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Original Research Article

A COMPARATIVE ANALYSIS OF NPH + R INSULIN VS. G + R INSULIN IN PEDIATRIC DIABETES: IMPACT ON ANTHROPOMETRIC MEASURES AND GLYCEMIC CONTROL

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ABSTRACT

Background: Diabetes mellitus presents unique challenges in Pediatric populations, necessitating careful consideration of insulin regimens. This study aims to compare the effects of neutral protamine Hagedorn (NPH) combined with regular insulin (R) versus glargine (G) with regular insulin on anthropometric measures and glycemic control in children with type 1 diabetes mellitus (T1DM).

Materials and Methods: In a prospective, comparative study conducted at SVS Medical College, Mahabubnagar, 50 pediatric patients aged 2-18 years with T1DM were randomized to receive either NPH + R (n=28) or G + R (n=22) insulin for six months. Baseline and follow-up assessments included weight, height, body mass index (BMI), and HbA1C levels. Paired t-tests were used to compare changes within each group.

Results: Patients on NPH + R exhibited significant weight gain (26.7 kg to 28.3 kg, p=0.001) and height increase (128.9 cm to 131.7 cm, p<0.001), while BMI changes were not significant (15.1 to 15.4, p=0.239). The HbA1C level decreased from 10.7% to 9.6% (p=0.023). Conversely, the G + R group showed no significant changes in weight (30.9 kg to 31.7 kg, p=0.123), height (140.9 cm to 139.0 cm, p=0.679), or BMI (15.9 to 15.8, p=0.875), but significant reductions in HbA1C (10.4% to 9.3%, p<0.001) were observed.

Conclusion: This study demonstrates that NPH + R insulin is associated with significant increases in weight and height compared to G + R insulin, which, while effective for glycemic control, does not impact growth parameters. These findings suggest that insulin regimen choice in pediatric diabetes management should consider both metabolic control and growth outcomes.

Keywords: Type 1 Diabetes mellitus, Insulin Regimens, Pediatric Endocrinology, Glycemic Control, Anthropometric Measures, NPH Insulin, regular, glargine.

INTRODUCTION

Diabetes mellitus is the most common endocrine disorder, with Type 1 diabetes mellitus (T1DM) being the leading chronic form of diabetes in children. Type 1 diabetes (T1DM) is a disorder of glucose homeostasis.[1] It is characterized by chronic hyperglycemia due to autoimmune destruction of pancreatic beta cells, leading to insufficient insulin secretion and resulting in abnormal metabolism of carbohydrates, fats, and proteins.[2]

T1DM accounts for approximately 10% of all diabetes cases. In 2017, the Diabetes Atlas estimated that 128,500 children and adolescents in India have T1DM,[3] with a prevalence of approximately 0.5 per 1000 in the Indian population.[4] Globally, more than 500,000 children under 18 are affected by T1DM, with an annual incidence increasing by 3-4%,[5,6] indicating a growing global health challenge. Managing T1DM in children presents unique challenges distinct from adult care, owing to differences in epidemiology, pathophysiology, and treatment responses that are further complicated by children's growth and developmental needs

Impaired growth is a recognized complication of pediatric diabetes, with studies emphasizing the need for optimal metabolic control to prevent stunted growth and other developmental issues. There is also evidence of abnormalities in the hypothalamic-pituitary-growth hormone axis, particularly in patients with poor glucose control or longer disease duration.[7]

The choice of insulin regimen is critical in managing pediatric diabetes. Traditional regimens, such as neutral protamine Hagedorn (NPH) insulin combined with regular insulin (NPH + R), have long been used. However, newer insulin analogues, such as glargine in combination with regular insulin (basal-bolus regimen: G + R), offer improved pharmacokinetics and greater convenience. Despite this, evidence comparing these regimens in children remains limited.[8]

Our study seeks to address this gap by comparing the NPH + R insulin regimen with the G + R regimen in the management of pediatric diabetes. In addition to evaluating glycemic control, we will examine the impact of these regimens on anthropometric parameters—specifically weight, height, and body mass index (BMI)—over a six-month follow-up period. These outcomes are crucial for both metabolic stability and normal growth in young patients, and the findings could provide important insights for optimizing diabetes care in this population.

Aims

To compare weight, height, BMI changes, and glycemic control between pediatric diabetes patients receiving NPH + R insulin and those receiving G + R insulin.

Objectives

1. To measure and compare the mean weight and height of pediatric patients before and after six months of treatment with NPH + R insulin and G + R insulin.
2. To calculate and compare the mean BMI of patients on NPH + R insulin and G + R insulin at baseline and after six months.
3. To measure and compare the HbA1C levels of patients in both the NPH + R insulin group and the G + R insulin group before and after six months of treatment.

