Contents available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

International Diabetes Federation

Review

Continuous subcutaneous insulin infusion versus multiple daily insulin injections in patients with Type 1 diabetes mellitus who fast during Ramadan: A systematic review and meta-analysis

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ARTICLE INFO

Article history:
Received 8 January 2019
Received in revised form
13 February 2019
Accepted 20 February 2019
Available online 27 February 2019

Keywords:
CSII
MDI
T1DM
Metabolic control
Ramadan fasting

ABSTRACT

Background: The benefits and risks of continuous subcutaneous insulin infusion (CSII) or multiple daily injections (MDI) in patients with Type 1 diabetes mellitus (T1DM) who fast during Ramadan are not known.

Methods: Systematic review and meta-analysis of observational studies conducted in PubMed, Embase (Ovid), and the Cochrane Library. Quality of included studies was assessed using the ROBINS-I tool for risk of bias assessment and analyses were performed using RevMan version 5.1.

Results: From 709 records, 306 full text studies were assessed. After exclusions, the final analysis included a total of 9 studies. Heterogeneity for outcomes was $I^2 = 0\%$. There was no significant difference for the change in glycemic control (HbA_{1c}) between CSII and MDI ($P > 0.05$). There was no change in weight or the lipid profile in patients with T1DM on MDI during Ramadan. There were insufficient data to assess the impact on glucose profiles and the incidence of hypoglycemia or diabetic ketoacidosis (DKA) in patients on CSII or MDI during Ramadan.

Conclusions: Studies assessing the effect of CSII or MDI in patients with T1DM who fast during Ramadan are limited to observational studies and show no difference in the change in $Hb_{A1}c$, weight or lipids during Ramadan.

Contents

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https://doi.org/10.1016/j.diabres.2019.02.019
0168-8227/

1. Introduction

Ramadan fasting is one of the five pillars of Islam and is mandatory for all healthy adult Muslims. It requires refraining from eating, drinking and the use of oral medications from sunrise to sunset for 29–30 consecutive days once a year. Although Ramadan fasting is not recommended for patients with Type 1 diabetes (T1DM) and a large proportion of patients with Type 2 diabetes (T2DM) [1–6], several recent studies show that many Muslim patients with diabetes do fast during Ramadan [7–9]. Previously, the epidemiology of diabetes and Ramadan (EPIDIAR) study of patients with diabetes from 13 countries across the MENA region found that 43% of patients with T1DM and 79% with T2DM fasted during Ramadan [10]. Fasting may lead to suboptimal management due to medication non-adherence [5] and result in hypoglycemia, hyperglycemia, dehydration and diabetic ketoacidosis (DKA) [7–9]. Indeed, the EPIDIAR study showed that the incidence of severe hypoglycemia requiring hospitalization during Ramadan increased by 4.7-fold in T1DM patients (3–14 events per 100 people) and by 7.5-fold in T2DM patients (0.4–3 events per 100 people) [10].

Continuous subcutaneous insulin infusion (CSII) is associated with better glycemic control and fewer hypoglycemic events compared to MDI [11]. CSII has been shown to reduce the risk of hypoglycemia in children and adolescents [11–14]. The Canadian Study of Longevity in T1DM showed that whilst those on CSII compared to multiple daily insulin (MDI) did not differ in HbA1c (7.4 ± 0.9% vs. 7.6 ± 1.2%) and had a higher incidence of minor hypoglycemic events (6.5 vs. 5.1 events/patient/month) they had fewer severe hypoglycemic events (0.5 vs. 1.3 events/patient/year) [15]. Petrovski et al found that treatment with CSII in T1DM over 1 year reduced HbA1c from 9.7 ± 1.3 to 8.1 ± 0.6%, with a low incidence of severe hypoglycemia of 0.01 events per patient per year [16].

