A comprehensive quality analysis of randomized controlled clinical trials of Asian ginseng and American ginseng based on the CONSORT guideline

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1. Introduction

Ginseng is an international herb that has been used for thousands of years. Two species most commonly applied and investigated in the ginseng family are Asian ginseng and American ginseng. The number of randomized controlled clinical trials (RCTs) has conspicuously increased, driven by the rapid development of ginseng. However, the reporting of RCT items of ginseng is deficient because of different trial designs and reporting formats, which is a challenge for researchers who are looking for the data with high quality and reliability. Thus, this study focused on providing an extensive analysis of these two species and examined the quality of the RCTs, based on the Consolidated Standards of Reporting Trials (CONSORT) guideline. Ninety-one RCTs conducted from 1980 to 2019 that were related to Asian ginseng and American ginseng used singly met our inclusion criteria. We found that the reporting quality of the two species has improved during the past 40 years. Publication date and sample size were significantly associated with the reporting quality. Rigorous RCTs designed for the species of ginseng are warranted, which can shed light on product research and development of ginseng in the future.

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have been conducted. A few investigations on quality assessment have been published in the past few decades [13–15]. Despite the increased research on the two species of ginseng, the overall RCT quality analysis of Asian ginseng and American ginseng has not been evaluated. No research on this subject is available. In consideration of these findings, we aimed to provide an extensive analysis of overall Asian ginseng and American ginseng RCTs reported globally and to examine the quality between them, which can track past and current evidence, as well as identify and highlight the potential future viewpoint of Asian ginseng and American ginseng RCT research and development.

2. Materials and methods

2.1. Data collection

Based on the tutorial of PubMed advanced search, we searched the data using the following strategy: “Ginseng” OR “Panax ginseng” OR “Panax quinquefolius” OR “Asian ginseng” OR “American ginseng” in the full fields. We screened the data, using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2009 Flow Diagram. The inclusion criteria were: (1) derived from the “Clinical Trial” type, (2) published before 2019, (3) written in English, (4) provided the full-text, (5) involved human clinical trials. The clinical trials were then assessed for eligibility: (1) Asian ginseng and American ginseng, (2) not a combination of different ginseng species, (3) not a combination of ginseng and other herbs, (4) not a ginseng-derived compound. Finally, completed RCTs with oral administration were included. To summarize, the RCTs that did not meet these criteria were excluded. A detailed flow chart was shown in the Fig. 1. In addition, the studies did not have any criteria regarding age, sex, or ethnicity.

2.2. Data extraction

All included RCTs were searched by two independent authors (WJ and XZ), based on the aforementioned search strategy. The RCTs were manually sought and had been conducted from 1980 to 2019, 40 years in total. According to the predefined criteria of the CONSORT 2010 checklist, a quality analysis form was designed to offer the extracting details in Table 1. The quality analysis contains six domains: title and abstract, introduction, methods, results, discussion, and other information. The six domains consisted of 37 items in total. Two authors (WJ and XZ) independently extracted the data, evaluated the quality, and calculated the score of the included RCTs. Any disagreements and uncertainties were discussed and resolved between the two authors. If necessary, a third author (SP) acted as judge. The final extraction data were presented in Supplementary Table 1.

2.3. Data evaluation

Ninety-one RCTs, which included 72 RCTs for Asian ginseng and 19 RCTs for American ginseng, were analyzed, based on the time distribution, country landscape, functional classification, preparation category, and product use. For the RCT quality score, an item was scored as “1” if it was fully reported, which was represented by “yes” (Y); it was scored as “0” if it was not reported or was inadequately reported, which was represented by “no” (N). Each RCT statistically had 37 items but four of them were not available (Item 6, 11, 13 and 25) in our study. Thus, every RCT quality score was calculated, based on the summarizing the individual Y score divided by 33. Other RCT information such as publication date, sample size, and trial length was simultaneously evaluated as potential factors of quality assessment between the two species.
2.4. Data analysis

Descriptive statistical analyses were conducted using Excel 2019 (Microsoft, Redmond, WA, USA), Prism 9.0 (GraphPad Software, San Diego, CA, USA), and SPSS 25.0 (IBM, Armonk, NY, USA). The mean and standard deviation (SD) quality score values were calculated for the two species to identify the characteristics associated with the quality score. Three factors (i.e., publication date, sample size, and trial length) were entered into the model to evaluate their relationship and significance, using the Pearson correlation and two-tailed significance.

