Meta Analysis

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Prevention of Blood Donation-related Vasovagal Response by Applied Muscle Tension: a Meta-analysis

Cong Wang[1], Li Chen[1], Chenyu Sun[2], Yan Zhang[1], Can Cao[1], Yuanyuan Ma[1] and Wenwen Shi[1]

Abstract

Objective: Vasovagal reaction (VVR) is an adverse reaction to blood donation. Applied muscle tension (AMT) has been reported to reduce the probability of VVR during blood donation; however, the results have been controversial. We therefore conducted a meta-analysis to systematically evaluate the effect of AMT in reducing VVR.

Methods: We searched six major databases using "applied muscle tension" and "blood donation-related vasovagal response" as keywords. Relevant articles published in English or Chinese between 1 January 2000 and 30 June 2021 were included in the analysis. The quality of the included articles was evaluated and publication bias was assessed by forest and funnel plots and by Egger's test.

Results: Fifty-one articles were identified, of which six were included according to the pre-defined inclusion and exclusion criteria. A fixed-effects model was adopted for effect size combination and revealed a relative risk of 0.52 (95% confidence interval 0.40 to 0.67). The AMT group was superior to the control in terms of VVR prevention. A funnel plot and Egger's test suggested that the findings were accurate and reliable with low publication bias.

Conclusion: AMT could effectively reduce VVR during blood donation. Further multicenter studies with large sample sizes are needed to confirm these results.

Keywords

Applied muscle tension, blood donation, vasovagal response, meta-analysis, volunteer, adverse reaction

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[1]Hebei Province Blood Center, Shijiazhuang 050011, China

[2]AMITA Health Saint Joseph Hospital Chicago, 2900 N. Lake Shore Drive, Chicago 60657, IL, USA

Corresponding author:
Cong Wang, Hebei Province Blood Center, No. 299 Heping West Road, Shijiazhuang 050011, China.
Email: 1042871772@qq.com

Introduction

About 118.4 million blood donations were collected worldwide in 2020 and the number of blood donors is increasing year after year; however, many countries and regions, especially among developing countries, still face transient or seasonal blood shortages. Over 800 million units of blood are collected worldwide each year, but only 38% of these are collected in developing countries.[1–7]

Recruiting more blood donors is thus crucial to ensuring a clinical blood supply. However, many first-time donors, especially younger donors, often lack knowledge about blood donation and experience discomfort during the process, including dizziness, sweating, and pallor, which are collectively referred to as the vasovagal response (VVR).[8–13]

VVR is caused by hypotension due to vasodilation. During the process, the blood donor usually goes through four phases: (1) early stabilization, (2) circulatory instability, (3) terminal hypotension, and (4) recovery.[14–17] It is therefore crucial to reduce the hypotensive state in the blood donor, especially during the second phase of circulatory instability. One study also noted that although most adults showed a decrease in cardiac output, only younger individuals showed a gradual decrease in vascular tone.[17] Stopping donors from entering the second phase may thus minimize the probability of VVR during blood donation.

The National Health and Family Planning Commission of the People's Republic of China issued their Guidelines on the Classification of Blood Donation Adverse Reaction (WS/T551-2017) in 2017, which specified the classification, severity assessment, and relevance of adverse reactions during blood donation. The manifestations of VVR are defined as general malaise, weakness, pallor, sweating, anxiety, dizziness, and nausea, while a few donors may experience more severe symptoms such as transient loss of consciousness (syncope), convulsions, or incontinence.[18] Fainting and falling can lead to accidental injury. The main contributors to the development of VVR in blood donors include psychological factors and reduced blood volume.[19] China has begun to consider the importance of donor responses to adverse reactions during blood donation. The occurrence of VVR during blood donation has also been reported to lead to termination of the donation procedure and to reduce the donor's willingness to donate again following a bad blood-donation experience.

Recent studies have indicated that practicing applied muscle tension (AMT) during blood donation could substantially alleviate the occurrence of adverse blood-donation reactions.[11] To practice AMT during blood donation, donors adopt a lying or sitting position with their legs crossed and tense the muscles in the legs, buttocks, and trunk 20 to 30 times for 5 to 10 s each time, before relaxing for 5 to 10 s each time.[11] Practicing AMT throughout the whole blood-donation process can effectively increase venous return and sympathetic excitation. In addition, the donors are distracted and their nervousness can effectively be relieved, thus reducing the occurrence of VVR. However, some studies found similar probabilities of VVR in AMT and control groups, i.e., the effect of AMT was not significant.[6] We therefore conducted a meta-analysis to systematically evaluate the effect of AMT in reducing blood donation-related VVR.

