EDITORIAL

1384  Remission of type 2 diabetes mellitus
      Nakhleh A, Halfin E, Shehadeh N

1390  Diabetes remission and nonalcoholic fatty pancreas disease
      Wu WJ

1394  Management of gestational diabetes mellitus via nutritional interventions: The relevance of gastric emptying
      Huang WK, Jalleh RJ, Rayner CK, Wu TZ

1398  MicroRNA-630: A promising avenue for alleviating inflammation in diabetic kidney disease
      Donate-Correa J, González-Luis A, Díaz-Vera J, Hernandez-Fernaud JR

1404  Adiposity in Chinese people with type 1 diabetes
      Wu NW, Lyu XF, An ZM, Li SY

1409  Diabetes and tuberculosis: An emerging dual threat to healthcare
      Shetty S, Pappachan JM, Fernandez CJ

REVIEW

1417  Patient-centered care in diabetes care-concepts, relationships and practice
      Chen TT, Su WC, Liu MI

1430  Insulin resistance as the molecular link between diabetes and Alzheimer's disease
      Abdalla MMI

MINIREVIEWS

1448  Obstructive sleep apnea: Overlooked comorbidity in patients with diabetes
      Tenda ED, Henrina J, Cha JH, Triono MR, Putri EA, Aristy DJ, Tahapary DL

1461  Update on evidence-based clinical application of sodium-glucose cotransporter inhibitors: Insight to uncommon cardiovascular disease scenarios in diabetes
      Tao SB, Lu X, Ye ZW, Tong NW
**/ORIGINAL ARTICLE/**

*Retrospective Cohort Study*

1477 Association between glucose levels of children with type 1 diabetes and parental economic status in mobile health application


*Retrospective Study*

1489 Association between glucose-lowering drugs and circulating insulin antibodies induced by insulin therapy in patients with type 2 diabetes

*Zhang P, Jiang Q, Ding B, Yan RN, Hu Y, Ma JH*

1499 Clinical efficacy of endovascular revascularization combined with vacuum-assisted closure for the treatment of diabetic foot

*Lei FR, Shen XF, Zhang C, Li XQ, Zhuang H, Sang HF*

1509 Magnetic resonance imaging combined with serum endolipin and galactagoglobin-3 to diagnose cerebral infarction in the elderly with diabetes mellitus

*Zhang YH, Liang D*

1518 Dapagliflozin in heart failure and type 2 diabetes: Efficacy, cardiac and renal effects, safety

*Yu PL, Yu Y, Li S, Mu BC, Nan MH, Pang M*

**Observational Study**

1531 Cut-off value of glycated hemoglobin A1c for detecting diabetic retinopathy in the Chinese population

*Wen Y, Wang Q*

1537 Glymphatic function and its influencing factors in different glucose metabolism states


**Clinical and Translational Research**

1551 Does type 1 diabetes serve as a protective factor against inflammatory bowel disease: A Mendelian randomization study

*Tong KK, Yu YF, Yang XY, Wu JY, Yu R, Tan CC*

1562 Network pharmacology and molecular dynamics study of the effect of the *Astragalus-Coptis* drug pair on diabetic kidney disease

*Zhang MY, Zheng SQ*

**Basic Study**

1589 Interactions between myoblasts and macrophages under high glucose milieus result in inflammatory response and impaired insulin sensitivity

*Luo W, Zhou Y, Wang LY, Ai L*
<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Natural product-based treatment potential for type 2 diabetes mellitus</td>
<td>1603</td>
<td>Shrivastav D, Kumbhakar SK, Srivastava S, Singh DD</td>
</tr>
<tr>
<td>Evaluation of teplizumab's efficacy and safety in treatment of type 1</td>
<td>1615</td>
<td>Ma XL, Ge D, Hu XJ</td>
</tr>
<tr>
<td>Atrial fibrillation and prediabetes: A liaison that merits attention!</td>
<td>1645</td>
<td>Batta A, Hatwal J</td>
</tr>
<tr>
<td>Serum tumor markers: Can they clinically implicate in type 2 diabetes</td>
<td>1648</td>
<td>Reddy KS, Pandiaraj IP, Gaur A, Varatharajan S</td>
</tr>
<tr>
<td>Bidirectional link between periodontitis and systemic inflammation in diabetic retinopathy</td>
<td>1651</td>
<td>Nishant P, Sinha S, Sinha RK, Morya AK</td>
</tr>
</tbody>
</table>
ABOUT COVER
Peer Review of World Journal of Diabetes, Erkan Gokce, MD, Professor, Department of Radiology, Tokat Gaziosmanpasa University, School of Medicine, Tokat 60100, Türkiye. drerkangokce@gmail.com