3. Results

3.1. Time distribution and country landscape

As shown in Fig. 1, 91 RCTs (i.e., 72 RCTs related to Asian ginseng and 19 RCTs related to American ginseng) were analyzed from 1980 to 2019 in the time distribution. The average annual RCT number for Asian ginseng was approximately 2 and the RCT number for American ginseng was close to 0.5. As Fig. 2A showed, the first RCT of Asian ginseng was published in 1986 and that of American ginseng, in 2001. Each year, the RCT number for Asian ginseng was much more than that for American ginseng, except in 2005, when it was equal. Country landscape is a summary of the number of...
countries where an RCT was conducted and provides a whole picture of the global distribution of the two different ginseng species, as shown in Fig. 2C. Obviously, Asian ginseng was concentrated in Asia, especially in South Korea with 38 RCTs. By contrast, American ginseng was most concentrated in Canada with 8 RCTs. At the same time, the Asian ginseng was more widely distributed than American ginseng.

3.2. Functional classification, preparation category, and product use

With regard to the functional classification in Fig. 2B, the functions of the two species of ginseng were primarily classified as “cognitive & behavior”, “glucose metabolism”, “cardiovascular function”, “cancer”, “sexual function”, “inflammation & immune”, and “organ symptoms”. Most functions were in the cognitive & behavior functional classification. The preparation category of the two species were also nearly the same. The capsule preparation accounted for most preparations of Asian ginseng (80%) and American ginseng (89%). Other preparation categories were also clearly presented in Fig. 2D. Fig. 2E showed the analysis of product use for Asian ginseng (with using rate 26%) and American ginseng (with using rate at 21%).

3.3. Quality score analysis

The quality analysis involved six domains with 37 items: title and abstract, introduction, methods, results, discussion, and other information. Fig. 3 showed the quality analysis for each item.
between Asian ginseng and American ginseng RCTs. It presented the percentage of \( Y \) for one item in all RCTs related to Asian ginseng and American ginseng. For both species, items 2, 3, 4, 5, 7, 20, 22, 23, 26, 27, 31, 33, and 37 were higher than 50%. For Asian ginseng, the items 8, and 32 were relatively high at 64% and 57%. For American ginseng, only item 34 was higher than 50% at 53%. Fig. 4 showed the six domains quality analysis of Asian ginseng (Fig. 4A) and American ginseng (Fig. 4B). The introduction, results, and discussion for Asian ginseng were more than 50%, at 99%, 53%, and 60%, respectively. By contrast, the title and abstract, introduction, and discussion for American ginseng were more than 50%, at 53%, 100%, and 56%, respectively.

Fig. 5A presented the results of the RCT quality score for the two species of ginseng. The RCT quality score for Asian ginseng was a minimum of 0.1818, maximum of 0.7879, mean of 0.4802, range of 0.6061, and SD of 0.1347. The quality score for American ginseng was a minimum of 0.1818, maximum of 0.7273, mean of 0.4577, range of 0.5455, and SD of 0.1498. The quality score showed that 95% CI was –0.09315 to 0.04819, and the \( P \)-value was 0.5155 but without significance. Fig. 5B, C and D showed that the three factors (i.e., publication date, sample size, and trial length) were included in the model to check their relationship with the quality score, using the Pearson correlation and two-tailed significance analysis. The results were in Table 2.

4. Discussion

The aim of this study was to provide an extensive analysis of these two species and examining the quality of the RCTs that have been conducted on American ginseng and Asian ginseng. Asian ginseng and American ginseng had a similar tendency, which can be preliminarily divided into three stages, the emerging stage with a muted growth, the boom stage with a rapid increase, and the down stage with a relevant decrease. Asian ginseng was more popular among the researchers. With regard to popularity among countries, South Korea was highest in the global country landscape for Asian ginseng, which was unanimous with the findings of a study conducted in 2010 [4]. Canada had an important role in American ginseng research, which is probably related to the native origin [16]. In general, Asia and North America were active research areas. The global network of Asian ginseng and American ginseng manifested distinct regional distribution.

With regard to the functional classification, the two species had similar functional fields. Both species had a rich source of bioactive phytochemicals such as ginsenosides and polysaccharides, which were the major biologically active ingredients in ginseng [17,18]. The two species have often been extensively used in various food products, alternative nutraceuticals, and dietary supplements, such as the G115 capsule [19], Ginsana capsule [20], and Cheonggukjang powder [21] for Asian ginseng, and the Cereboost™ capsule [22], HT1001™ capsule [23], and CNT 2000 capsule [24] for American ginseng with fewer preparation categories in RCTs. Based on different marketed product using rates, we conjectured the possibility that different medication customs in different regions such as Asian would accept a decoction well; therefore, researchers may choose an original ginseng plant with a lower product using rate to conduct an RCT.