Methods

Literature search strategy

We performed a literature search of PubMed, Web of Science, MEDLINE, the

Cochrane Library, China National Knowledge Infrastructure database, VIP database, and China Biomedical Database for articles reporting randomized controlled trials (RCTs) on the effect of AMT in reducing VVR during blood donation. The search strategies used were: (MeSH "vasovagal reaction" OR MeSH "Vasovagal response" OR MeSH "Syncopes, Vasovagal" OR Mesh "VVR") AND (MeSH "applied muscle tension" OR MeSH "Contraction, Muscle" OR MeSH "AMT"). Relevant articles published in English or Chinese between 1 January 2000 and 30 June 2021 were included in the analysis. The references of the included articles were also screened to identify further relevant studies.

Literature selection

The inclusion criteria for this meta-analysis were as follows: (1) studies based on RCTs investigating the use of AMT during blood donation; (2) studies based on whole-blood donations (articles on other subjects such as plateletpheresis were excluded to ensure comparability); and (3) articles reporting a clear outcome in terms of donor VVR during blood donation.

The exclusion criteria are as follows: (1) studies not examining the use of AMT to reduce VVR during blood donation; (2) articles for which full data extraction was not possible; (3) animal studies; (4) all grey literature, e.g., conference papers, letters, and case reports; (5) and systematic evaluations and meta-analyses.

After removing duplicate data using Endnote X9, the titles and abstracts were screened independently by two authors (Li Chen & Yan Zhang) to remove articles that did not meet the inclusion criteria. The remaining articles were then read in their entirety and the final articles were included based on the pre-determined criteria.

Data extraction

Two authors (Wenwen Shi & Yuanyuan Ma) simultaneously and independently extracted the following relevant information from the included literature, using a pre-designed extraction form: (1) first author's name, (2) year of publication, (3) country of study, (4) age range of blood donors, (5) sex of blood donors, (6) total number of blood donors, (7) site of blood donation, (8) grouping, and (9) type of scale. Disagreements over data extraction were resolved through discussion or by consultation with a third person. Authors of articles with missing data or not-extractable data were contacted by email, and the articles were excluded if the full data were still not available.

Literature quality assessment

Literature quality was assessed independently by two authors (Cong Wang & Can Cao) using the Cochrane risk bias assessment tool, with the primary focus of evaluating bias in the included literature. This tool consists of seven domains: (1) random sequence generation; (2) allocation concealment; (3) participants and personnel blinding; (4) outcome assessment blinding; (5) incomplete outcome data; (6) selective reporting; and (7) other sources of bias. Each of these domains is further divided into three levels: low, unclear, and high risk of bias. Disagreements were resolved through discussion or by consultation with a third person.

Statistical analysis

The outcome indicator in this study was a two-category variable and we therefore calculated the relative risk (RR) and 95% confidence interval (95% CI). The primary outcome indicator was donor VVR during blood donation. A fixed-effects or random-effects model was selected based on the P-value and I^2, with a fixed-effects

model for $I^2 < 50\%$ and $P > 0.1$, otherwise, a random-effects model was selected. If the heterogeneity was excessive (e.g., $I^2 > 75\%$), the source of the heterogeneity was explored. Publication bias was evaluated by examining the left-right symmetry of the funnel plot and the results of Egger's test using Stata ($P > 0.05$ indicated no publication bias). Subgroup analyses were conducted if sufficient studies and sample sizes were available. All statistical analyses were performed using RevMan 5.3 and Stata 14.0.

Results

Literature selection

Fifty-one articles were identified from the seven databases, according to the pre-defined search strategy. Thirty-one papers were retained after removing duplicates, and 12 relevant papers were left after screening the titles and abstracts. Six papers, five in English and one in Chinese, finally remained after screening the entire article according to the inclusion and exclusion criteria. The study flow is shown in Figure 1.

Research features

The six papers included in this study reported on a total of 4226 unpaid voluntary blood donors, of whom 2236 were randomly assigned to AMT groups and 1990 were randomly assigned to control groups. Most of the included studies were conducted in European and American populations, with only one trial from China.

