

Glycemic Control for Type 1 Diabetic Children on Multiple Daily Insulin Therapy Tripoli Children Hospital

Faten BenRajab^{1,2@}, Salha Gliwan^{1,2} and Asma Moktar¹

Pediatric endocrin Unit, Tripoli Children Hospital, Libya

Department of Pediatric, Faculty of Medicine, University of Tripoli- Libya

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ABSTRACT

Diabetes is a the most common chronic endocrine disorder of childhood; the management of type 1 DM has changed dramatically over the past 30 years; to maintain near-normal glycaemia.

The aim of study to compare two different strategies of insulin therapy ; twice daily insulin and multiple daily injections by assessment of patient's growth, level of HbA1c and occurrence of acute complications. A prospective study includes patients who were diagnosed as T1DM for at least 1 year at endocrine clinic in Tripoli children's hospital (2006-2007). 20 Patients who were on conventional therapy (twice daily insulin injections) for ≥ 1 year and changed to MDI before our study were reviewed; 30 patients who on twice daily injections with poor diabetic control ($HbA1c > 9$) were switched to MDI, then all (50 patients) followed up for 1 year to compare between HbA1c results, growth parameters & occurrence of acute complications before and after 1 year of MDI therapy.

The age of patients at the time of diagnosis of DM ranged from 2-16 yrs old with mean $8.2 (\pm 3.2)$ years, 88% of patients were on twice daily therapy for about 1-6 years before we switch them to MDI; mean age at starting MDI $13 (\pm 2.4)$ years. After one year of follow up we assess the growth of patients; we found 70% of them have normal weight, 24% were under weight and 6% were overweight. Regarding HbA1c we found 2% of patients who were on conventional therapy had good glycemic control ($HbA1c < 7\%$) raised to 26% after one year on MDI. 30% of conventional therapy had accepted control ($HbA1c 7-9\%$) which raised to 56% after one year on MDI and 68% of those on conventional therapy had poor glycemic control ($HbA1c > 9\%$), which reduced markedly to 18% on MDI for one year; it was statistically significant P value < 0.001 . 26% of patients on conventional insulin therapy had attacks of hypoglycemia reduced to only 2% after 1 year on MDI, occurrence of DKA: 14% of patients on conventional insulin therapy were suffered from DKA episodes and no episode of DKA recorded after one year therapy on MDI therapy.

We concluded most of our patients who were receiving MDI have better growth, good glycemic control & less occurrence of hypoglycemia and diabetic ketoacidosis.

Key words- MDI in Libyan children; Insulin in type 1 DM; HbA1c after MDI.

INTRODUCTION

Diabetes Mellitus is a complex disorder with profound consequences and is the most common chronic endocrine disorder of childhood, characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both.

The management of Type 1 DM has changed dramatically over the past 30 years in particular, new insulin strategies have improved the ability to maintain near- normal glycaemia.⁵

Treatment strategies:

To reach physiological insulin replacement with subcutaneous injections of insulin by definition very difficult. The more sophisticated the treatment regimen, the more closely can physiological insulin release be

mimicked with new treatment options like insulin pump and basal-bolus therapy. This goal can possibly be reached in better way.¹

Twice daily split and mixed insulin regimen: Rapid or short acting insulin combined with intermediate acting insulin administered before breakfast and before evening meal; beyond remission period, it is not generally possible to achieve near- normal glycaemia with two injections per day¹.

Basal- bolus regimens:

Insulin therapy with at least 3-4 injections each day can move closely simulate normal insulin profiles and permit greater flexibility with respect to timing and content of meals.²

Continuous subcutaneous insulin infusion (pump therapy).²



The optimal glycemic control in Type I DM requires intensive insulin therapy as suggested by Diabetes control and complications trial (DCCT) which showed 34-70% reduction in clinically diabetic micro vascular complications in patients randomized to intensive diabetes therapy compared to patients assigned to standard diabetes management¹⁰.

This study aimed to compare two different strategies of insulin therapy (twice daily insulin & multiple daily injections) by assessment of patient's growth parameters, level of HbA1c and occurrence of acute complications before & after one year of MDI therapy.

