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Astragalus injection enhances the sensitivity of clinical cancer patients to chemotherapy: a systematic meta-analysis

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 04 July 2024 and was last updated on 04 July 2024.

INTRODUCTION

Review question / Objective This is a meta-analysis of the included eligible studies was performed to evaluate the effect of Astragalus injection (AGI) or its main component, Astragaloside polysaccharides (APS) injection, on the resensitization of cancer cells to chemo-drugs and clarify the exact therapeutic value of AGI or APS in clinically resistant cancers. P: cancer. I: chemo-drugs treatment in combination with AGI or APS. C: standand clinical chemotherapy. O: 1-year survival rate, Karnofsky Performance Score (KPS) increase and clinical efficacy.

Condition being studied Drug resistance of cancers results in chemotherapy failure and cancer relapse, finally leads to the death of cancer patients. Resistance reversal agents need an extremely high concentration to effectively eliminate resistant cells, consequently causing toxicity to the normal cells. Traditional Chinese Medicine Astragalus was commonly used to assist chemo-drug treatment in clinical cancer patients. In recent years, many studies have revealed that AGI significantly enhanced cancer cells' sensitivity to chemo-drugs. Given that 1-year survival could be used to evaluate the effectiveness of the therapy and the Karnofsky Performance Score increase is utilized to assess the quality of life improvement, with an increase of ≥10 points being considered a quality of life improvement, the present study investigated the clinical efficacy of the combination of AGI or APS with chemotherapy in cancer patients through a systematic meta-analysis.

METHODS

Search strategy MeSH terms included Astragalus (or AS) combined with words correlating to chemotherapy (chemo-drug or chemo*), and terms

referring to cancer (cancer* or adenocarcinoma* or carcinoma* or tumor*) were used to search for eligible studies.The entry terms for same MeSH term were initially combined using logical word "OR" and subsequently different combinations for MeSH term were re-combined using logical word "AND".

Participant or population Cancer patients diagnosed with pathology.

Intervention Chemo-drugs treatment in combination with Astragalus injection or astragaloside polysaccharides injection.

Comparator Standand clinical chemotherapy.

Study designs to be included The studies presenting tumor response rates in cancer patients receiving chemo-drugs treatment in combination with AGI were systematically searched from six common scientific databases until February 2024. The relative risks (RRs) indicating the tumor response rate, 1-year survival rate, and quality of life improvement in clinical patients among two groups were calculated in metan package. The pooled RRs with 95% confidence intervals (CIs) were used to explore the effect of AGI or APS on enhancing drug sensitivity in terms of tumor response, 1-year survival rate and quality.

Eligibility criteria Only studies that satisfied the following conditions were included: (1) the study involved human cancer patients; (2) all patients underwent basic treatment; (3)all patients were classified into two groups randomly, one group only received basis treatment, the other group received basic treatment combined with AGI-related therapeutics agents; (4) presenting tumor response events in both groups. Studies that met the following criteria were excluded as described previously (Zeng, R., H. Li, L. Jia, et al., 2022): (1) duplicative analysis; (2) abstracts, case reports, reviews, news reports, or protocols; (3) subjects were cell lines or xenografted animals using patient-derived cancers; (4) AGI combined with other Chinese medicines.

Information sources PubMed, EMBASE, Cochrane Library, ISI Web of Science, VIP and CNKI until February 2024 without a lower limit on publication date.PubMed, EMBASE, Cochrane Library, ISI Web of Science, VIP and CNKI.

Main outcome(s) Tumor response rate, 1-year survival rate and Karnofsky Performance Score (KPS) increase rate.

Additional outcome(s) None.

Data management The downloaded pubilications were managed using endnote sofware.

Quality assessment / Risk of bias analysis Cochrane TOOL, the GRADE approach.

Strategy of data synthesis The type of extracted data was count and pooled together using the random (M-H) effects model. Pooled RRs with 95% CIs, evaluating the effect of AGI or APS on the resensitization of cancer patients to chemo-drugs, were represented using a forest plot. A pooled RR> 1 indicates AGI enhanced the effect of chemo-drug in cancer treatment. Cochran's Q test and I2 statistic were used to evaluate the heterogeneity from the pooling model, where I2 ≤ 50% indicates no or moderate heterogeneity and I2 >50% indicates strong heterogeneity, along with phet <0.05 presenting significance[19]. If heterogeneity occurred, the subgroup analysis and regression analysis were conducted to analyze the heterogeneity source. To assess the stability of the pooling model for pooled RRs, a sensitivity analysis was conducted by sequentially removing one study at a time. A funnel analysis was carried out using Begg's test to estimate publication bias, where a significance with a p-value less than 0.05. The statistical analysis was done using STATA software version 17.0 (STATA Corporation, College Station, TX, USA).

Subgroup analysis The pooled RRs for tumor response rate in lung cancer was 1.27 (1.16, 1.38), which indicated that AGI significantly increased the chemo-sensitivity of NSCLC patients. However, the pooled RR for tumor response rate in gastric cancers was 1.18 (0.99, 1.42), with the lower 95% CI below 1, suggesting there is no significant enhancement of AGI for chemo-sensitivity in gastric cancers. Additionally, the pooled RRs for tumor response rate in other cancer patients revealed AGI significantly enhanced chemo-sensitivity. Taken together, AGI increased chemo-sensitivity in cancer patients except for gastric cancer.

Because the sample size of cancer patients enrolled in clinical studies might affect the overall effect of AGI, subgroup analysis for sample size was also conducted. The result showed that the pooled RRs of sample size 100 was 1.23(1.14, 1.34) , which indicated that the effect of AGI on enhancing chemo-sensitivity was not varied by sample size.

Sensitivity analysis The leave-one-out approach was used in the sensitivity analysis to investigate

the effect of each study on the pooled RRs, and to determine the stability of the pooled model. The pooled RRs were recalculated after removing one study from the pool at a time to assess the impact of eliminating the study on the pooled outcomes. The pooled model remained steady even after every study was eliminated sequentially, suggesting that none of these studies had significant effects on the pooled results.

Language restriction None.

Country(ies) involved China.

Other relevant information None

Keywords AGI, drug resistance, tumor response, survival, quality of life.

Dissemination plans None.

Contributions of each author

Author 1 - Tingjie Ye - Tingjie Ye was responsible for the initial idea, data collection, analysis, interpreted the findings and manuscript review.
Author 2 - Xiaofeng Yan was responsible for data collection, analysis, and manuscript.
Author 3 - Wenhao Xiu aided in data gathering, analysis and manuscript review.
Author 4 - Changtai Qin obtained data and revised the manuscript.
Author 5 - Yuxi Yang obtained data and revised the manuscript.
Author 6 - Jinzu Yang contributed to manuscript revisions.
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