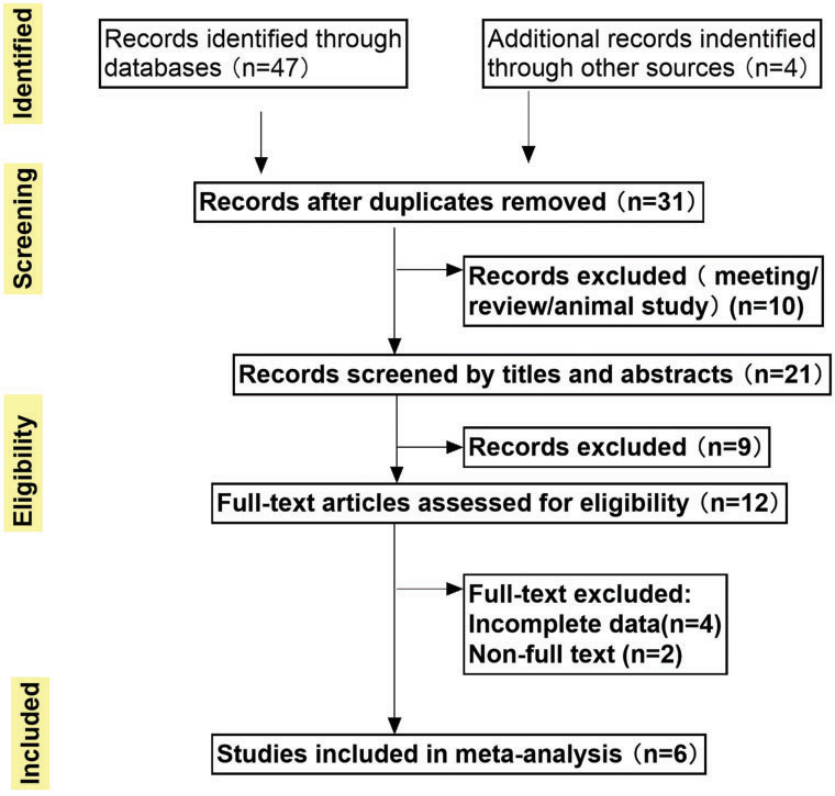

Figure 1. PRISMA flow chart of literature selection and literature search processes.

Five of the included studies were based on studies conducted at fixed blood-donation sites, and one study was based on mobile blood-donation sites. All the included studies adopted the Blood Donation Reactions Inventory (BDRI) scale. The basic characteristics of the included studies are shown in Table 1.

Literature quality evaluation

The overall literature quality evaluation showed that the six included papers had high-quality ratings. The quality-evaluation chart for each study showed that none of the included studies mentioned whether blinding was used (for subjects, investigators, or evaluators). In addition, the 2003[20] and 2007[21] studies by Ditto et al. also failed to mention whether the allocation was based on randomized numbers, and only the use of RCTs was mentioned. All other items were mentioned in each of the included articles. The risk of bias assessment results included in the RCT are shown in Figure 2.

Overall meta-analysis results

The heterogeneity test of the six included papers showed $I^2 = 0$, $P = 0.75$, suggesting that the heterogeneity among the included articles was not statistically significant, and a fixed-effects model was therefore selected for the meta-analysis. The combined RR of the six studies was 0.52 (95% CI 0.40 to 0.67), which was statistically significant ($Z = 5.10$, $P < 0.001$), suggesting that blood donation-related VVR was lower in patients with AMT (Figure 3).

Sensitivity analysis

The sources of heterogeneity in each study were investigated using RevMan 5.3 software, and no significant differences were found, proving the high stability of this study.

Publication bias

Funnel plots for the six included studies were basically left-right symmetrical, indicating no significant publication bias (Figure 4). Egger's test using Stata 14.0 also showed no publication bias in this meta-analysis.

Discussion

This meta-analysis focused on the effectiveness of AMT for preventing VVR in blood donors. To the best of our knowledge, this is the first independent meta-analysis to examine the use of AMT as a primary intervention to reduce the occurrence of VVR. The six included articles were all high-quality RCTs, comprising a total of 4226 blood donors. The combined RR of the six studies was 0.52 (95% CI 0.40 to 0.67; $Z = 5.10$, $P < 0.001$), suggesting that AMT significantly reduced the risk of blood donation-related VVR compared with the control group.