Whilst CSII may offer an advantage in patients with T1DM who choose to fast during Ramadan [17,18], there are limited and contrasting data on CSII during Ramadan [17]. Khalil et al showed an improvement in HbA1c and a reduction in the total daily insulin dose [19], but another study showed an increased incidence of hypoglycemia [20] in patients on CSII during Ramadan. Kaplan et al showed no difference in the mean interstitial glucose or in the duration of euglycemia, hypoglycemia, or hyperglycemia comparing periods of Ramadan fasting and non-fasting, in T1DM patients on CSII compared to MDI [21]. Similarly, in a study comparing 61 T1DM patients on CSII with 95 T1DM patients on MDI who fasted during Ramadan, there was no difference in the rates of hypoglycemia or hyperglycemia, although the glucose variability captured via self-monitoring of blood glucose (SMBG) and continuous glucose monitoring (CGM) was lower in those on CSII compared to MDI [22]. The aim of this systematic review and meta-analysis was to quantitatively synthesize the available literature on the effect of CSII compared to MDI on metabolic control and occurrence of hypoglycemia in patients with T1DM who fasted during Ramadan.

2. Methods

The systematic review and meta-analysis is reported in accordance with PRISMA guidelines [23]. The review protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) on 9 November 2017 (CRD42017078057).

2.1. *Data sources and extraction*

Three databases were chosen to search for this systematic review: PubMed, Embase (Ovid), and the Cochrane Library. In the PubMed database and Cochrane Library; both MeSH subject headings and keywords were searched; in Embase Emtree subject headings and keywords were utilized. Numerous terms were tested for relevancy and the final search strings for the three databases can be found in Appendix A. Article languages were limited to those in English and no date

restrictions were set. A segment of the grey literature was searched through the use of Dissertation and Theses (ProQuest) and Conference Proceedings Citation Index- Science (CPCI-S) --1990-present/Conference Proceedings Citation Index- Social Science & Humanities (CPCI-SSH) --1990-present (Web of Science). The databases were searched from inception to January 2019. Citations resulting from the searches were all compiled into an EndNote library where they were de-duplicated. Citations were then uploaded into Covidence systematic review software where they were selected/deselected according to inclusion and exclusion criteria.

We included observational studies that reported on HbA1c in patients with T1DM on either CSII or MDI and fasted during Ramadan. Randomized controlled trials were also eligible. Studies from any country and ethnic group were included. All study designs were included except literature reviews and systematic reviews, correspondence and newspaper articles. Studies were included if they reported on at least one of the following at two time points (pre and post Ramadan or during-Ramadan and post-Ramadan): HbA1c; fasting plasma glucose; pre-prandial glucose; postprandial glucose; weight; BMI; neck, waist, hip; body fat mass; fat percent; lipid profile (total cholesterol; LDL-C; TG; HDL-C); SBP/DBP; hypoglycemic episodes, DKA; HONK; DVT; Hospital admission; emergency hospital visits; QoL; adherence to medication. Studies were excluded if they reported on fasting for other religious or spiritual purposes and if reporting on the outcome was at one-time point only (pre, during, or post Ramadan).

2.2. Data extraction

After removal of duplicates, all citations were screened for relevance using the full citation, abstract and indexing terms, before excluding studies deemed as not relevant. Where there was a lack of consensus a third author was consulted (RM). Duplicates were removed and the most recent and complete versions of the studies were reviewed for eligibility. Relevant studies were assessed by two reviewers (HG and HA) to assess eligibility according to the pre-specified inclusion and exclusion criteria. Possible full manuscripts of these potentially eligible citations were obtained. Two reviewers made the final inclusion and exclusion decisions independently. In case of disagreement, a third reviewer (RM) was consulted to resolve the conflicts. A PRISMA flow chart of search results was produced. A data extraction sheet was developed for extracting the data from each study. The data included specific details about the patients, exposure, setting and outcomes. Data extraction was done by one reviewer (HG), and all included studies were double checked by the second reviewer (HA). In the event of missing data, authors were contacted by email or telephone in order to obtain the unpublished information in writing

2.3. Assessment of risk of bias

Included studies were assessed using the Risk of Bias In Non-randomized Studies – on Interventions (ROBINS-I) tool [24]. This tool categorizes the risk of bias as low, moderate, serious, critical, and unclear. Quality assessment was undertaken by one reviewer and checked by a second reviewer and disagreements regarding the quality of a trial were resolved by consensus, or after consultation with the third reviewer (RM). If a study's risk of bias was serious, critical or unclear, the effect of removing this study was checked and relevant outcomes were reported.

