ABSTRACT

Objectives: To assess the risk of bias (RoB) of randomized controlled trials (RCTs) published in dental journals in the Spanish language. Methods: A systematic retrospective survey was conducted of all RCTs published from 1980 to 2019 in dentistry Spanish and Latin American journals. We extracted data and performed RoB assessments using the Cochrane Risk of Bias tool. Results: 292 RCTs published in 51 journals were included. The best-rated domains were incomplete outcome data, selective reporting, and other biases. The domains assessed with higher proportions of an unclear or high risk of bias were sequence generation, allocation concealment, and blinding of outcome assessment. There is a low proportion of RCTs published in Spanish language journals. However, the number has been increasing over the years, and the low risk of bias assessment rates across domains show an increasing trend. Conclusions: A low percentage of Spanish-language dental journals issue RCTs. Our assessment of these RCTs' RoB suggests higher difficulties in the design and conduction phase than in the posterior reporting stage.

KEY WORDS
Randomized clinical trial; Dentistry; Risk of bias; Reporting.

INTRODUCTION

Randomized controlled trials (RCTs) are considered the best approach to assess the effects, benefits, and harms of therapeutic intervention, drug, device, or technique in human beings\(^1\sim3\). RCTs are also the foundation of systematic reviews and other evidence synthesis documents\(^4\sim6\). Evidence-based hierarchies place RCTs just below systematic reviews as the highest form of evidence\(^6\) that could be achieved from an in vivo/clinical trial. RCTs are widely accepted as the “gold standard” for obtaining unbiased estimates of treatment effects\(^6\). However, the reliability of individual test conclusions depends largely on internal validity, based on the quality of the research methodology and execution\(^6\). Therefore, high-quality reporting of the details of such research is essential\(^1\sim3\).

RCTs can have weaknesses in the design or analyses that could lead to underestimating or overestimating the intervention; this is known as bias and can affect in any direction\(^6\). It is usually impossible to know the extent to which biases have affected a particular study’s results. Consequently, to draw reliable conclusions, reviewers should consider the possible limitations of the studies, which relate to the extent to which their design, conduct, analysis, and presentation were appropriate to answer your research question\(^6\). Therefore, assessing the validity of included studies is a fundamental component of any systematic review and should influence the review’s analysis, interpretation, and conclusions.

Many tools have been proposed to assess RCTs’ quality in the context of systematic reviews or other evidence syntheses. Most of them are
The Cochrane Collaboration, 2020., n.d.) to elaborate the risk of bias for each selected trial using the 7 domains. Responses were entered into RevMan (Review Manager) [Computer Program]. Version 5.4. The Cochrane Collaboration, 2020, n.d.) for graphics and analysis.

RESULTS

Identification of RCTs

The search for RCTs was carried out in all Spanish-speaking countries (Spain and Latin America), and clinical trials (CT) were sought in the journals of Argentina, Bolivia, Chile, Colombia, Costa Rica, Cuba, Dominican Republic, Ecuador, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, Spain, Uruguay and Venezuela. In most of these countries it was not possible to locate any clinical trials. RCTs were identified in the following countries: Argentina, Chile, Colombia, Spain, Mexico, Peru, Uruguay and Venezuela. Table 2 shows the number of journals identified by country and the number of CCTs and RCTs found. The distribution of clinical trials is published in a previous article [18].

We reviewed a total of 25,810 articles in 114 journals. We excluded 25,423 because they corresponded to case reports, narrative reviews, in vitro studies, animal studies or observational studies. Only 387 (1.5%) of the published articles were potentially eligible for inclusion. After the full-text review, 292 (1.13%) RCTs were included for analysis, published in 51 of the reviewed journals, whereas 95 (0.4%) Controlled Clinical Trials (CCTs) were excluded. Figure 1 presents the flow diagram for the
Risk of bias in dentistry-related randomized controlled trials in Spanish language journals.

Table 2. Details of the number of journals identified by country, number of articles reviewed, and number of CCTs and RCTs found

<table>
<thead>
<tr>
<th>Country</th>
<th>N° JOURNAL</th>
<th>TOTAL OF ARTICLES</th>
<th>RCTs</th>
<th>CCTs</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARGENTINA</td>
<td>17</td>
<td>1.965</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>BOLIVIA</td>
<td>1</td>
<td>212</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>CHILE</td>
<td>16</td>
<td>3.008</td>
<td>63</td>
<td>18</td>
</tr>
<tr>
<td>COLOMBIA</td>
<td>10</td>
<td>2.041</td>
<td>25</td>
<td>7</td>
</tr>
<tr>
<td>ESPANA</td>
<td>38</td>
<td>10.954</td>
<td>152</td>
<td>34</td>
</tr>
<tr>
<td>MEXICO</td>
<td>17</td>
<td>3.598</td>
<td>22</td>
<td>13</td>
</tr>
<tr>
<td>PERU</td>
<td>6</td>
<td>1.483</td>
<td>12</td>
<td>81</td>
</tr>
<tr>
<td>URUGUAY</td>
<td>2</td>
<td>249</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>VENEZUELA</td>
<td>7</td>
<td>2.301</td>
<td>8</td>
<td>13</td>
</tr>
<tr>
<td>TOTAL</td>
<td>114</td>
<td>25.811</td>
<td>292</td>
<td>168</td>
</tr>
</tbody>
</table>

Figure 1. Flow diagram for the article selection process

The article selection process and details of the number of articles reviewed and excluded. Of the included RCTs, 152 were published in Spain (52%), 63 in Chile (22%), 25 in Colombia (11.9%), 22 in Mexico (8%), 12 in Peru (4%), 8 in Argentina (3%), 8 in Venezuela (3%), and 2 in Uruguay (1%). Spain and Chile were the countries with the highest number of clinical trials found. Chile had the highest number of RCTs per number of articles reviewed (2.09%), followed by Spain (1.39%).