MATERIALS AND METHODS

Study Design: This prospective, comparative study was conducted in the Pediatrics department, SVS Medical College, Mahabubnagar, from Jan 2023 to June 2024.

Participants

We enrolled a total of 50 Pediatric patients diagnosed with type 1 diabetes according to the criteria of the ISPAD 2018. (2) Patients were recruited from our Pediatric endocrinology clinic at SVS Medical College and Hospital.

Inclusion Criteria: Patients with T1D M on regular insulin therapy for at least three months before enrolment, aged between 2 and 18 years, and diagnosed for at least 6 months were included in the study.

Exclusion Criteria: Patients with associated medical conditions such as celiac disease or autoimmune thyroiditis, patients with other types of diabetes mellitus, liver disease, kidney disease.

Randomization and Intervention

Randomization: Patients were randomly assigned to either the NPH + R or G + R insulin group using computer-generated random numbers. Allocation concealment was ensured through sealed envelopes.

Insulin Regimens: The NPH + R insulin group (n = 26) received a combination of neutral protamine Hagedorn insulin (NPH) and regular insulin (R). The G + R insulin group (n = 24) received a combination of glargine insulin (G) and regular insulin(R). Insulin doses were adjusted based on individual patient needs and glycemic control targets.

All participants were asked to refrain from substantial changes in their lifestyle habits including food supplements and heavy exercise in the course of the study.

Data Collection

Baseline Assessment: Detailed medical history was obtained regarding demographic data, age of onset of diabetes, disease duration, and history of complications, if any. A thorough physical examination was done including anthropometric measurement- weight in kilograms (kg) and height in centimetres (cm) were recorded and body mass index (BMI) was calculated. HbA1C levels were measured using standardized laboratory assays.

Follow-Up Visits: All the patients were followed monthly during the study period for six months. Health education was provided during each visit. Weight was measured every month and height was measured after 6 months. HbA1C levels were assessed every 3 months. Adverse events and hypoglycemic episodes were documented.

Statistical Analysis

Sample Size Calculation: Our sample size of 50 patients was determined based on a power analysis, aiming for 80% power to detect a clinically significant difference in HbA1C levels between the two insulin regimens.

Statistical Tests: Descriptive statistics (mean, standard deviation) were used to summarize continuous variables. Paired t-tests were used to compare changes within each group (baseline vs. follow-up). The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, a p-value < 0.05 was considered statistically significant.

Ethical Approval: The Institutional Ethical Committee at SVS Medical College, Mahabubnagar approved the study protocol. Informed consent was obtained from all participants or their legal guardians.

Limitations: Our study was limited by the relatively small sample size and the single-centre design. Compliance with insulin regimens was self-reported and subject to recall bias.

RESULTS

In our study, 26 children (52%) were treated with NPH and regular insulin (split-mix regimen, NPH + R) and 24 children (48%) with glargine and regular insulin (basal-bolus regimen, G + R). We compared the weight, height, and glycemic control at the beginning and 6 months of follow-up. (Table 1)

The mean age of the children was 11.52±4.12 years; 26 (52%) were females and 24 (48%) were males. 30 (60%) children were from rural backgrounds and 20 (40%) belonged to urban areas.

Weight: In this six-month follow-up study comparing NPH + R insulin with G + R insulin in Pediatric diabetes patients, we observed distinct weight-related outcomes. Patients receiving NPH + R insulin exhibited a statistically significant increase in weight, with a mean change from 26.7 kg (baseline) to 28.3 kg after six months (p = 0.001). Notably, this weight gain suggests that the NPH + R regimen is associated with substantial increases in body weight within this patient group. Conversely, patients on the G + R insulin regimen did not experience a statistically significant weight change. The mean weight at baseline was 30.9 kg, which remained relatively stable at 31.7 kg after six months (p = 0.123). These findings highlight the differential impact of insulin regimens on weight dynamics in pediatric diabetes management.

Height: The mean baseline height in the patients in NPH + R insulin group was 128.9 cm (SD: 22.6). Patients receiving NPH + R insulin experienced a significant increase in height, with a mean height of 131.7 cm (SD: 22.2) after six months (p < 0.001). This suggests that the NPH + R regimen may positively influence growth in height during the study duration. Patients in the G + R insulin group had a mean baseline height of 140.9 cm (SD: 28.8). There was no statistically significant change in height for patients on the G + R insulin regimen. The mean height remained relatively stable at 139.0 cm (SD: 23.1) after six months (p = 0.679).