2.4. Data synthesis

Meta-analysis was performed in RevMan (version 5.3) [25]. Random effects meta-analysis was used in anticipation of heterogeneity due to differences in study design and population. Standard mean differences (SMD) with 95% confidence intervals were calculated for the continuous variable; HbA_{1c}%, weight (kg), lipid profile (mmol/L). The I^2 statistic was calculated, which is derived from Cochran's chi-squared test Q and is used to describe the percentage of between-study variations that is attributable to variability in the true exposure effect [26]. An I^2 value of 0–30% was classified as not important, 31–60% as moderate, 61–90% as substantial, and 91–100% as considerable [27]. Where studies presented different types of insulin or different modules on the insulin pump, continuous data were grouped and then averaged to obtain overall means and standard deviations.

3. Results

3.1. Study selection

The search strategy identified 709 records (Fig. 1). After removing duplicates, 658 papers were screened on the basis of their titles and abstracts, out of which 352 were excluded, resulting in 306 papers being assessed using their full text. After exclusions, 17 citations were included in the systematic review (15 full-text articles and 2 conference proceedings). The final analysis on HbA1c included 9 studies (254 individuals on CSII compared to 264 on MDI); weight included 4 studies (190 individuals); total cholesterol, LDL-C, HDL-C and TG included 2 studies (96 individuals on MDI). Funnel plots were created to test for small-study effects.

3.2. Study characteristics

Nine studies reported on the primary outcome of HbA_{1c} at two time-points [17,28–35], and three studies reported on it prior to Ramadan fasting only [36–38] (Appendix B). Only one study reported on fasting plasma glucose (FPG) and post prandial glucose at two time-points [39] and another study reported on FPG at one time-point only [36]. Four studies reported on weight at two time-points [28,30,31,36], and one study reported on it pre-Ramadan only [40]. Change in BMI pre and post Ramadan was assessed in one study [36] and was assessed at one time-point, pre-Ramadan by another study [32]. Waist circumference was reported pre and post-Ramadan by one study only [36]. Two studies reported on the lipid profile (TC, LDL-C, HDL-C, TG) at two time-points [30,31], while Ahmedani et al reported on the lipid profile pre-Ramadan only [36]. Only one study reported on SBP and DBP at two time-points [36]. One study reported on hypo-