MATERIALS AND METHODS

A prospective study includes the patients who were diagnosed as T1DM for at least 1 year at endocrine clinic in Tripoli Children's Hospital (2006-2007). 20 Patients who were on twice daily insulin injections; regular with NPH or Mixtarad Insulin (conventional therapy), and changed to multiple daily injections (MDI) before our study were reviewed. 30 patients who on twice daily injections with poor diabetic control (HbA1c > 9) were switched to MDI, 3 doses of Premeal insulin (Regular insulin) and 2 doses of basal insulin as NPH or 1 dose as Glargine; then All (50 patients) followed up for 1 year to compare between HbA1c results, growth parameters by using growth charts And occurrence of acute complications before MDI & after 1 year of MDI therapy. Insulin dose was 0.7-1.5 u/kg/day according to requirement of individual patient and dietary advice was given at most of clinic visits.

Data were analyzed according to Wt., Ht. BMI (According to CDC a BMI over 95th percentile indicates overweight, between 85th and 95th percentile is risk of overweight & below the 5th percentile is underweight)³. HbA1C; we considered HbA1c < 7% good control, 7 - 9 accepted control, > 9 poor control. and occurrence of hypoglycemia (either symptomatic or if BS < 70 mg/dl) or DKA. Statistically by using SPSS (P. value < 0.05).

RESULTS

The total number of patients in our study were 50 patients, the age of patients at the time of diagnosis of DM ranged from 2-16yrs old with mean = 8.2 ± 3.2 years, the majority of our patients age ranged from 5-13yrs old, only 2% of them aged between 14-16yrs old which can be explained by a tendency of these patients to attend adults diabetic clinic instead of the pediatric clinic (Figure 1).

Figure 2 showed 48% of our patients had DM for 1-4 years and another 48% for 5-8 years, only 4% had DM for long period (9-12 years). Distribution of patients according to duration of twice daily therapy (Figure 3), we found 46% of our patients were on conventional therapy for 1-3 years, another 42% for 4-6 years and 2% for about 10-12 years. So about 88% of patients were on twice daily therapy for about 1-6 years before switching them to MDI.

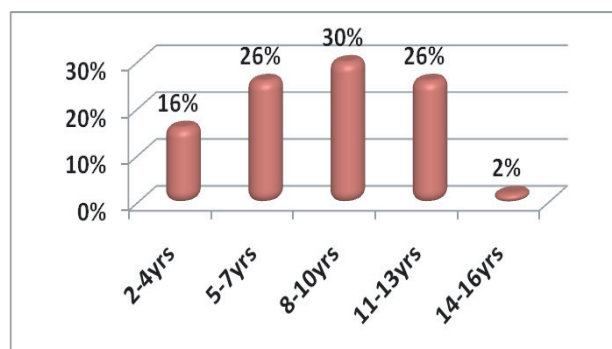


Figure 1: Age of patients at presentation of diabetes

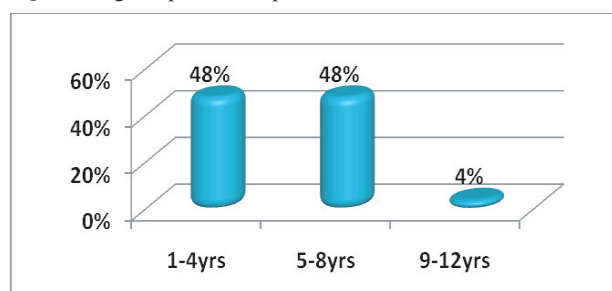


Figure 2: Distribution of patients according to diabetes duration

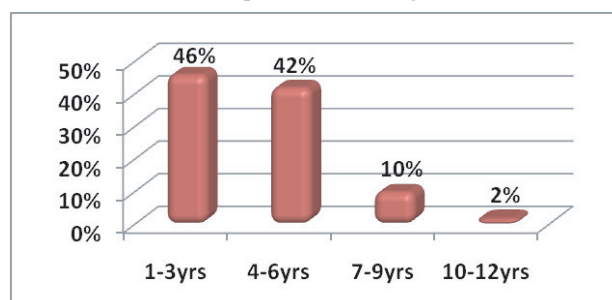


Figure 3: Distribution of patients on twice daily insulin according to diabetes duration

