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Comparison of Glycemic Control between Intensive Insulin Regimen and Continuous Subcutaneous Insulin infusion: A Meta-Analysis Report of Type-1 Diabetics from Randomized Controlled Trials

Editorial

Kamran Mahmood Ahmed Aziz[1*], Abdullah Othman

[1] Consultant Diabetologist and Research Scientist, Aseer Endocrine and Diabetes Center, Aseer Central Hospital, MOH, Saudi Arabia.
[2] Consultant Pediatric Endocrinologist and Director Aseer Endocrine and Diabetes Center, Aseer Central Hospital, MOH, Saudi Arabia.

Introduction

There has been a debate that continuous subcutaneous insulin infusion (CSII) or pump therapy (first introduced in 1970s) is superior to insulin injections including multiple daily injections (MDI), intensive insulin therapy or the basal bolus therapy. Furthermore, some studies have demonstrated that insulin dosages were less in CSII with better patient satisfaction [1, 2]. However, there are several other studies with some conflicting results and some authors have concluded that both are equally effective in term of reduction of glycated hemoglobin (HbA1c) [3-5]. The main outcome of these studies was HbA1c, which shows the control of diabetes for the past two months. HbA1c is important, as if this worsens, diabetes complications initiates and progress [6]. Under this debate, we collected randomized clinical trials (RCTs) conducted on type-1 diabetic patients comparing the HbA1c results between MDI and CSII and conducted meta-analysis.

Materials and Methods

PRISMA guidelines were used for reporting of individual patient data meta-analyses [7]. We performed internet database survey (PubMed, Google Scholar) and reviewed literature. Only randomized controlled trials (RCTs) on type-1 diabetic patient were included. Observational studies, reviews, surveys, and short term studies (less than two months) were excluded. Also studies with incomplete data and those studies which did not provide complete data details (such as mean ± SD or the numbers randomized/exact number of subjects) were excluded from meta-analysis. HbA1c mean ± SD was calculated for MDI and CSII. Heterogeneity between trials was quantified by conventional Q-statistic (Cochran's heterogeneity statistic) and Higgins I^2 statistic (the degree of inconsistency in the results between studies or the percentage of variability in effect due to heterogeneity rather than sample error) with 0-40% representing negligible heterogeneity, 30-60% moderate heterogeneity, 50-90% substantial heterogeneity and 75-100% considerable heterogeneity. Additionally, tau-squared (τ^2), estimates for the between-study random-effects variance was calculated as well. Standardized statistical techniques and Meta Analyst software was used to analyze the data and to conduct meta-analysis [8-12]. Data was also entered in SPSS to find mean HbA1c differences (t-test) for MDI and CSII. A random-effect analysis was performed on these studies to find out overall effect measure.

Results

According to inclusion criteria, ten studies were identified as RCT on type-1 diabetics, with 809 patients randomized to receive either MDI (N=394) or CSII (N=415). Table-1 demonstrates details and characteristics of the trials included in the meta-analysis [13-22].

Figure-1 shows a forest plot and results of aggregate meta-analysis with the effect size of all ten studies, their confidence intervals (95% CI), and the summary with overall effect measure for the mean HbA1c difference between MDI and CSII.

A random-effect analysis (DerSimonian-Laird method) performed on ten studies found that the percentage of glycated Haemoglobin (HbA1c) was lower in patients receiving continuous subcutaneous insulin infusion compared with those receiving insulin injections; standardized mean difference (SMD) was 0.441, 95% confidence interval 0.267 to 0.616, $p < 0.001$; equivalent to a difference of 0.39%, favoring CSII. I^2 statistic was 20.9 ; $\tau^2 = 0.016$; $Q = 11.378$ with $df = 9$, indicating that heterogeneity

***Corresponding Author**:
Kamran Mahood Ahmed Aziz (MBBS, DDM, PhD),
Consultant Diabetologist; Research Scientist and Clinical Investigator Diabetology Clinic, Aseer Endocrine and Diabetes Center, Aseer Central Hospital, Ministry of Health, P.O.Box 34, Abha, Saudi Arabia.
Tel: 00966-568361040
E-mail: drkamran9999@yahoo.com