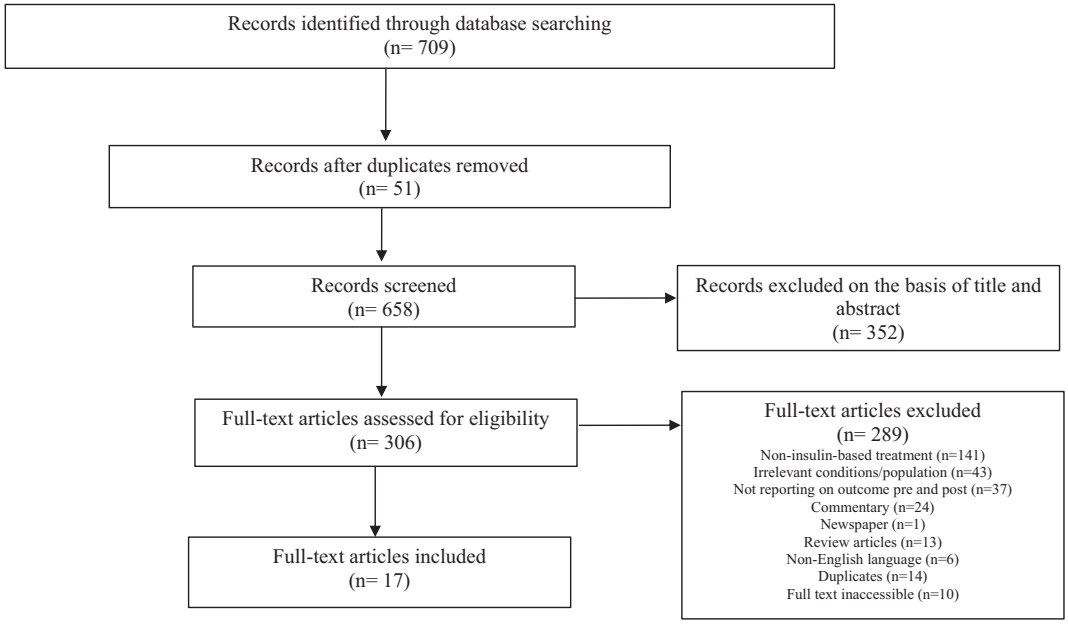

Fig. 1 – PRISMA diagram of included studies.

glycemia at one time-point pre-Ramadan [17], three studies reported at one time-point during Ramadan [30,35,36] and one study reported at one time-point post-Ramadan [37]. Only 1 study reported on hypoglycemia pre and during-Ramadan [40]. One study reported on DKA during Ramadan and the following month [29]. The incidence of hospitalization was assessed in two studies during and post-Ramadan [29,41] and at one time point prior to Ramadan by Ahmedani et al [36]. Hassanein et al reported on HbA1c%, weight, lipid profile, SBP and DBP before and after-Ramadan fasting in both T1DM and T2DM combined [42]. Another study reported on interstitial glucose (IG) levels during the Ramadan and non-Ramadan periods in T1DM patients on CSII and MDI [21]. Fourteen studies were of a prospective observational design [17,21,28,29,31–38,40], one was a prospective interventional study [42], one was a retrospective observational study [41], and one was a case-control study [30]. Studies were conducted in different geographical locations: Bangladesh [28]; Pakistan [36]; Malaysia [34]; UAE [17,21,29,42]; Saudi Arabia [30,32,35,37–39]; Lebanon [33]; Libya [41]; Tunisia [40]; and Egypt [31,32].

3.3. *Synthesis of results*

Data were available from 3 studies on 254 patients with T1DM on CSII who fasted during Ramadan [17,32,35]. There was no significant effect on HbA_{1c} in the CSII group (SMD −0.16,

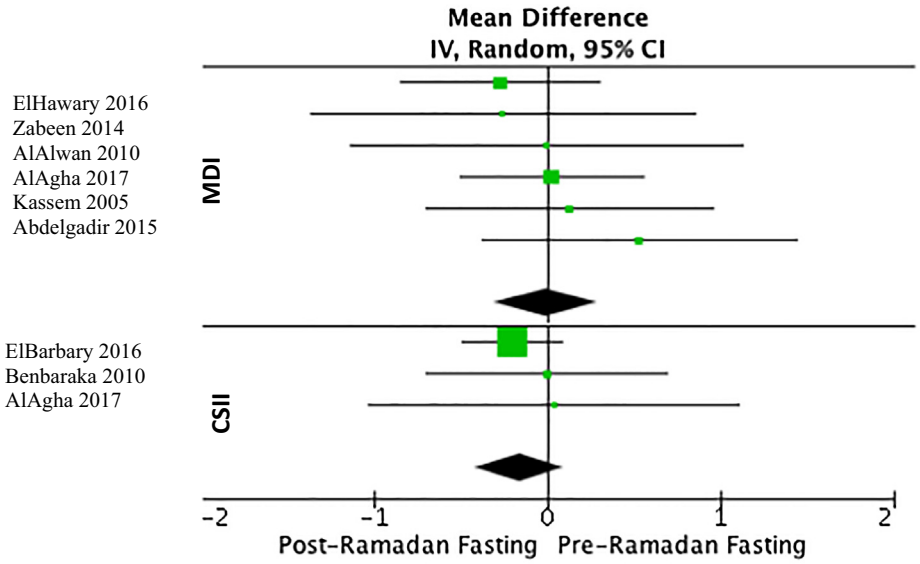

Fig. 2 – Forest Plot showing the mean difference in change in HbA_{1c} pre and post Ramadan in patients on CSII and MDI. *Data on the forest plot were sorted by an effect size. CSII: Continuous Subcutaneous Insulin Infusion; MDI: Multiple Daily Injections.