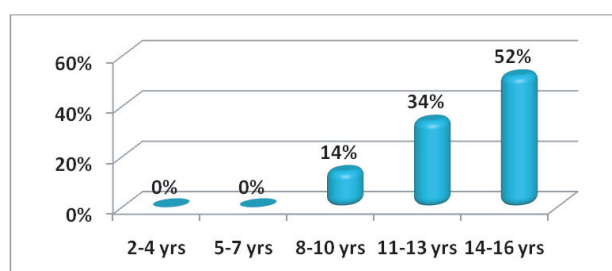


Figure 4: Distribution of age at starting MDI

Age at starting MDI (Figure 4), patients were distributed in 2 groups, 1st group includes patients aged from 2-7 years (younger age group) and they were on twice daily therapy not on MDI. The other group on MDI includes patients who were > 7 years old with mean 13 (± 2.4) years. Duration of MDI therapy (Figure 5), 40% of patients were already on MDI for a period ranged from 2-5 years, another 60% of them switched to MDI, then all followed for about 1 year.

About growth (Figure 6) BMI charts showed 70% of our patients (on MDI) have normal Wt, 24% were



under Wt. 6% were over Wt.; Unfortunately we could not get BMI for patients while they were on twice daily therapy because our data lack of height measurement. We found 2% of patients on twice daily have good glycemic control (HbA1c < 7%) which raised to 26% on MDI, 30% of patients have accepted control (HbA1c 7-9%) on conventional therapy which raised to 56% on MDI, 68% of our patients on twice daily therapy have poor glycemic control (HbA1c > 9%), which reduced markedly to 18% on MDI (Figure 7); The difference between means of HbA1c of patients in each group is statistically significant P value < 0.001. Occurrence of hypoglycemia (Figure 8) 26% of patients on twice daily therapy had attacks of hypoglycemia reduced to only 2% on MDI. Occurrence of DKA (Figure 9) 14% of patients while on twice daily therapy were suffered from DKA, but no any patients after switched on MDI suffered from DKA.

DISCUSSION

The incidence of type 1DM is rapidly increasing in specific regions, the rate of increase is greatest among the youngest children.

In the USA, the overall prevalence of diabetes among school aged children is about 1.9/1000, increasing from a prevalence of 1/1430 at 5 years of age to 1/360 children at 16 years.³

In our study we found the age of patients at the time of diagnosis ranged from 2 to 16 years old with mean 8.2 ± 3.2 years, 16% diagnosed on age 2 to 4 years, 26% diagnosed on age 5 to 7 years and 30% diagnosed at age 8 to 10 years, 26% diagnosed at age 11 to 13 years, this mean that DM increase in frequency with age, also these results achieved by Kadiki et al (1991-2002).⁴

However only 2% of our patients presented at 14 to 16 years, this can be explained by a tendency of those patients to attend adult diabetic clinic instead of the pediatric clinic.

Insulin regimens: The conventional insulin therapy (Twice daily injections regular with NpH or Mixtarad Insulin) usually works adequately while endogenous insulin is still being produced, as more complete insulin deficiency develops this regimen becomes less effective and we need intensive therapy (Multiple Daily Injection) to maintain normal-near normal glucose control.⁵

In this study we observed our patients were distributed in 2 groups, 1st group includes patients aged from 2-7 years (younger age group) and they were on twice daily therapy still none of them need to switch to MDI. The other group (2nd group) includes patients who were > 7 years old with mean $13 (\pm 2.4)$ years, we found the number of patients on MDI increased with increased age because when children are getting older the requirements of Insulin will increase and twice daily therapy was not enough to control their blood sugar and we need to switch them to MDI for more optimal control.

Normal growth: The prognosis with regards to growth in children and adolescents with type 1 DM has improved considerably with better disease management. The introduction of multiple Insulin injection, Glucose monitoring has achieved near-normal Glucose level.