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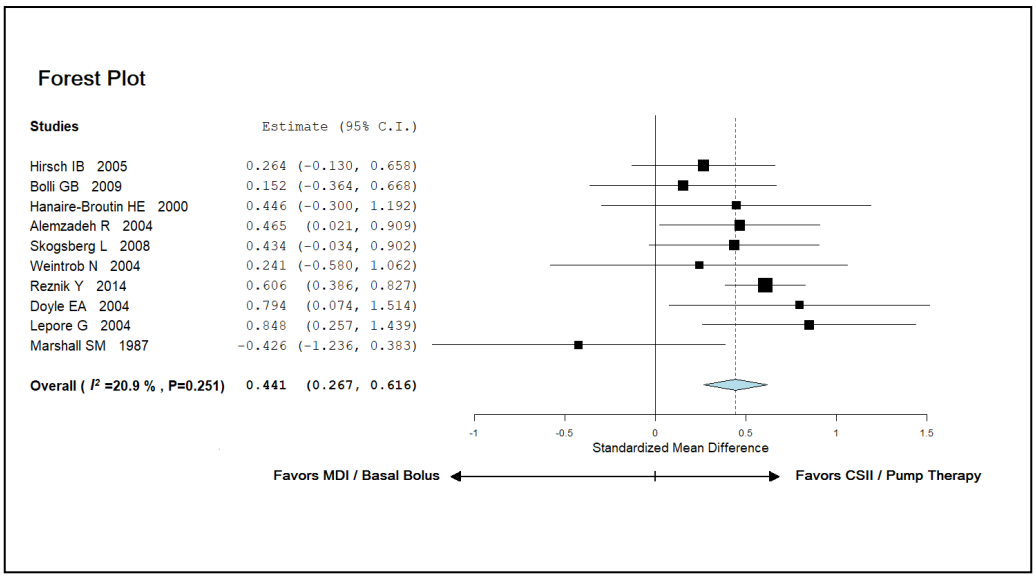
Table 1. Randomized controlled trail name, year, duration, number of participants with HbA1c mean ± SD for MDI and CSII.

Name of Study (Randomized trial)	year	MDI (N)	MDI HbA1c Mean ± SD	CSII (N)	CSII (N) HbA1c Mean ±SD	Study Duration
Hirsch IB, et al.	2005	50	7.3 ± 0.7	50	7.1 ± 0.8	10 weeks
Bolli GB, et al.	2009	30	7.8 ± 0.6	28	7.7 ± 0.7	24 weeks
Hanaire-Broutin, HE et al.	2000	9	8.24 ± 0.77	32	7.89 ± 0.77	16 weeks
Alemzadeh R, et al.	2004	40	8.2 ± 0.9	40	7.8 ± 0.8	12 months
Skogsberg L, et al.	2008	38	6.7 ± 0.5	34	6.5 ± 0.4	24 months
Weintrob N, et al.	2004	12	8.2 ± 0.8	11	8 ± 0.8	14 weeks
Reznik Y, et al.	2014	163	8.6 ± 1.1	168	7 ± 1.2	24 weeks
Doyle EA, et al.	2004	16	8.1 ± 1.2	16	7.2 ± 1	16 weeks
Lepore G, et al.	2004	24	9 ± 1.3	24	8 ± 1	12 months
Marshall SM, et al.	1987	12	9 ± 0.4	12	9.2 ± 0.5	24 weeks

Figure 1. Forest Plot results of random effect meta-analysis model (DerSimonian-Laird random effects method) with standardized mean differences (SDM), 95% confidence intervals for percentage of glycated hemoglobin (HbA1c%) compared with insulin pump (CSII) versus MDI or basal bolus therapy (*SMD=0.441 (95% CI 0.267 to 0.616) I^2 =20.9; τ2= 0.016; Q=11.378 df=9; p=0.251).*



was not significant (heterogeneity p-value = 0.251). When mean HbA1c values of MDI and CSII were compared, patients on CSII demonstrated significantly lower values (8.2 ± 0.72 versus 7.73 ± 0.72 ; p-value < 0.001 respectively). This statistical and meta-analysis favors the usage of insulin pump therapy.

Conclusion and Recommendations

Although different studies in medical literature have given different conclusions, however, our meta-analysis favors the use of insulin pump in type-1 diabetics for better glycemic control. Some studies conducted in past have also concluded that insulin pump provides only satisfaction to the patients and that glycemic control was equally effective with MDI or CSII [17]. While on the other hand, some studies have reported lower risk of hypoglycemia with CSII [13]. Conversely, other authors have proved that the incidence of hypoglycemia was similar with CSII and MDI [14, 22]. Under this discussion and meta-analysis, physicians and diabtologists should use patient centered approach for managing hyperglycemia in type-1 diabetics [23, 24]. Patient's selection for the insulin pump with diabetes education is as essential aspect. Furthermore, cost effectiveness should also be considered while selecting MDI and CSII. Further studies are required to confirm the findings of the current study.

Conflict of Interest

Authors declare no competing conflict of interest.

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