AIMS AND SCOPE
The primary aim of World Journal of Diabetes (WJD, World J Diabetes) is to provide scholars and readers from various fields of diabetes with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJD mainly publishes articles reporting research results and findings obtained in the field of diabetes and covering a wide range of topics including risk factors for diabetes, diabetes complications, experimental diabetes mellitus, type 1 diabetes mellitus, type 2 diabetes mellitus, gestational diabetes, diabetic angiopathies, diabetic cardiomyopathies, diabetic coma, diabetic ketoacidosis, diabetic nephropathies, diabetic neuropathies, Donohue syndrome, fetal macrosomia, and prediabetic state.

INDEXING/ABSTRACTING
The WJD is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Current Contents/Clinical Medicine, Journal Citation Reports/Science Edition, PubMed, PubMed Central, Reference Citation Analysis, China Science and Technology Journal Database, and Superstar Journals Database. The 2024 Edition of Journal Citation Reports® cites the 2023 journal impact factor (JIF) for WJD as 4.2; JIF without journal self cites: 4.1; 5-year JIF: 4.2; JIF Rank: 40/186 in endocrinology and metabolism; JIF Quartile: Q1; and 5-year JIF Quartile: Q2.

RESPONSIBLE EDITORS FOR THIS ISSUE
Production Editor: Yu-Xi Chen; Production Department Director: Xu Guo; Cover Editor: Jia-Ru Fan.
Evaluation of teplizumab's efficacy and safety in treatment of type 1 diabetes mellitus: A systematic review and meta-analysis

Xiao-Lan Ma, Dan Ge, Xue-Jian Hu

**Specialty type:** Endocrinology and metabolism  
**Provenance and peer review:** Unsolicited article; Externally peer reviewed.  
**Peer-review model:** Single blind  
**Peer-review report's classification**  
**Scientific Quality:** Grade B  
**Novelty:** Grade B  
**Creativity or Innovation:** Grade B  
**Scientific Significance:** Grade B  
**P-Reviewer:** Rasool A, Pakistan  
**Received:** January 24, 2024  
**Revised:** March 5, 2024  
**Accepted:** April 30, 2024  
**Published online:** July 15, 2024  
**Processing time:** 166 Days and 0.3 Hours

**Abstract**

**BACKGROUND**  
Islets of Langerhans beta cells diminish in autoimmune type 1 diabetes mellitus (T1DM). Teplizumab, a humanized anti-CD3 monoclonal antibody, may help T1DM. Its long-term implications on clinical T1DM development, safety, and efficacy are unknown.

**AIM**  
To assess the effectiveness and safety of teplizumab as a therapeutic intervention for individuals with T1DM.

**METHODS**  
A systematic search was conducted using four electronic databases (PubMed, Embase, Scopus, and Cochrane Library) to select publications published in peer-reviewed journals written in English. The odds ratio (OR) and risk ratio (RR) were calculated, along with their 95% CI. We assessed heterogeneity using Cochrane Q and P statistics and the appropriate P value.

**RESULTS**  
There were 8 randomized controlled trials (RCTs) in the current meta-analysis with a total of 1908 T1DM patients from diverse age cohorts, with 1361 patients receiving Teplizumab and 547 patients receiving a placebo. Teplizumab was found to have a substantial link with a decrease in insulin consumption, with an OR of 4.13 (95% CI: 1.72 to 9.90). Teplizumab is associated with an improved C-peptide response (OR 2.49; 95% CI: 1.62 to 3.81) and a significant change in Glycated haemoglobin A1c (HbA1c) levels in people with type 1 diabetes [OR 1.75 (95% CI: 1.03 to 2.98)], and it has a RR of 0.71 (95% CI: 0.53 to 0.95).