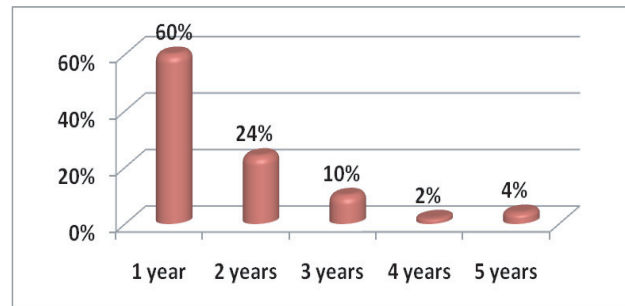


Figure 5: Distribution of patients according to MDI therapy

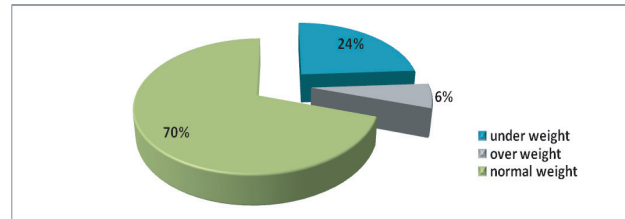


Figure 6: Patients distribution according to BMI

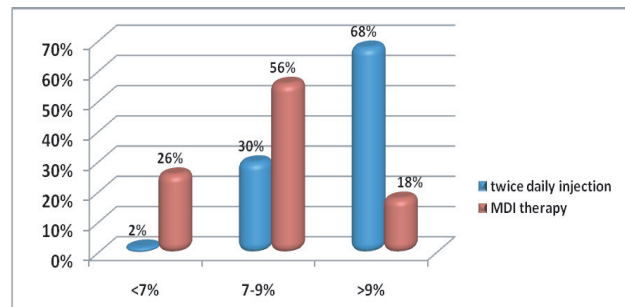


Figure 7: Patient's HbA1C in relation to treatment.

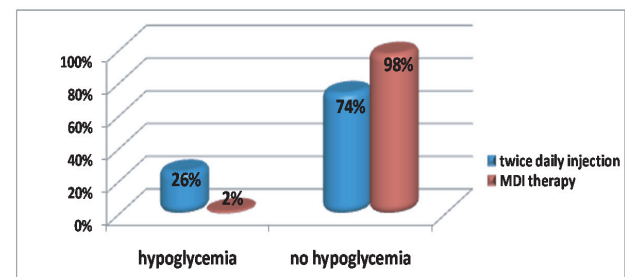


Figure 8: Occurrence of hypoglycemia in relation to insulin therapy.

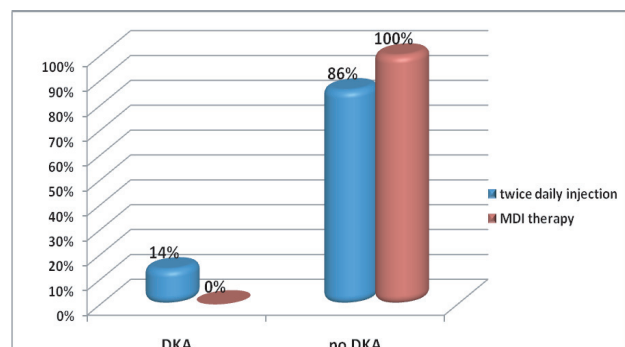


Figure 9: Occurrence of DKA in relation to insulin therapy.



The latter is thought to be responsible for good growth perspectives in children with diabetes.⁶

In our study the results showed 70% of those patients on MDI have normal weight, 24% under wt and another 6% over weight. Unfortunately we couldn't get BMI for patients while on conventional insulin therapy because the data for Height was not available.