Most of the journals identified and reviewed were not indexed in any of the main databases and do not have an impact factor. In fact, only one journal from Spain is indexed in PubMed and Journal Citation Report.

Risk of Bias (RoB) analysis

Figure 2 presents the distribution of RoB assessment by domain across studies. Among the domains that were most evaluated as unclear or high risk of bias are those assessing selection bias: sequence generation with 164 (56%) and 18 (6.1%) studies, respectively, and allocation concealment with 213 (72.7%) and 6 (2%) studies, respectively. Furthermore, the blinding of outcome assessment was evaluated in 138 (47.1%) studies as unclear and in 57 (19.5%) studies as high risk of bias.

For the domain of blinding of participants and personnel, 118 (40.3%) studies were assessed as low risk of bias, 110 (37.5%) as unclear, and 64 (21.8%) as high risk.

The best evaluated domains were incomplete outcome data, selective reporting, and other biases, with 223 (76.1%), 263 (99.8%), and 183 (62.5%) studies evaluated with low risk of bias, respectively.

RoB assessment over time.

Figure 3 shows the number of RCTs found per year in the reviewed journals. When assessing changes in risk of bias evaluations over the years, the rates of low risk of bias across domains show an increasing trend (Figure 4A). Unclear (Figure 4B) and high (Figure 4C) risk of bias assessment rates show a decreasing trend. There is a marked decrease in the high risk of bias rates in the blinding domains, but in turn a slight increase in the unclear risk of bias rates for these domains. (Figure 4).
In this study, 292 RCTs published in 51 dental journals of Spanish language were identified. Surprisingly, less than half (42.1%) of the dental journals that publish articles in Spanish language issue RCTs. This aspect might be explained by the low number of Spanish speaking journals indexed in main databases, discouraging authors of these countries from publishing their RCT in these sources, making them resort to foreign English language journals with a higher impact factor. To achieve an improvement, Spanish-language journals must have editorial committees that are better prepared to achieve a better level of peer review that will lead them to be included in indexed databases. In this sense, researchers and reviewers should be trained and professionalized. Obtaining these points will lead to studies such as RCTs being published in Spanish-language journals, thus bringing the evidence closer to a public that reads scientific literature and is limited by the English language. In this way, the importance of RCTs in clinical decision making will be known and, therefore, have a direct impact on the oral health of the population.

A risk of bias evaluation was performed for all the included RCTs using the RoB Tool developed by the Cochrane Collaboration. As previously mentioned, the items with lower risk of bias were Incomplete Outcome Data, Selective Reporting, and Other Biases. Conversely, the ones most weakly evaluated were related to blinding, either for the participants and personnel or the evaluators, in which 21.8% and 19.5% of the studies reported high risk of bias, respectively. This data reveals higher difficulties in the design and elaboration phase of the study than in the posterior reporting stage. One possible explanation for this phenomenon is the implementation of the new version of the CONSORT guideline of that year, leading to the production of studies judged as having high risk of bias over the years (Figure 4). This tendency in the low RoB evaluations shows a clear breakpoint around the year of 2010, increasing significantly. This phenomenon could also be explained by the implementation of the new version of the CONSORT guideline of that year, leading to the production of studies of higher quality.

Despite the low proportion of RCTs published in Spanish language journals, the number is increasing over the years. The findings of this study show a low steady publication rate until 1998, heterogeneously increasing until a peak incrementation is produced in 2008, surrounding the mean of 25 studies published per year (Figure 3).

These findings are consistent with previous research regarding the RoB of RCTs published in the Cochrane Databases of Systematic Reviews.

Our study has certain limitations. Firsthand, our search was developed only in dentistry related journals. Therefore, studies on this discipline published in journals from other specialties could have been left out. Moreover, we only reviewed journals from Latin America and Spain that publish in Spanish language, leaving aside articles written by authors residing in these countries of possible higher quality, published in English or in foreign journals. Finally, the assessment of the RoB was performed from the publication alone, without considering protocols, web materials or other useful data for a more complete evaluation and analysis.

For the main strengths in our study, we highlight the exhaustive comprehensive hand search in journals published in Spanish language in Latin America and Spain. Furthermore, the data extraction and RoB assessments were performed in duplicate and independently by two authors. To our knowledge, this is the first published study that evaluates the RoB of RCTs in Spanish speaking dental journals.

CONCLUSIONS

A low percentage of Spanish-language dental journals issue RCTs. Our assessment of these RCTs’ RoB suggests that there are greater difficulties in the design and conduction phase of the study than in the posterior reporting stage.

However, our findings suggest an increase in the proportion of the low risk of bias assessments across domains over the years. We encourage researchers and editors to improve the quality of the design, conduction, and reporting of RCTs, to reduce potential biases and their impact on the certainty of the findings. A low percentage of dental journals in Spanish publish RCTs. Our evaluation of the RB of these RCTs suggests that there are greater difficulties in the study design and conduct phase than in the subsequent reporting phase.

However, our findings suggest an increase in the proportion of low risk of bias evaluations in all domains over the years. We encourage investigators and publishers to improve the quality of RCT design, conduct, and reporting to reduce potential biases and their impact on the certainty of results.

FUNDING

There was no funding available for this study.

ETHICS APPROVAL

No ethical approval was required for this study.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.
Risk of bias in dentistry-related randomized controlled trials in Spanish language journals.

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