**CONCLUSION**  
In type 1 diabetics, teplizumab decreased insulin consumption, improved C-peptide response, and significantly changed HbA1c levels with negligible side effects. Teplizumab appears to improve glycaemic control and diabetes management with...
INTRODUCTION

Type 1 diabetes mellitus (T1DM) is a pathological condition of an autoimmune type wherein there is a progressive degeneration of beta cells located inside the islets of Langerhans[1]. Despite advancements in healthcare, the majority of individuals with type 1 diabetes struggle to reach the ideal glycaemic targets, resulting in a continued elevated risk of complications and mortality[2,3]. The development of immunotherapy targeting beta-cell destruction represents an unresolved requirement in the management of autoimmune type 1 diabetes, with potential future applicability in prediabetes[4]. The initiation of treatment during the clinical onset presents a favorable circumstance wherein individuals can be readily diagnosed and there is still a preserved functional beta-cell mass. The maintenance of residual beta-cell function, as indicated by elevated levels of C-peptide, contributes to improved glycaemic control, hence reducing the risk of retinopathy, nephropathy, hypoglycemia, and ketoacidosis. The use of immunotherapy at the time of diagnosis seeks to extend and enhance this impact by inhibiting additional B-cell mortality and potentially facilitating the restoration of functional capacity in surviving B-cells following the resolution of inflammation[5-7]. Various clinical trials evaluating different therapeutic drugs have demonstrated limited success in this context; nonetheless, treatment responses have frequently exhibited a decline within a span of two years[8,9]. Teplizumab is a monoclonal antibody that has been engineered to have a non-activating Fc region. It is believed to inhibit the activity of autoreactive T lymphocytes, which are responsible for inducing the death of beta-cells. It targets the CD3 protein specifically and is considered to be effective in this function.

The T cells undergo a transient depletion from the peripheral circulation throughout the course of immunotherapy, followed by their reconstitution within a few weeks upon discontinuation of the treatment[10,11]. Based on preclinical and clinical investigations, it has been observed that teplizumab medication has the potential to stimulate regulatory T-cell function, hence indicating an enhancement in immunological tolerance[12-14]. According to recent research, the administration of teplizumab has been found to effectively mitigate beta-cell apoptosis after one year of treatment, modulate CD8+ T lymphocytes as well as enhance C-peptide reactions in clinical trials involving individuals with type 1 diabetes[15,16]. However, additional study is necessary to examine the long-term effects on B-cell activity and survival, as well as to ascertain the safety and efficacy of teplizumab therapy in modifying the progression towards clinical type 1 diabetes. Therefore, in this systematic review and meta-analysis, we assessed the effectiveness and safety of teplizumab as a therapeutic intervention for T1DM via analysis of 8 randomized controlled trials (RCTs)[17-24] selected as per the predetermined inclusion and exclusion criteria.

This meta-analysis and systematic review was conducted with the purpose of determining whether or not teplizumab is an effective and safe treatment intervention for people who have T1DM.

MATERIALS AND METHODS

Search strategy

The present meta-analysis was conducted following a comprehensive search across various databases, including PubMed, Embase, Scopus, and Cochrane library. The search covered from the year 2000 to 2023 and utilized specific keywords such as “Type-1 Diabetes mellitus”, “T1DM”, “Teplizumab”, “anti-CD3 monoclonal antibody”, “Insulin”, “Glycated haemoglobin A1c”, “HbA1C”, “C-peptide”, “Adverse events”, “Randomized controlled trials”, “RCT”,
A thorough search of a number of databases was carried out with the use of electronic scanning tools, which led to the creation in order to assess the glycaemic control. A fixed-effect model was utilized for the pooled analysis which was demonstrated by an and the utilization of OR. This was done by employing the DerSimonian Lair method. The examination of dichotomous outcomes included the investigations. A 2 × 2 table software, the categorization, extraction, and elimination of duplicate references were made easier. The development of software package Review Manager (RevMan) 5.3 for the purpose of evaluating and analyzing the influence of a number of dichotomous and continuous outcomes, the Statistical analysis MedCalc program. The potential for bias in the papers that were examined was evaluated using a pre-established and standardized qu. Through the utilization of a funnel plot the presence of publication bias was evaluated, and Begg’s test was carried out with the assistance of the MedCalc program in order to ascertain the statistical significance of the findings.