Body Mass Index (BMI): In the NPH + R Insulin Group, the mean BMI at baseline was 15.1 (SD: 2.6). There was slight increase in BMI, with a mean BMI of 15.4 (SD: 2.4) after six months. However, this change was not statistically significant (p = 0.239). Therefore, while there was weight gain, it did not substantially alter BMI in this group. Patients in the G + R insulin group had a mean baseline BMI of 15.9 (SD: 2.5). The mean BMI remained stable at 15.8 (SD: 2.4) after six months (p = 0.875).

HbA1C Levels: Patients in the NPH + R Insulin group had a mean baseline HbA1C of 10.7% (SD: 2.0). There was a significant reduction in HbA1C levels, with a mean of 9.6% (SD: 2.1) after six months (p = 0.023). This improvement indicates enhanced glycemic control associated with the NPH + R regimen. Patients in the G + R Insulin group had a mean baseline HbA1C of 10.4% (SD: 1.9). These patients also had a statistically significant reduction in HbA1C levels. The mean HbA1C decreased to 9.3% (SD: 1.2) after six months (p < 0.001), demonstrating effective glycemic control with this regimen.

Table 1: Comparison of Anthropometric Changes and Glycemic Control Between NPH + R Insulin regimen and G + R Insulin regimen: 6-Month Follow-Up

Variable	Regimen	Baseline (Mean±SD)	After 6 months (Mean±SD)	P value (paired t-test)
Weight	NPH+R	26.7±11.6	28.3±11.5	Significant p =0.001
	G+R	30.9±11.7	31.7±11.4	p=0.123
Height	NPH +R	128.9±22.6	131.7±22.2	Significant p < 0.001
	G+ R	140.9±28.8	139± 23.1	p = 0.679
BMI	NPH +R	15.1± 2.6	15.4±2.4	p =0.239
	G+R	15.9± 2.5	15.8±2.4	p = 0.875
HbA1C	NPH +R	10.7±2	9.6±2.1	Significant p = 0.023
	G+R	10.4 ±1.9	9.3± 1.2	Significant p < 0.001

DISCUSSION

Diabetes mellitus is the most prevalent endocrine disorder and one of the most common chronic diseases in children.[1] According to the International Diabetes Federation's 2015 report, India ranks second globally in the number of children living with type 1 diabetes mellitus (T1DM). The estimated prevalence of T1DM in India is 10.2 cases per 100,000 children.[9] Among children aged 5–16, the current prevalence is reported at 22.2 per 100,000. The mortality rate from diabetic ketoacidosis (DKA) in India is alarmingly high at

13.2%, compared to 0.15–0.31% in developed countries.[10]

In recent years, the incidence of T1DM has been increasing by approximately 3–5% annually. As an autoimmune disease, T1DM is characterized by the gradual destruction of pancreatic beta cells, leading to decreased insulin production and the eventual onset of insulin-dependent diabetes mellitus.[11]

The management of T1DM requires a lifelong commitment to daily insulin injections, regular blood sugar monitoring, adherence to a proper diet, and maintaining physical activity. The primary goal of insulin therapy is to mimic physiological insulin patterns as closely as possible. Effective glycemic control is critical, as it influences the quality of life, the risk of complications, and the overall progression of the disease.

This study compared the effects of NPH + R insulin versus G + R insulin on weight, height, BMI, and glycemic control in pediatric patients over six months. Our findings revealed notable differences between the two regimens, offering valuable insights into their relative efficacy in managing growth and blood sugar levels.

Patients receiving the NPH + R regimen showed significant increases in both weight and height over the study period. These findings contrast with the results from a study by Parthasarathy et al., which involved 160 children with T1DM. Their research indicated that children on basal-bolus therapy achieved better metabolic control and higher growth velocity compared to those on the split-mix regimen (HbA1c 8.4 ± 1.7% vs. 9.0 ± 1.8%; growth velocity 0.5 ± 1.6 vs. -0.3 ± 1.4, respectively).[12]

Despite the significant weight gain, BMI changes in the NPH + R group were not statistically significant. This stability in BMI suggests that while weight increased, body composition may have shifted, highlighting the nuanced effects of different insulin regimens. Similar observations were reported by Hassan K et al.[13]

A notable reduction in HbA1c levels was seen in the NPH + R group, indicating improved glycemic control. This is consistent with findings from Rostami P et al.[8] Similarly, the G + R regimen also led to a significant reduction in HbA1c levels, corroborating results from Donepudi A et al.[14] Both regimens demonstrated effectiveness in controlling blood glucose, though their impact on growth and weight varied.