The literature search also identified four large cohort studies, based on a total of 450,000 observations, which were excluded because the meta-analysis was limited to RCTs. However, a review of the abstracts of those excluded articles supported the findings of this study, i.e., the risk of VVR was significantly reduced by AMT.

We also identified one article, the abstract of which suggested similar risks of VVR in the AMT and control groups (both 0).[6] Twelve randomly selected blood donors practiced AMT during blood donation while 12 other donors with matching conditions received no intervention, and the risk of VVR was observed in both groups. None of the 24 blood donors experienced VVR, and the authors thus concluded that AMT did not reduce the risk of VVR in blood donors. However, the probability of VVR during blood

Table 1. Basic characteristics of the included studies

Study	Year	Country	Site	Number of participants	Age (years)	Percentage males	Group	Evaluation scale
Thijsen et al.[11]	2018	Australia	F	734	33.3 ± 12.6	39.2	AMT/placebo/time points	BDRI
Holly et al.[24]	2012	Canada	M	282	1: AMT pre-donation and during donation 20.8; 2: AMT pre-donation only 20.7; 3: AMT during donation only 19.7; 4: no-treatment control 21.1	53.5	1: AMT pre-donation and during donation; 2: AMT pre-donation only; 3: AMT during donation only; 4: no-treatment control	BDRI/SSAI
France et al.[29]	2010	USA	M	414	20.2	48.1	1: Standard donation; 2: placebo; 3: pre-donation water; 4: pre-donation water and leg exercise during donation	STAI-Y/BDRI/BDSS/MSS/FS
Ditto et al.[21]	2007	Canada	M	1209	21.9 ± 3.4	50	1: No-treatment control group; 2: full-AT group; 3: lower-body-tension group; 4: upper-body-tension group; 5: upper-body tension with distraction group; 6: expectation-placebo group	BDRI
Ditto et al.[26]	2003	Canada	M	605	n	n	1: No-treatment control group; 2: placebo control; 3: AMT	BDRI
Jia et al.[7]	2020	China	M	1784	18–23	49.9	1: AMT; 2: placebo	STAI/BDRI

AMT, applied muscle tension; F, fixed site; M, mobile site; BDRI, Blood Donation Reactions Inventory; SSAI, Spielberger State Anxiety Inventory; STAI, State Anxiety Inventory; BDSS, Blood Donation Satisfaction Survey; MSS, Muscle Soreness Scale; FS, Fatigue Scale; n, not described.

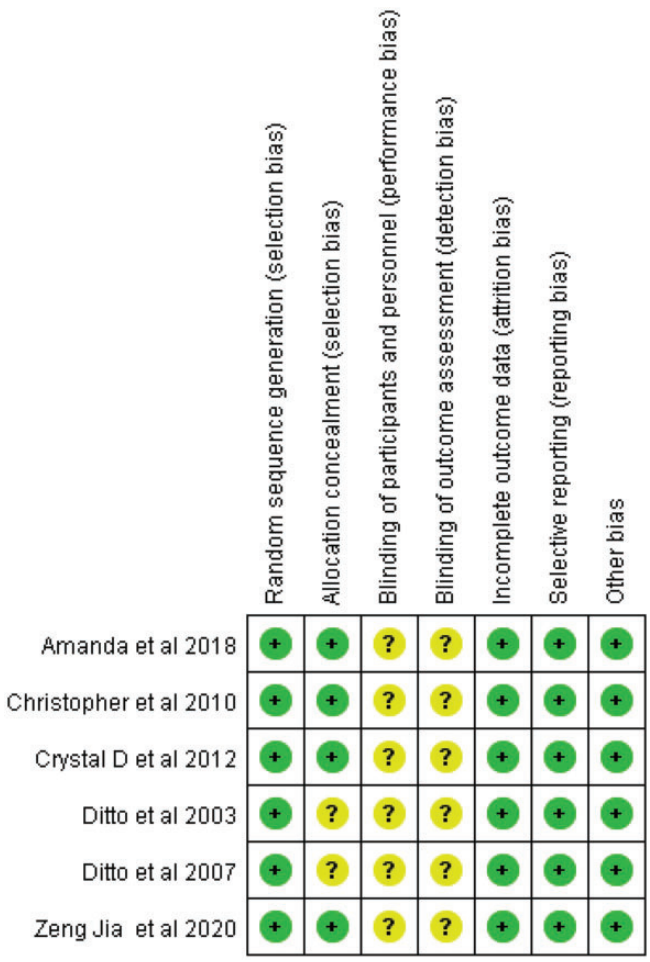

Figure 2. Literature quality assessment.