Criteria for inclusion and exclusion
The current analysis comprised studies that showed data on the efficacy and safety of Teplizumab for the treatment of T1DM. Those studies that satisfied the subsequent inclusion criteria were incorporated: (1) Including patients with T1DM; (2) Adolescents and adult patients ranging in age from 7 to 40 years; (3) Evaluating the comparative efficacy and safety of teplizumab for the treatment of T1DM; and (4) Implementation of RCT as the chosen study design. From the year 2000 all the way up until the year 2023, the selection of studies covered the entire time span. We chose papers that were available in full text and offered sufficient information for a table that was two by two. Several clinical outcomes were used as primary measures in this meta-analysis. These outcomes included a decrease in insulin utilization, a change in response to C-peptide, a change in the level of HbA1C, and adverse events that occurred in participants who were treated with teplizumab and those who were in the control group. Additionally, the comparative glycemic control experienced by the teplizumab group in comparison to the control group was also assessed. We did not include references that were either out of date, anecdotal, or based on the opinions of experts. Additionally, we did not include studies that were not cross-sectional, studies that contained experimental data from animal studies or trials, and studies for which we were unable to receive primary data and key information from the authors. Studies that included patients with diabetes in addition to those with HIV, cancer, and other systemic problems were also removed from consideration. Additionally, articles that were not research papers, qualitative studies, and papers published in languages other than English were also removed. Separately, the researchers (Xiao-Lan Ma and Dan Ge) acquired demographic profiles of the patients as well as event data with important components from the studies that were included.

Risk of bias evaluation of studies incorporated
The potential for bias in the papers that were examined was evaluated using a pre-established and standardized questionnaire. For the purpose of determining the potential for bias, a tool developed by the Cochrane Collaboration and included in the Cochrane Handbook (version 5.3) was utilized. The instrument consisted of five components: Bias resulting from the randomization process, bias resulting from deviations from the interventions that were intended, bias resulting from the absence of outcome data, bias resulting from the assessment of the outcome, and bias resulting from the selection of the outcomes that were presented. Two different reviewers, Xiao-Lan Ma and Dan Ge, each carried out their own research in order to determine the potential for bias. An additional reviewer, who will be referred to as Xue-Jian Hu, acted as an arbiter to settle any disagreements that were still outstanding. At the end of the day, the potential bias was evaluated and classified as either "high risk," "low risk," or "unclear risk." Through the utilization of a funnel plot the presence of publication bias was evaluated, and Begg’s test was carried out with the assistance of the MedCalc program in order to ascertain the statistical significance of the findings.

Statistical analysis
For the purpose of evaluating and analyzing the influence of a number of dichotomous and continuous outcomes, the software package Review Manager (RevMan) 5.3 was applied. Through the employment of reference management software, the categorization, extraction, and elimination of duplicate references were made easier. The development of forest plots was attempted with the purpose of evaluating the influence of outcome determinants across all of the investigations. A 2 × 2 table that was generated with event data was utilized in order to compute the odds ratio (OR). This was done by employing the DerSimonian Lair method. The examination of dichotomous outcomes included the utilization of OR and risk ratios (RR) in addition to a CI covering 95% of the possible outcomes. The assessment of heterogeneity was examined through the utilization of statistical techniques, such as the χ² test with a matching P value and the I² test. A random-effects model was utilized in the event that there was heterogeneity between the studies, which was demonstrated by an F value that was greater than fifty percent or a P value that was less than five percent. A fixed-effect model was utilized for the pooled analysis, which was otherwise not the case. It was determined that a P value that was lower than 0.05 to be statistically significant. In addition to this, a box and whisker plot was also created in order to assess the glycaemic control in the Teplizumab administration group with the control group.

RESULTS

Literature search results
A thorough search of a number of databases was carried out with the use of electronic scanning tools, which led to the
The current meta-analysis was comprised of a sample of eight RCTs, which included a total of seventeen thousand eight patients. The selection of patients for this trial was carried out through the use of a random sampling technique. The group that received Teplizumab consisted of 1361 individuals, whereas the group that served as the control consisted of exactly 547 people. The demographic features of the studies that were included are presented in Table 2. It is stated in the text that the author identification number, the year of publication, the journal of publication, the country of publication, the study setting, the study design, the total number of participants, the diagnosis, the age of participants, the number of participants in the teplizumab group and the control group, the duration of the study, the gender (male/female ratio), and the primary outcomes that were measured are all included. After that, the data from the events that were described earlier were utilized for the purpose of carrying out the meta-analysis later on.

**Assessment of risk of bias**

Table 3 presents the results of the risk of bias assessment for the studies that were included, which were derived from the questionnaire that was designed beforehand. As can be seen from the graph depicting the risk of bias (Figure 2A) and the summary depicting the risk of bias (Figure 2B), the current meta-analysis appears to have a low probability of being biased. Out of the eight studies that were considered for inclusion in the analysis, six of them had a low risk of bias, while one of them had a substantial risk of bias. It was determined that the bias that occurred as a result of the randomization technique was caused by the moderate risk. In spite of this, there was a specific study that displayed a substantial high risk because of the bias in the selection of the data that were published. The symmetrical form of the funnel plot that is represented in Figure 3 and the statistically insignificant value of Begg's test (0.249) that is higher than the preset significance level of 0.05 both indicate that there is a minimal risk of publishing bias. In addition, the symmetrical form of the funnel plot is used to illustrate the little risk of publication bias.

