INPLASY PROTOCOL

To cite: Liu et al. Rikkunshito for upper gastrointestinal syndrome in patients with cancer: a systematic review and meta-analysis protocol. Inplasy protocol 2020100068. doi: 10.37766/inplasy2020.10.0068

Received: 19 October 2020

Published: 19 October 2020

Corresponding author:
Yifeng Ren

ryfdoctor@163.com

Author Affiliation:
Hospital of Chengdu University of Traditional Chinese Medicine

Support: **Evidence-based construction.**

Review Stage at time of this submission: **Formal screening of search results against eligibility criteria.**

Conflicts of interest:
None.

Rikkunshito for upper gastrointestinal syndrome in patients with cancer: a systematic review and meta-analysis protocol

Liu, H[1]; Zheng, C[2]; Wang, Y[3]; Yan, R[4]; You, F[5]; Ren, Y[6].

Review question / Objective: **Investigating the effects and safety of rikkunshito for upper gastrointestinal syndrome in patients with cancer, and provide more reliable evidence for clinical treatment.**

Condition being studied: **Nausea, vomiting and anorexia, such upper gastrointestinal dysfunction are common adverse events caused by chemotherapy or cancer surgery, which intrigue a severe impact on quality of life in cancer patients. Although standard antiemetic therapy in accordance with the ASCO, NCCN and MASCC/ESMO has been carried out, the symptoms still can't be fully contolled. Rikkunshito, an herbal medicine, has been wildly used to prevent upper gastrointestinal symptoms in cancer patients in recent years due to its effectiveness in digest disease. Although a systematic review and meta-analysis for the effect of Rikkunshito in upper gastrointestinal syndrome has been issued in 2019, no subgroup analysis was performed for patients with cancer. It is well known that the occurrence frequency, severity and evaluation index of upper digestive tract syndrome are different between patients with cancer and general digestive diseases. The efficacy of rikkunshito in patients with cancer remains uncertain. Otherwise, observational studies and new clinical studies reported in 2019 and 2020 have not yet been included. Therefore, a systematic evaluation for the efficacy and safety of Rikkunshito in upper gastrointestinal syndrome in cancer patients is necessary.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 19 October 2020 and was last updated on 19 October 2020 (registration number INPLASY2020100068).

INTRODUCTION

Review question / Objective: **Investigating the effects and safety of rikkunshito for upper gastrointestinal syndrome in patients with cancer, and provide more reliable evidence for clinical treatment.**

Condition being studied: Nausea, vomiting and anorexia, such upper gastrointestinal dysfunction are common adverse events caused by chemotherapy or cancer surgery, which intrigue a severe impact on quality of life in cancer patients. Although standard antiemetic therapy in accordance with the ASCO, NCCN and MASCC/ESMO has been carried out, the symptoms still can't be fully contolled. Rikkunshito, an herbal medicine, has been wildly used to prevent upper gastrointestinal symptoms in cancer patients in recent years due to its effectiveness in digest disease. Although a systematic review and meta-analysis for the effect of Rikkunshito in upper gastrointestinal syndrome has been issued in 2019, no subgroup analysis was performed for patients with cancer. It is well known that the occurrence frequency, severity and evaluation index of upper digestive tract syndrome are different between patients with cancer and general digestive diseases. The efficacy of rikkunshito in patients with cancer remains uncertain. Otherwise, observational studies and new clinical studies reported in 2019 and 2020 have not yet been included. Therefore, a systematic evaluation for the efficacy and safety of Rikkunshito in upper gastrointestinal syndrome in cancer patients is necessary.

METHODS

Participant or population: Diagnosed with cancer with an indication for chemotherapy or surgery; estimated life expectancy ≥ 3 months; Age ≥ 20 years; gender is not limited; Provided signed informed consent and agreed to cooperate with treatment.

Intervention: Take Rikkunshito orally.

Comparator: Placebo; Common drugs that prevent nausea, vomiting and anorexia; No treatment.

Study designs to be included: We tend to include clinical randomized controlled trials (RCTs) as a high level of evidence. Non-inferiority non-RCTs, observational studies will also be considered if the numbers of RCTs are insufficient. Full article not available is excluded.

Eligibility criteria: 1. Type of studies: randomized controlled trials (RCTs), random crossover studies, controlled (non-randomized) clinical trials, observational study carried out in humans will be considered. These following literary types are not taken into account: case reports, animal mechanism studies, self-controlled; 2. Types of participants: participants diagnosed with cancer and suffered upper gastrointestinal symptoms induced by chemotherapy or surgery are eligible to be included. The exclusion criteria are as follows: patients with renal dysfunction, cardiac dysfunction, or bone-marrow dysfunction; predicted survival ≤3 months, women who were pregnant, breastfeeding, or of childbearing potential were not enrolled; 3. Types of interventions: the intervention group will take Rikkunshito orally, while the control group adopts a placebo, or no treatment, standard treatment.

Information sources: We will search relevant studies through the following databases from their inception to October 2020: Pubmed, MEDLINE, Embase, Cochrane Library, Web of Science, National Institute of Informatics, Google scholar. Grey articles, reference lists of articles retrieved and related journals will be searched manually. We applied a language restriction of English, Japanese and Chinese.

Main outcome(s): The difference in nausea, vomiting and anorexia symptoms before and after treatment is considered as primary outcome: nausea, vomiting and anorexia grade (any scale).

Additional outcome(s): Complete response (CR) rates (no emesis and no rescue medication) in the overall, acute and delayed phases; Food intake (any scale) ; Quality of life (any scale); Plasma ghrelin level; Incidence rate of adverse events associated with Rikkunshito.

Quality assessment / Risk of bias analysis: The risk of bias of the RCTs will be assessed in accordance with the Cochrane Handbook, including "high risk" of bias, "low risk" of bias, or "unclear risk" of bias. The types of bias will be evaluated as follows: 1. Random sequence generation (selection bias); 2. Allocation concealment (selection bias); 3. Blinding of participants and personnel (performance bias); 4. Blinding of outcome assessment (detection bias); 5. Incomplete outcome data (attrition bias); 6. Selective reporting (reporting bias); 7. Other bias. The Newcastle-Ottawa Scale (NOS) will be applied for the non-RCTs.

Strategy of data synthesis: Review Manager (V.5.3) statistical software will be applied. At least two studies are need for this analysis. In addition, if the study is a cross-over study, we will only analyze the data from the period before the first crossover. A fixed-effect model will be applied if there is little heterogeneity or insufficient numbers of studies. The random effect model will be considered if there is a level of heterogeneity.

Subgroup analysis: We will execute the following subgroup analyses if there is significant heterogeneity among the researches: 1. types of clinical trials (RCTs or non-RCTs); 2. types of anti-tumor therapy (chemotherapy or surgery); 3. dose and duration of Rikkunshito.

Sensibility analysis: Sensitivity analysis will be mainly carried out to evaluate the robustness of meta-analysis results. We can exclude each included study 1 by 1 and the results will be repeated after omitting the low-quality studies. Moreover, we will also measure whether the statistics model (random-effects model and fixed-effects model) will affect the current results.

Country(ies) involved: China.

Keywords: Rikkunshito; patients with cancer; Nausea; Vomiting; Anorexia.

Contributions of each author:
Author 1 - Hong Liu.
Author 2 - Chuan Zheng.
Author 3 - Yuting Wang.
Author 4 - Ran Yan.
Author 5 - Fengming You.
Author 6 - Yifeng Ren.