95% CI −0.41 to 0.10). Six studies assessed the effect of Ramadan fasting on change in HbA_{1c} in 264 T1DM patients on MDI [17,28–31,33,35] and showed no significant change (SMD −0.01, 95% CI −0.46 to 0.44) (Fig. 2). Heterogeneity for outcomes was $I^2 = 0\%$ (Table 1). Studies reporting on outcomes at one time-point (pre, during, or post-Ramadan) were not included in the meta-analysis as they did not allow for a comparison of the effect of fasting on glycemic and metabolic control. Single studies reporting on the outcomes of interest were not eligible to be included in the quantitative synthesis of this meta-analysis as recommended by the Cochrane group, the meta-analysis should combine results from two or more separate studies [43]. None of the included studies reported on any of the secondary outcomes.

Studies that reported on patients with T1DM and T2DM were included and data were extracted for T1DM only [29]. Nor Azlin et al provided HbA1c data at two time-points, but the study could not be included in the meta-analysis as the data was presented as cumulative values from participants with T1DM, T2DM, and GDM [34]. Similarly Hassanein et al reported on outcomes as cumulative values for patients with T1DM and T2DM [42] and Kaplan et al reported on cumulative interstitial glucose values in T1DM patients on either CSII or MDI [21].

Four studies reported on the effect of Ramadan fasting on weight change in patients with T1DM on MDI and showed a non-significant reduction (SMD −0.39, 95% CI −3.35 to 2.57; $P = 0.080$) (Fig. 3) [28,30,31,36]. There were insufficient data reporting on weight change during Ramadan in patients on CSII. Only one study reported on the change in BMI and waist circumference pre and post Ramadan fasting [36], but could not be included in the meta-analysis as per the Cochrane recommendations [43]. Elbarbary et al reported on the BMI of patients on CSII at baseline only [32]. Only 2 studies [30,31] reported on a change in the lipid profile in patients on MDI (Fig. 4): total cholesterol (SMD 0.24, 95% CI −0.24 to 0.72); LDL-C (SMD −0.14, 95% CI −0.03 to 0.31); HDL-C (SMD −0.04, 95% CI −0.14 to 0.06); TG (SMD 0.01, 95% CI −0.09 to 0.11) (Table 2).

Table 1 – Results of the meta-analysis of the studies investigating the effect of CSII vs. MDI on change in HbA_{1c} before and after Ramadan.

Studies	Weight (%)	Standard mean difference (SMD) (%)	95% CI		P value for difference	I^2 (%)	P value for publication bias
			Lower	Upper			
CSII							
Elbarbary 2016 [32]	93.4	−0.20	−0.48	0.08	0.22	0	0.81
Benbaraka 2010 [17]	13.6	0	−0.69	0.69			
Alagha 2017 [35]	6.6	0.04	−1.03	1.11			
MDI							
Elhawary 2016 [31]	19.3	−0.40	−1.26	0.46	0.97	0	0.78
AlAlwan 2010 [30]	5	0	−1.70	1.70			
Alagha 2017 [35]	23.2	0.04	−0.75	0.83			
Kassem 2005 [33]	9.3	0.20	−1.05	1.45			
Abdelgadir 2015 [29]	7.8	0.80	−0.56	2.16			
Zabeen 2014 [28]	5.3	−0.38	−2.04	1.28			

*CSII: Continuous Subcutaneous Insulin Infusion; MDI: Multiple Daily Injections.

Table 2 – Meta-analysis of the change in lipid profile in T1DM patients on MDI before and after Ramadan.