**Statistical analysis findings**

The current meta-analysis was comprised of a sample of eight RCTs, which included a total of seventeen thousand eight patients. The funnel plot is used to illustrate the little risk of publication bias. In addition, the symmetrical form of the funnel plot that is represented in Figure 3 and the statistically insignificant value of Begg’s test (0.249) that is higher than the preset significance level of 0.05 both indicate that there is a minimal risk of publishing bias. In addition, the symmetrical form of the funnel plot is used to illustrate the little risk of publication bias.

**Table 1 Database search strategy**

<table>
<thead>
<tr>
<th>Database</th>
<th>Search strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scopus</td>
<td>1. “Type-1 Diabetes mellitus” OR “T1DM” OR “Teplizumab” OR “anti-CD3 monoclonal antibody”&lt;br&gt;2. “Insulin” OR “Glycated hemoglobin A1c” OR “HbA1C” OR “C-peptide” OR “Adverse events” OR “Randomized controlled trials” OR “RCT” OR “Systematic review” OR “meta-analysis”&lt;br&gt;3. ‘1’ AND ‘2’</td>
</tr>
<tr>
<td>PubMed</td>
<td>1. “Type-1 Diabetes mellitus” OR “T1DM” (MeSH Terms) OR “Teplizumab” (all fields) OR “anti-CD3 monoclonal antibody” (all fields)&lt;br&gt;2. “Insulin” (MeSH Terms) OR “Glycated hemoglobin A1c” (all fields) OR “HbA1C” (all fields) OR “C-peptide” (all fields) OR “Adverse events” OR “Randomized controlled trials” (all fields) OR “RCT” (all fields) OR “systematic review” OR “meta-analysis”&lt;br&gt;3. ‘1’ AND ‘2’</td>
</tr>
<tr>
<td>Embase</td>
<td>“Type-1 Diabetes mellitus” / exp OR “T1DM” / exp OR “Teplizumab” / exp OR “anti-CD3 monoclonal antibody” / exp&lt;br&gt;2. “Insulin” / exp OR “Glycated hemoglobin A1c” / exp OR “HbA1C” / exp OR “C-peptide” / exp OR “Adverse events” / exp OR “Randomized controlled trials” / exp OR “RCT” / exp OR “systematic review” / exp OR “meta-analysis”&lt;br&gt;3. ‘1’ AND ‘2’</td>
</tr>
<tr>
<td>Cochrane library</td>
<td>1. (Type-1 Diabetes mellitus): Ti, ab, kw OR (T1DM): Ti, ab, kw OR (Teplizumab): Ti, ab, kw OR (anti-CD3 monoclonal antibody): Ti, ab, kw OR (Cortisol): Ti, ab, kw (Word variations have been searched)&lt;br&gt;2. (Insulin): Ti, ab, kw OR (Glycated hemoglobin A1c): Ti, ab, kw OR (HbA1C): Ti, ab, kw OR (C-peptide): Ti, ab, kw OR (Adverse events): Ti, ab, kw OR (Randomized controlled trials): Ti, ab, kw OR (systematic review): Ti, ab, kw OR (meta-analysis): Ti, ab, kw (Word variations have been searched)&lt;br&gt;3. ‘1’ AND ‘2’</td>
</tr>
</tbody>
</table>

1 MeSH terms: Medical subject headings.<br>2 exp: Explosion in emtree- searching of selected subject terms and related subjects.<br>3 Ti, ab, kw: Either title or abstract or keyword fields.
Table 2 Brief summary of the included studies