There is one study was done on 2002 in USA on 44 patients (2–16 years old) on conventional Insulin regimen, these patients were transitioned from conventional Insulin therapy to multiple daily injection and BMI was obtained before and after initiation of Multiple Daily Injection therapy results showed there was improvement of Glycemic control without producing an abnormal increase in BMI.⁷

Good Glycemic control: considered the recommendations of the Diabetes control and complications trial (DCCT), HbA1c measurements is the gold standard for monitoring Glycemic control and served as a surrogate for diabetes related complications.⁸

The Glycosylated Haemoglobin values currently recommended for children and adolescents with type 1DM are $\leq 8.5\%$ for toddler and preschool age group (≤ 6 years), $< 8\%$ for school age (6 to 12 years), 7.5% for adolescents and young adults (13 to 19 years of age).⁹

In our study if we compare between two regimen (conventional therapy and MDI) by HbA1c level we found only 2% of patients on Twice daily therapy have good Glycemic control (HbA1c $< 7\%$) which raised to 26% on MDI while patients on Multiple Daily Injection, 68% of patients on conventional therapy have poor control HbA1c $> 9\%$ which reduced markedly to 18% while patients on Multiple Daily Injection the difference between mean of HbA1c of patients in each group is statistically significant (P value was < 0.00).

DCCT has conclusively proven that intensive therapy by Multiple Daily Injection improves long term Glycemic control (HbA1c)¹⁰, also the results of study which done in USA which mentioned before showed when patients transitioned to Multiple Daily Injection there was improvement in Glycemic control (i.e. near target HbA1c).

Despite the results of DCCT/EDIC (Epidemiology of diabetes interventions and complications) study and some calls to reassess the Glycemic control set by ADA (American diabetes association) particularly for adolescents, Unfortunately, even the current suggested age-specific Glycemic goals for children and adolescents with type 1 diabetes are difficult to reach and having these patients reach the target Glycosylated HbA1c value remains a challenge for even the most skilled provider.

Risk of acute complications:¹⁰ 82% of our patients on Multiple daily injection have HbA1c below 9%, hypoglycemic episodes decrease from 26% to only 2% on MDI; No episodes of DKA in this year on MDI if compared by 14% while on conventional therapy previously. Many

studies confirmed that the introduction of MDI will decrease risk of hypoglycaemia compared to conventional therapy. There is study carried in Torrecardenas Hospital paediatrics, Al Mera Spain 2007 comparing conventional treatment and intensive treatment (Multiple Daily Injections) in type 1DM pre pubertal patients, results showed intensive treatment during first year to four years was safer than conventional therapy (twice daily injection) and decreasing risk of severe Hypoglycaemia this is because of more flexibility of treatment.

CONCLUSION

Most of our patients who were receiving multiple daily insulin injections have better growth, good glycemic control and less occurrence of hypoglycemia and diabetic ketoacidosis.

RECOMMENDATION

We recommend to use Multiple Daily Injections for type 1 diabetes to achieve good control soon after diagnosis.

REFERENCES

1. Dahl- Jorgensen K and Kiess W (2005) Insulin treatment, *Diabetes in childhood and Adolescence* 122-138 **10**.
2. Charles Brook Brook's (2009) Clinical Pediatric -Endocrinology, Sixth edition Insulin therapy in type 1 DM, pp 474-475.
3. Behrman Richard E, Killieganman, Jenson (2003) Nelson text book of pediatrics .Growth and development; assessment of growth pg 61.Type I DM, Epidemiology, Genetic and Environment pp. 1948-1950.
4. Kadiki et al. (2002) Incidence of type 1 diabetes in children (0-14years) in Benghazi Libya 1991- 2000, *Diabetes Metabolism Journal* **6**(1), 463-467.
5. Hirsch IRLB (1999) Type 1 diabetes mellitus and the use of flexible Insulin regimens, *American Family Physician Journal* 2-7.
6. Chiarelli F (2005) Medical nutrition therapy of children and adolescents with diabetes, *Diabetes in childhood and adolescence* **10**, 139-149.
7. Cummins E (2003) Beneficial effects of flexible Insulin therapy in children and adolescents with type 1DM, *Acta Diabetologica Journal*, **40**, 143-149.
8. Sacks DB, Bruns DE, Goldstein DE, Maclaren NK, McDonald JM and Paroot M (2002) Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus, *Clinical Chemistry* **48**(3), 436-472.
9. Standards of medical care in diabetes supp 1. January (2013) Glycemic control, *Diabetes care*, **36**, 541-542.
10. The diabetes control and complications trial research group DCCT(1993) The effects of intensive therapy of diabetes on the development and progression of long term complication in IDDM, *N Engl Med.* **329**, 977-986.