Studies	Weight (%)	Standard Mean Difference (SMD) (%)	95% CI		P value for difference	I^2 (%)	P value for publication bias
			Lower	Upper			
Total Cholesterol (mmol/L)							
AlAlwan 2010 [30]	75.1	0.10	−0.12	0.32	0.33	42	0.19
Elhawary 2016 [31]	24.9	0.67	−0.15	1.49			
LDL-C (mmol/L)							
AlAlwan 2010 [30]	84	0.10	−0.09	0.29	0.12	0	0.32
Elhawary 2016 [31]	15.4	0.34	−0.10	0.78			
HDL-C (mmol/L)							
AlAlwan 2010 [30]	79	−0.06	−0.18	0.06	0.46	0	0.44
Elhawary 2016 [31]	21	0.04	−0.18	0.26			
TG (mmol/L)							
AlAlwan 2010 [30]	94	0	−0.10	0.10	0.85	0	0.42
Elhawary 2016 [31]	5.2	0.18	−0.25	0.61			

*TC: total cholesterol; LDL-C: Low-density lipoprotein cholesterol; HDL-C: High-density lipoprotein cholesterol; TG: Triglycerides.

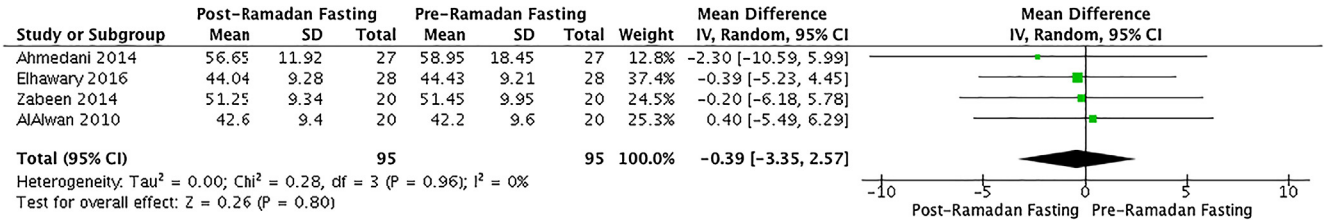

Fig. 3 – Forest Plot showing the mean difference in change in weight (kg) pre and post Ramadan in patients on MDI. *Data on the forest plot were sorted by an effect size.

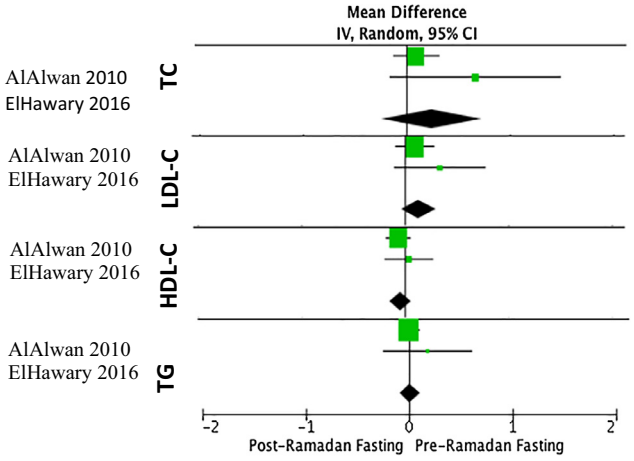

Fig. 4 – Forest Plot showing the mean difference in change in lipid profile (mmol/L) pre and post Ramadan in patients on MDI. *Data on the forest plot were sorted by an effect size. TC: total cholesterol; LDL-C: Low-density lipoprotein cholesterol; HDL-C: High-density lipoprotein cholesterol; TG: Triglycerides.

3.4. *Risk of bias of the included studies*

Egger's test resulted in a value of $P = 0.81$ in the CSII group and $P = 0.78$ in the MDI group, which indicates that there was no significant influence of small study effects on the results. No studies were assessed as having a high risk of bias so the analyses presented include results from all selected studies (Table 3). When removing small studies from the analysis, the SMD and 95% CI changed, but I^2 remained the same and the *P*-value remained non-significant ($P > 0.05$), thus all studies were included in calculating the overall effect size.