<table>
<thead>
<tr>
<th>Ref.</th>
<th>Year of publication</th>
<th>Journal of publication</th>
<th>Country of study</th>
<th>Study setting</th>
<th>Study design</th>
<th>Total number of participants (n)</th>
<th>Diagnosis</th>
<th>Age of patients</th>
<th>Teplizumab group (n)</th>
<th>Control group (n)</th>
<th>Duration of study</th>
<th>Sex (M/F)</th>
<th>Primary outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herold et al [17]</td>
<td>2002</td>
<td>The New England Journal of Medicine</td>
<td>United States</td>
<td>HIC</td>
<td>RCT</td>
<td>24</td>
<td>Type-1 diabetes</td>
<td>7-30 years</td>
<td>12</td>
<td>12</td>
<td>1 year</td>
<td>18/6</td>
<td>Positive outcomes: Lower insulin uses and decrease in value of HbA1c, Adverse events</td>
</tr>
<tr>
<td>Hagopian et al [18]</td>
<td>2013</td>
<td>Diabetes</td>
<td>Sweden</td>
<td>HIC</td>
<td>RCT</td>
<td>410</td>
<td>Type-1 diabetes</td>
<td>8-35 years</td>
<td>311</td>
<td>99</td>
<td>2 years</td>
<td>295/115</td>
<td>Positive outcomes: Change in area under the curve for C-peptide, lower insulin uses and decrease in value of HbA1c, Adverse events</td>
</tr>
<tr>
<td>Herold et al [19]</td>
<td>2013</td>
<td>Diabetologia</td>
<td>United States</td>
<td>HIC</td>
<td>RCT</td>
<td>58</td>
<td>Type-1 diabetes</td>
<td>12-15 years</td>
<td>31</td>
<td>27</td>
<td>1 year</td>
<td>30/28</td>
<td>Positive outcomes: Change in area under the curve for C-peptide, and decrease in value of HbA1c, Adverse events</td>
</tr>
<tr>
<td>Herold et al [21]</td>
<td>2023</td>
<td>Diabetes care</td>
<td>United States</td>
<td>HIC</td>
<td>RCT</td>
<td>609</td>
<td>Type-1 diabetes</td>
<td>8-35 years</td>
<td>375</td>
<td>234</td>
<td>1 year</td>
<td>370/239</td>
<td>Positive outcomes: Change in area under the curve for C-peptide, and decrease in value of HbA1c, Adverse events</td>
</tr>
<tr>
<td>Perdigoto et al [22]</td>
<td>2019</td>
<td>Diabetologia</td>
<td>United States</td>
<td>HIC</td>
<td>RCT</td>
<td>43</td>
<td>Type-1 diabetes</td>
<td>8-30 years</td>
<td>31</td>
<td>12</td>
<td>2 years</td>
<td>26/17</td>
<td>Positive outcomes: Change in area under the curve for C-peptide, and decrease in value of HbA1c, Adverse events</td>
</tr>
<tr>
<td>Sherry et al [23]</td>
<td>2011</td>
<td>Lancet</td>
<td>United States</td>
<td>HIC</td>
<td>RCT</td>
<td>763</td>
<td>Type-1 diabetes</td>
<td>8-35 years</td>
<td>513</td>
<td>99</td>
<td>2 years</td>
<td>325/438</td>
<td>Positive outcomes: Lower insulin uses and decrease in value of HbA1c, Adverse events</td>
</tr>
<tr>
<td>Sims et al [24]</td>
<td>2021</td>
<td>Science Translation medicine</td>
<td>United States</td>
<td>HIC</td>
<td>RCT</td>
<td>76</td>
<td>Type-1 diabetes</td>
<td>8-39 years</td>
<td>44</td>
<td>32</td>
<td>2 years</td>
<td>40/36</td>
<td>Positive outcomes: Change in area under the curve for C-peptide and decrease in value of HbA1c, Adverse events</td>
</tr>
</tbody>
</table>

HbA1c: Glycated haemoglobin A1c; RCT: Randomized controlled trial; M: Male; F: Female; HIC: High income countries.

hundred eight individuals with T1DM. Among the whole population, Teplizumab was delivered to 1361 patients, while 547 patients were given a control medication for the treatment of type 1 diabetes. On the basis of the statistical analysis that was carried out on the most important results of the study, the following conclusions were reached:

**Reduction of insulin use in teplizumab vs control group:** To investigate the reduction in insulin-use in patients treated with either Teplizumab or a control drug, an OR was calculated using the event data extracted from the included studies, as depicted in Figure 4A. From the calculated results, it was found that the patients in the teplizumab group have a higher likelihood of reduction in insulin use, with an OR of 4.13 (95% CI: 1.72 to 9.90) and a tau² value of 0.41, $\chi^2 = 9.64$, degree of freedom(df) = 2, $Z = 3.18$, $I^2 = 79\%$ and $P = 0.001$. 
Table 3 Risk of bias assessment of included studies

<table>
<thead>
<tr>
<th>Did the study avoid inappropriate exclusions</th>
<th>Y</th>
<th>Y</th>
<th>Y</th>
<th>Y</th>
<th>Y</th>
<th>Y</th>
<th>Y</th>
<th>Y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Did all patients receive the same reference standard</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Were all patients included in the analysis</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Was the sample frame appropriate to address the target population</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Were study participants sampled in an appropriate way</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Were the study subjects and the setting described in detail</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Were valid methods used for the identification of the condition</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Was the condition measured in a standard, reliable way for all participants</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
</tbody>
</table>

Y: Yes; N: No.