CONCLUSION

This study highlights that while combination of neutral protamine Hagedorn insulin and regular insulin (NPH + R) and glargine in combination with regular insulin (G + R) are effective in managing glycemic control, they have distinct effects on weight, height, and BMI. NPH + R insulin is associated with significant weight and height increases, while G + R insulin does not significantly affect these parameters but also achieves substantial improvements in glycemic control. These findings suggest that the choice of insulin regimen may need to be tailored based on individual patient needs, considering both metabolic control and growth outcomes.

REFERENCES

1. Urbano F, Farella I, Brunetti G, Faienza MF. Pediatric Type 1 Diabetes: Mechanisms and Impact of Technologies on Comorbidities and Life Expectancy. International Journal of Molecular Sciences. 2023; 24(15):11980. https://doi.org/10.3390/ijms241511980.
2. Mayer-Davis EJ, Kahkoska AR, Jefferies C, Dabelea D, Balde N, Gong C, Aschner P, Craig M (2018) ISPAD Clinical Practice Consensus Guidelines 2018: definition, epidemiology, and classification of diabetes in children and adolescents. Pediatr Diabetes 19(27):7–19. https://doi.org/10.1111/pedi.12773 18. World Health Organization (2006) Department of Nutrition.
3. Pavadigoudra MK, Sajjanar SB, Uday K, Ushakiran CB. Assessment of growth among children with type 1 diabetes mellitus. Int J Contemp Pediatr 2024; 11:1057-60.
4. Gupta, P., Sharma, R. Glycemic Control in Indian Children and Adolescents with Type 1 Diabetes Mellitus. Indian J Pediatr (2024). https://doi.org/10.1007/s12098-024-05252-5
5. Alkarani T Patil, Rajashekara Murthy GR, Hema GR. A study on glycemic control and related complications in type I diabetic children. Pediatr Rev: Int J Pediatr Res 2015; 2(4): 128-134.doi:10.17511/ijpr.2015.4.018.
6. Habteyohans BD, Hailu BS, Meseret F, Mohammed A, Berhanu Y, et al. Poor glycemic control and its associated factors among children with type 1 diabetes mellitus in Harar, eastern Ethiopia: A cross-sectional study. BMC Endocr Disord. 2023 Sep 28; 23(1):208. doi: 10.1186/s12902-023-01453-9. PMID: 37759193; PMCID: PMC10538014.
7. VV, Parthasarathy LS, Mallade BB, Khadilkar AV, Chiplonkar SA, Borade AB. Growth status of children and adolescents with type 1 diabetes mellitus. Indian J Endocr Metab 2013; 17:1057-60.
8. Rostami P Md, Setoodeh A Md, Rabbani A Md, Nakhaei-Moghadam M Md, Najmi-Varzaneh F Md, Rezaei N Md PhD. A Randomized Clinical Trial of Insulin Glargine and Aspart, Compared to NPH and Regular Insulin in Children with Type 1 Diabetes Mellitus. Iran J Pediatr. 2014; 24(2):173-178.
9. Lohiya NN, Kajale NA, Lohiya NN, et al. Diabetes distress in Indian children with type 1 diabetes mellitus and their mothers. Journal of Pediatric Endocrinology & Metabolism: JPEM. 2021 Feb; 34(2):209-216. DOI: 10.1515/jpem-2020-0339. PMID: 33180040.
10. Ayyavoo A, Ravikulan A, Palany R. Treatment of diabetic ketoacidosis with subcutaneous regular insulin in a non-ICU setting is effective and economical: A single-centre experience. J Pediatr Endocrinol Diabetes 2022; 2:50-5.
11. Santi E, Tascini G, Toni G, Berioli MG, Esposito S. Linear Growth in Children and Adolescents with Type 1 Diabetes Mellitus. Int J Environ Res Public Health. 2019; 16(19):3677. Published 2019 Sep 30. doi:10.3390/ijerph16193677.
12. Parthasarathy, L., Khadilkar, V., Chiplonkar, S., & Khadilkar, A. (2016). Longitudinal Growth in Children and Adolescents with Type 1 Diabetes. Indian pediatrics, 53(11), 990–992. https://doi.org/10.1007/s13312-016-0974-1.
13. Hassan, K., Rodriguez, L. M., Johnson, S. E., Tadlock, S., & Heptulla, R. A. (2008). A randomized, controlled trial comparing twice-a-day insulin glargine mixed with rapid-acting insulin analogs versus standard neutral protamine Hagedorn (NPH) therapy in newly diagnosed type 1 diabetes. Pediatrics, 121(3), e466–e472. https://doi.org/10.1542/peds.2007-1679.
14. Donepudi A, Donepudi HS, Ayyagari M. Insulin usage and practices in children and adolescents with type 1 diabetes. Indian J Endocr Metab 2021; 25:38-42.