4. Discussion

There are no published randomized head to head studies comparing CSII with MDI in patients with T1DM who fast during Ramadan. Nine studies reporting on the change in HbA_{1c} during Ramadan in patients on CSII or MDI were included in the meta-analysis. There was no significant effect of Ramadan fasting on HbA_{1c} in individuals with T1DM on CSII or MDI. There were insufficient data to perform meta-analysis on the other primary and secondary outcomes including: fasting plasma glucose; pre-prandial glucose; postprandial glucose; SBP/DBP; hypoglycemic episodes, DKA; DVT; hospital admissions; QoL and medication adherence to compare between CSII and MDI. There was no effect on weight in patients with T1DM on MDI who fasted during Ramadan in four studies [28,30,31,36] and there was no change in total cholesterol, LDL-C, HDL-C and TG in two studies [30,31]. Five studies reported on hypoglycemic events at one time point; either before Ramadan [17], during Ramadan [30,35,36], or following the month of Ramadan [37], which did not allow their inclusion in the meta-analysis to assess the impact of Ramadan fasting. Of the 17 studies included in the systematic review, only one study reported on the incidence of DKA and hospital admission during Ramadan and the following month [29]. Thirty-percent of hospital admissions with DKA were considered to be due to non-compliance, while the remaining 70% of hospital admissions with DKA were due to missed doses (21%); urinary tract infection (19%); fever (8%); gastroenteritis (6%) newly diagnosed T1DM (4%); gastritis (2%) and appendicitis (2%) [29]. The studies reporting on hypoglycemia did not follow a standard measure in defining and reporting hypoglycemic episodes. One study reported hypoglycemic events as the number of episodes (273 in the CSII group and 354 in the MDI group) and a mean ± SD and range (0.56 ± 0.35 (range, 0–7) [35]. Similarly, Abid et al reported on the number of hypoglycemic episodes experienced by the overall population of patients with T1DM and T2DM, pre-Ramadan (1.31 ± 2.22), severe hypoglycemic episodes (0.22 ± 0.70), number of hypoglycemic episodes during Ramadan (0.75 ± 1.62) and no severe hypoglycemic episodes [40]. Two studies reported the number of cases/total population with hypoglycemia during Ramadan fasting with 17/49 in one study [17] and 6/27 in the other [36]; and 1 study stated that patients experienced hypoglycemia during Ramadan without any quantitative measure [30]. Other studies have reported on the incidence of hypoglycemia during Ramadan in patients with T1DM on CSII with the low-glucose suspend (LGS) feature on and off in relation to the number of hypoglycemic excursions (3.68 ± 1.62 vs. 6.7 ± 2.1, $P = 0.001$) and the duration of hypoglycemia in minutes (110.5 ± 74.8 vs. 167.1 ± 53.1, $P = 0.001$) [32]. Self-Monitoring of Blood Glucose (SMBG) in T1DM patients during Ramadan showed no difference in the rate of mild (CSII-8.6 ± 6.1 vs. MDI-9.85 ± 9.34) or severe (CSII-0.99 ± 1.7 vs. MDI-1.7 ± 4.7) hypoglycemia [22]. Continuous Glucose Monitoring (CGM) in T1DM patients during Ramadan has shown that the rate of hyperglycemia (48%) was higher than hypoglycemia (10%), with only 4/22 patients experiencing mild hypoglycemia [44]. Another study of CGM in patients with T1DM during Ramadan showed no significant difference in the mean low IG index during Ramadan (5.67

Table 3 – Risk of bias assessment for Non-Randomized studies.

Studies	Bias due to confounding	Bias in selection of participants	Bias in classification of intervention	Bias due to deviations from intended intervention	Bias due to missing data	Bias in measurement of outcome	Bias in selection of the reported results
Elbarbary 2016 [32]	-	-	-	-	-	-	-
Alagha 2017 [35]	-	-	-	-	?	+	+
Benbaraka 2010 [17]	-	-	-	-	-	-	-
Elhawary 2016 [31]	+	+	-	-	-	-	-
AlAlwan2010 [30]	-	-	-	-	-	-	-
Kassem 2005 [33]	-	-	-	-	?	-	-
Abdelgadir 2015 [29]	+	+	?	?	-	-	-
Zabeen 2014 [28]	-	-	-	-	-	-	-
Ahmedani 2014 [36]	-	-	-	-	-	-	-

*Yes = +; No = −; unclear = ?.