Figure 1  Flow of selection of studies.

Change in C-peptide response in teplizumab vs control group: To examine the change in C-peptide response in patients treated with either Teplizumab or a control drug, an OR was calculated using the event data extracted from the included studies. From the calculated results shown in Figure 4B, it was found that the patients in the teplizumab group have a higher likelihood of change in C-peptide response, with an OR of 2.49 (95%CI: 1.62 to 3.81) and a $\tau^2$ value of 0.08, $\chi^2 = 6.12$, df = 4, $Z = 4.19$, $I^2 = 75\%$ and $P < 0.0001$.

Change in HbA1C level in teplizumab vs control group: To assess the change in HbA1C level in Teplizumab vs control group, a comparative analysis of glycated haemoglobin value in the patients treated with either teplizumab or control drug was carried out, as depicted in Figure 4C. From the calculations, it was found that the patients in the teplizumab group have a higher likelihood of change in HbA1C level, with an OR of 1.75 (95%CI: 1.03 to 2.98) and a $\tau^2$ value of 0.32, $\chi^2 = 23.06$, df = 7, $Z = 2.05$, $I^2 = 70\%$ and $P = 0.04$.

Comparison of adverse events in patients of teplizumab vs control group: In order to assess the comparative risk of adverse events between the Teplizumab and control groups, a RR analysis was conducted. This analysis specifically examined the occurrence of adverse events, such as systemic inflammations and allergic responses, in patients who received either teplizumab or the control medicine. The results of this analysis are presented in Figure 5. Based on the
computed data, it was determined that the individuals in the control group exhibit a greater susceptibility to experiencing unfavorable outcomes, as shown by a RR of 0.71 (95% CI: 0.53 to 0.95). Additionally, the $\tau^2$ value turned out to be 0.14, the $\chi^2$ value was 44.64 with df 7, the Z score was 2.26, the $I^2$ value was 84%, and the $P$ value was 0.02.

Comparison of glycaemic control in patients of teplizumab vs control group: Box and whisker plot was generated using the event data obtained from the studies included in the analysis to evaluate the relative effectiveness of teplizumab vs the control medication in managing glycaemic control in patients. This figure is depicted in Figure 6. The plot exhibited a symmetrical distribution of data points with a median positioned at the centre of the box, and the whiskers extending to almost equal ranges on both sides of the box. The group receiving teplizumab has favorable glycaemic control, characterized by optimal serum glucose concentrations, in comparison to the control group. This effect contributes to the prevention of diabetes complications.

**DISCUSSION**

T1DM is an autoimmune disorder resulting from the destruction of pancreatic β-cells responsible for insulin production, either with or without any remaining functional tissue[41]. Type 1 diabetes can be attributed to various factors, such as viral infections, drug-induced effects, and autoimmune mechanisms. These variables contribute to the death of β-cells and result in a complete absence of insulin in the bloodstream, leading to elevated levels of blood glucose[42,43]. Individuals diagnosed with T1DM necessitate the continuous administration of insulin throughout their whole lifespan. The majority of individuals necessitate a minimum of two injections of insulin each day, wherein the dosage is modified in accordance with self-monitoring of blood glucose levels[44]. Teplizumab, also known as teplizumab-mzwv, is a monoclonal antibody of the IgG1 kappa class that has been humanized. It is primarily utilized for the purpose of delaying the onset of type 1 diabetes and as a therapy option for those with T1DM[45]. In November 2022, teplizumab was granted approval as the
inaugural medication for the purpose of postponing the initiation of stage 3 type 1 diabetes in individuals aged eight years and older, encompassing both adults and children\[46\].