donation has been reported to be low (1.4% to 7%),[19] and the conclusions may thus be biased if the sample size is too small, resulting in less-credible results. Although VVR is mostly mild, a poor blood-donation experience may still affect the donor's willingness to give blood again.[19,20,22–24] Studies[25] have pointed out two reasons for the low incidence of VVR: subjectively, the on-site staff may not consider that the donor's discomfort meet the criteria for VVR and therefore do not record it, and objectively, the donor may have mild symptoms but may be unwilling to show physical discomfort and thus suppresses them.

It has been increasingly reported that the occurrence of VVR can decrease the number of blood donors.[21,25–28] Notably, the motivation of first-time donors to donate blood again can be drastically reduced by an unpleasant blood-donation experience.[29,30] This leads to a vicious cycle in that more effort must be directed to recruiting new donors to replace discouraged blood donors, but these replacements may lose motivation due to VVR.

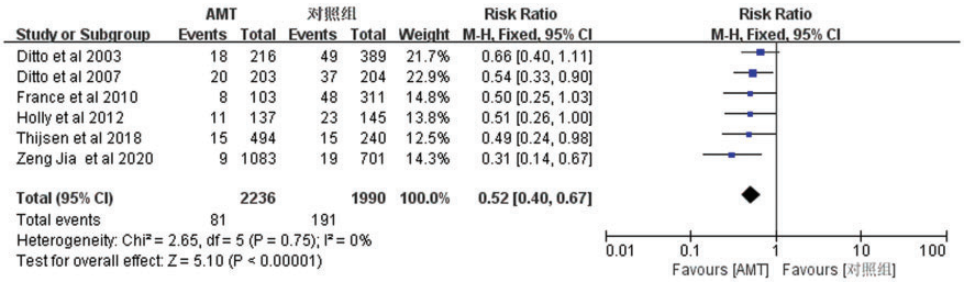

Figure 3. Forest plot of the overall meta-analysis.
M-H, Mantel–Haenszel; CI, confidence interval; AMT, applied muscle tension.

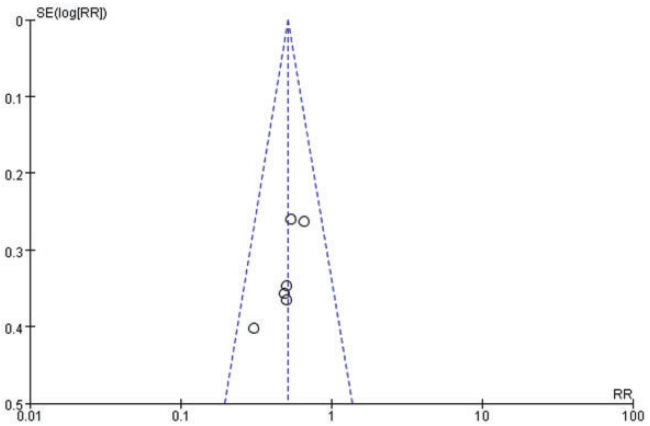

Figure 4. Funnel plot for publication bias of the included studies.
RR, relative risk; SE, standard error.

This study had some limitations. First, the number of included articles was small, with only six papers meeting the inclusion criteria. Second, the literature search was limited to articles published in English or Chinese, and articles in other languages were excluded, which could limit further research. Finally, no subgroup analyses were performed due to the small number of included articles.

Conclusion

The current meta-analysis indicated that AMT may effectively reduce the occurrence of VVR during blood donation. In the future, 5G network technology and one-on-one on-site education could potentially open up new avenues for reducing the incidence of VVR. However, the current sample size was insufficient due to the small number of included articles, and further large-scale multicenter RCTs should be designed and conducted in the future to confirm the effectiveness of AMT in reducing VVR during blood donation.

Declaration of conflicting interest

The authors have no conflicts of interest to declare.

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ORCID iD

Cong Wang https://orcid.org/0000-0002-7506-6747

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