The quality analysis of six domains, which comprised 37 items, revealed unique characteristics between the two species. The two species showed a quite high level for the introduction between item 3 and item 4. However, the overall adherence to the CONSORT guideline in the other domains was relatively poor, especially from item 1 to item 2 for the title and abstract part. Most RCT researches did not use “randomized” in the title for Asian ginseng [25–27] and American ginseng [28–30]. In another aspect, the word restriction and the reporting format in the abstract were universally considered key influencing factors for the item 2 quality score.

A barrier may exist in using the CONSORT guideline in an all-around manner. Numerous journals restricted the abstract word count and the reporting format when researchers intended to submit their research for publication [31]. Two research studies may be examples of RCTs lacking a structured abstract containing a background, aim, methods, results, and conclusion sections for Asian ginseng [32] and American ginseng [33]. The structured format can influence reporting quality, which was closely linked with other research results [34]. Thus, we strongly recommended that the title and abstract should be as accurate, comprehensive and structured as possible within the restrictions of the guidelines of a journal. The collaboration between authors and journals should be improved to avoid rigid requirements that limit the quality level.

The quality score of Asian ginseng was higher than that of American ginseng in our research findings. RCT quality scores were compared with regard to three potential factors. In our model, the RCT quality score was significantly associated with the publication date for Asian ginseng and with the sample size for American
ginseng, which was similar to the results of a systematic review conducted in 2008 [35]. However, this finding was the opposite for trial length, based on a review conducted in 2009 [36]. The item was probably scored using different rules. In some studies, the quality score was regarded as 1 score, when all elements were reported [37,38], but in other studies may be regarded as partial compliance [39] or unclear [40], which should be accounted for in the analysis. Furthermore, authors’ awareness of the CONSORT statement also may lead to different results [41].

The reporting RCT quality of the two species of ginseng improved overall during the past 40 years. The CONSORT statement has been updated many times. It has become increasingly comprehensive, accurate and clear, which may have influenced the quality assessment.

A focus on another important aspect, how the sample size was determined, revealed that the sample size was poorly reported at less than 30% for both Asian ginseng and American ginseng. Other researchers similarly found that this item had poor quality [42–44]. In general, the two factors of publication date and sample size may be significant and powerful factors in reported RCT quality, which should be well researched in future RCTs. Rigorous RCTs for ginseng species also seem warranted in the future.

The current study introduced quality analysis, based on CONSORT guideline, for two species of ginseng. Considering the current systematic analysis findings, we are confident that our research was a comprehensive and integral summary of all available RCT evidence-based data.

However, our study also had several limitations. First, we could not provide a whole picture for all types of ginseng species, but only for the two ginseng species commonly used in researches. Thus, our findings do not represent all ginseng species situation. Second, the samples of the two species in our research were different and

Fig. 4. The quality analysis of the six domains: title and abstract, introduction, methods, results, discussion, and other information. The length of the internal radius represents the percentage of “reported” and the external radius represents the percentage of “not reported”. The indigo issue represents “title and abstract”, the yellow issue represents “introduction”, the orange issue represents “methods”, the green issue represents “results”, the blue issue represents “discussion”, and the pink issue represents “other information”.

A. The Asian ginseng pie chart. B. The American ginseng pie chart.
relatively small. Therefore, some investigators’ opinions may have had viewer bias. Finally, all studies we used were published in English so that non-English publications were not analyzed.

5. Conclusions

The extensive analysis of the two ginseng species revealed that each had their own characteristics. The reporting RCT quality of the two species of ginseng improved during the past 40 years. The analysis revealed that publication date and sample size were significantly associated with reporting RCT quality, which should be investigated and developed further in future research. The reporting format will be improved in terms of accuracy, comprehensiveness and structure. Rigorous RCTs designed for the species of ginseng seems warranted in the future, which could shed light on the product research and development of potential future fields of both Asian ginseng and American ginseng.

**Declaration of competing interest**

The authors have declared no conflict of interest.

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Compliance with ethics requirements

This research does not contain any studies with human or animal subjects.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jgr.2021.05.003.

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