 2006 Oct; 5: 273-86.
6. Hahr AJ, Molitch ME. Management of diabetes mellitus in patients with chronic kidney disease. Clinical diabetes and endocrinology, 2015 Dec; 1(1): 1-9.
7. DAFNE Study Group. Training in flexible, intensive insulin management to enable dietary freedom in people with type 1 diabetes: dose adjustment for normal eating (DAFNE) randomised controlled trial. Bmj, 2002 Oct 5; 325(7367): 746.
8. Griesdale DE, de Souza RJ, van Dam RM, Heyland DK, Cook DJ, Malhotra A, Dhaliwal R, Henderson WR, Chittock DR, Finfer S, Talmor D. Intensive insulin therapy and mortality among critically ill patients: a meta-analysis including NICE-SUGAR study data. Cmaj, 2009 Apr 14; 180(8): 821-7.
9. Ilkova H, Glaser B, Tunçkale A, Bagriaçik N, Cerasi E. Induction of long-term glycemic control in newly diagnosed type 2 diabetic patients by transient intensive insulin treatment. Diabetes care, 1997 Sep 1; 20(9): 1353-6.
10. American Diabetes Association. Standards of medical care in diabetes—2015 abridged for primary care providers. Clinical diabetes: a publication of the American Diabetes Association, 2015 Apr; 33(2): 97.
11. RAJARAMAN MM. Therapeutics POSTERS.
12. Vajo Z, Fawcett J, Duckworth WC. Recombinant DNA technology in the treatment of diabetes: insulin analogs. Endocrine reviews, 2001 Oct 1; 22(5): 706-17.
13. McKeage K, Goa KL. Insulin glargine: a review of its therapeutic use as a long-acting agent for the management of type 1 and 2 diabetes mellitus. Drugs, 2001 Sep; 61(11): 1599-624.
14. Davis S, Alonso MD. Hypoglycemia as a barrier to glycemic control. Journal of Diabetes and its Complications, 2004 Jan 2; 18(1): 60-8.
15. Hoogma, R.P.L.M., Hammond, P.J., Gomis, R., Kerr, D., Bruttomesso, D., Bouter, K.P., Wiefels, K.J., De La Calle, H., Schweitzer, D.H., Pfohl, M. and Torlone, E., Comparison of the effects of continuous subcutaneous insulin infusion (CSII) and NPH-based multiple daily insulin injections (MDI) on glycaemic control and quality of life: results of the 5-nations trial. Diabetic Medicine, 2006; 23(2): 141-147.
16. Kaiserman K, Jung H, Benabbad I, Karges B, Polak M, Rosilio M. 20 Years of insulin lispro in pediatric type 1 diabetes: a review of available evidence. Pediatric diabetes, 2017 Mar; 18(2): 81-94.
17. Odhaib SA, Mansour AA, Khalifa SF, Shegem N, Thannon W, Abi Saad M, Abdulrazaq H, Belkhadir J, Sandid M, Masood SN. Impact of humanitarian crises on diabetes care in Iraq and Syria—IDF-MENA region. Journal of Diabetology, 2022 Dec 1; 13(Suppl 1): S38-47.
18. Rosner B, Roman-Urrestarazu A. Health-related quality of life in pediatric patients with Type 1 diabetes mellitus using insulin infusion systems. A systematic review and meta-analysis. PloS one, 2019 Jun 25; 14(6): e0217655.
19. Kharode I, Coppedge E, Antal Z. Care of children and adolescents with diabetes mellitus and hyperglycemia in the inpatient setting. Current Diabetes Reports, 2019 Oct; 19: 1-0.
20. Malik FS, Taplin CE. Insulin therapy in children and adolescents with type 1 diabetes. Pediatric Drugs, 2014 Apr; 16: 141-50.
21. Almotawa AA. Prevalence and Risk Factors of Diabetes and Insulin Resistance in Patients Attending a Health Care Centre in Kuwait, and the Accuracy of a Point of Care Device to Measure Glycated Haemoglobin to Monitor Patients with Diabetes. The University of Liverpool (United Kingdom); 2018.
22. Riddle MC, Rosenstock J, Vlajnic A, Gao L. Randomized, 1-year comparison of three ways to initiate and advance insulin for type 2 diabetes: twice-daily premixed insulin versus basal insulin with either basal-plus one prandial insulin or basal-bolus up to three prandial injections. Diabetes, Obesity and Metabolism, 2014 May; 16(5): 396-402.
23. Raskin P, Bode BW, Marks JB, Hirsch IB, Weinstein RL, McGill JB, Peterson GE, Mudaliar SR, Reinhardt RR. Continuous subcutaneous insulin infusion and multiple daily injection therapy are equally effective in type 2 diabetes: a randomized, parallel-group, 24-week study. Diabetes care, 2003 Sep 1; 26(9): 2598-603.
24. Janka HU, Plewe G, Riddle MC, Kliebe-Frisch C, Schweitzer MA, Yki-Järvinen H. Comparison of basal insulin added to oral agents versus twice-daily premixed insulin as initial insulin therapy for type 2 diabetes. Diabetes care, 2005 Feb 1; 28(2): 254-9.
25. Shimizu H, Monden T, Matsumura M, Domeki N, Kasai K. Effects of twice-daily injections of premixed insulin analog on glycemic control in type 2 diabetic patients. Yonsei medical journal, 2010 Nov 11; 51(6): 845.
26. Liu J, Jiang X, Xu B, Wang G, Cui N, Zhang X, Liu J, Mu Y, Guo L. Efficacy and safety of basal insulin-based treatment versus twice-daily premixed insulin after short-term intensive insulin therapy in patients with type 2 diabetes mellitus in China: study protocol for a randomized controlled trial (BEYOND V). Advances in Therapy, 2020 Apr; 37: 1675-87.
27. Olafsdottir AF, Polonsky W, Bolinder J, Hirsch IB, Dahlqvist S, Wedel H, Nyström T, Wijkman M, Schwarcz E, Hellman J, Heise T. A randomized clinical trial of the effect of continuous glucose monitoring on nocturnal hypoglycemia, daytime hypoglycemia, glycemic variability, and hypoglycemia confidence in persons with type 1 diabetes treated with multiple daily insulin injections (GOLD-3). Diabetes Technology & Therapeutics, 2018 Apr 1; 20(4): 274-84.

28. Mathieu C, Gillard P, Benhalima K. Insulin analogues in type 1 diabetes mellitus: getting better all the time. Nature Reviews Endocrinology, 2017 Jul; 13(7): 385-99.