Multiple investigations have revealed that Teplizumab demonstrates disease-modifying characteristics through the preservation of β-cell functioning. In a recent systematic review and meta-analysis conducted by Nourelden \textit{et al} \[47\], the authors examined the effects of teplizumab on insulin use, C-peptide response, and adverse effects in patients with type 1 diabetes. The study included eight randomized clinical trials with a total of 866 participants. The findings of the analysis revealed that Teplizumab was associated with a significant reduction in insulin use [mean difference (MD) = -0.17, 95%CI (-0.24, -0.09)]. Additionally, the administration of Teplizumab resulted in a higher C-peptide response [MD = 0.08, 95%CI (0.01, 0.15)] and a lower incidence of adverse effects. In a systematic review and meta-analysis conducted by \textit{Ashraf et al} \[48\] in 2023, the authors examined 11 RCTs with a total of 1397 participants. Their findings indicated that treatment with teplizumab resulted in a significant increase in the C-peptide response, as evidenced by a MD of 0.114 (95%CI: 0.069 to 0.159). Additionally, teplizumab treatment was found to significantly reduce patients' insulin intake across all time-frames, with a MD of -0.123 (95%CI: -0.151 to -0.094). Similarly, \textit{Liu et al} \[49\] and \textit{Evans-Molina and Oram} \[50\] have documented in their respective research investigations that Teplizumab, an anti-CD3 monoclonal antibody, exhibits promise as a therapeutic intervention for enhancing the area under the curve of C-peptide and insulin utilization in individuals with type 1 diabetes.

Our findings align with the aforementioned results, indicating positive correlation between teplizumab and a decrease in insulin usage, with an OR of 4.13 (95%CI: 1.72 to 9.90). Additionally, teplizumab is associated with an improved C-peptide response (OR 2.49; 95%CI: 1.62 to 3.81) and a significant change in HbA1c levels among individuals diagnosed with type 1 diabetes [OR 1.75 (95%CI: 1.03 to 2.98)], while exhibiting minimal adverse effects, as indicated by a RR of 0.71 (95%CI: 0.53 to 0.95). In addition, teplizumab has been shown to offer improved glycaemic management. Nevertheless, our analysis solely encompasses studies conducted exclusively in high-income nations. This highlights the need of conducting such studies in low- and middle-income countries (LMICs), where the prevalence of T1DM is higher among adults and adolescents.

\section*{Limitations}

One of the most important aspects of this research is the utilization of all-encompassing search phrases that encompass the investigation of "type-1 diabetes mellitus" and "teplizumab" across a number of different databases.

However, it is necessary to illustrate certain limitations. Firstly, studies done in languages other than English were not included in this analysis. Given that a sizable number of the publications included in our meta-analysis were eliminated, it is also imperative to recognize the possibility of selection bias in our research. Furthermore, it was not possible to determine a correlation between the results and factors like gender, age, or ethnicity, and it is unclear whether these conclusions will apply to people who do not appear to be at risk for type 1 diabetes but do not have first-degree relatives who have the disease. Thirdly, the limited sample size used in the current meta-analysis—just eight studies—showed notable variability and heterogeneity. It is impossible to determine whether repeated doses will prolong therapeutic effects or offer additional advantages in comparison to the drug administered for a single course. Finally, one more limitation of our analysis is that it only includes studies from high-income nations. This emphasizes the importance of doing this kind of research in LMICs, where T1DM is more common in adults and adolescents.
Ma XL et al. Teplizumab and T1DM

CONCLUSION

Based on the results of the present meta-analysis, it can be concluded that the utilization of teplizumab is linked to a reduction in insulin use, an enhanced C-peptide response, and a significant alteration in HbA1c levels among individuals diagnosed with type 1 diabetes, while exhibiting minimal adverse effects. The findings indicate that teplizumab exhibits favorable safety and efficacy profiles in promoting improved glycaemic control and managing diabetes mellitus. However, additional study is necessary to investigate the potential synergistic effects of combining immune and...
metabolic therapy. This research is crucial in order to maintain the immunological responses that are related with the preservation of C-peptide responses and the attainment of good outcomes that have a significant therapeutic impact.

Figure 6  Box and Whisker plot for comparative Glycaemic control in Teplizumab vs control group.

FOOTNOTES

Author contributions: Ma XL contributed to concept and designed the study; Ge D contributed to analyzed data and drafting of the manuscript; Hu XJ contributed to collect the data and helped in data analysis.

Conflict-of-interest statement: All the authors report no relevant conflicts of interest for this article.

PRISMA 2009 Checklist statement: The authors have read the PRISMA 2009 Checklist, and the manuscript was prepared and revised according to the PRISMA 2009 Checklist.

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Country of origin: China

ORCID number: Xue-Jian Hu 0009-0001-1335-2553.

S-Editor: Li L
L-Editor: A
P-Editor: Zhao YQ

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