± 5.04) compared to the non-Ramadan (6.63 ± 53.16) period [21]. The lack of a standard method of reporting hypoglycemia did not allow comparison of the incidence of hypoglycemia among the included studies. This highlights the need for further studies with accurate reporting on the type of hypoglycemia (mild, moderate, severe), the number of patients/total population and number of patients with severe hypoglycemia requiring hospitalization. One study assessed hospital admissions during Ramadan and after Ramadan (13 patients vs. 9 patients), however data was presented for the overall population of patients with T1DM and T2DM and did not state the incidence of hospital admissions in T1DM only [41]. None of the included studies reported on the incidence of DVT, emergency visits, adherence to medications and QoL in T1DM patients during Ramadan fasting.

The use of CSII has increased in patients with T1DM and studies support the use of CSII based on the potential for better glycemic control and a lower incidence of hypoglycemia [19,22]. Indeed, the National Institute of Clinical Excellence (NICE) in the United Kingdom, the American Diabetes Association (ADA), and the European Association for the study of diabetes (EASD) recommend CSII as the best option for insulin treatment in individuals with T1DM [45–49]. However, there are limited data on the benefits or harm of CSII during Ramadan fasting and therefore, opinions are divided regarding the use of CSII during Ramadan fasting [50–52]. Al-Arouj and colleagues considered the use of CSII during Ramadan as an absolute contraindication [50]. Whereas another study suggested that CSII had appeal but they were concerned regarding its cost and the frequency of glucose monitoring [49]. Shaikh et al advised that patients using CSII should adjust their infusion rates according to their home glucose monitoring, but without any supporting evidence [52].

4.1. *Strengths and limitations*

This is the first meta-analysis to compare the effect of CSII and MDI in T1DM patients who fast during Ramadan. It highlights the scarcity of data in this area and identifies a current gap in the literature and the need for future research on CSII during Ramadan. The limitations of our systematic review are that the number of included studies in this review is very small and the number of patients in these studies was few, limiting our ability to draw firm conclusions. The studies were also undertaken in different geographical areas and different cultural conditions as well as dietary habits. Also, only resources published in English were included in this review.

4.2. *Context, implications for health policy, and future research*

Systematic reviews and meta-analysis are not without critics; however, they summarize the best available evidence and identify deficiencies in current evidence. Our data show no significant difference in the change in HbA_{1c} during fasting in individuals with T1DM on either CSII or MDI. Thus, there was neither advantage nor harm in relation to glycemic control for either intervention during Ramadan in patients with T1DM. It may be argued that HbA_{1c} does not adequately capture change in glycemic control over the short period (~30 days) of fasting during Ramadan. Thus, alternate measures such as change in SMBG profiles and continuous glucose monitoring may be more useful. Whilst CSII should impact on hypoglycemia, this was not adequately assessed in the studies to date and could not be included as an endpoint in the analysis. Additionally, other metabolic benefits such as an alteration in lipids, BMI and acute complications such as DKA were not captured in these studies.

5. Conclusion

With the rising number of T1DM Muslims who fast during Ramadan, healthcare professionals are required to be aware of the risk and benefits of fasting during Ramadan and to provide Ramadan specific diabetes care. Hypoglycaemia and hyperglycaemia represent the greatest health concerns for both patients and caregivers and any measures to limit these complications should be considered. On the basis of the limited available evidence, this meta-analysis shows that CSII and MDI are comparable in relation to change in glycaemic control during Ramadan fasting in patients with T1DM. MDI has no impact on weight or the lipid profile. Larger more carefully designed studies are needed to establish the impact of CSII on the incidence of minor and major hypoglycemia, overall glycemic perturbations captured via continuous glucose monitoring and DKA.

6. Availability of data and materials

All data generated or analyzed during this study are included in this published article and its supplementary information files.

Acknowledgements

We thank Sarwat Mahmud, Epidemiologist, from the Biostatistics, Epidemiology, & Biomathematics Research Core at Weill Cornell Medicine-Qatar who provided insight and expertise that greatly assisted the research.

Funding

This review was not funded. Supported by Qatar National Research Fund Grant BMRP20038654.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.diabres.2019.02.019.

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