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Study Protocol

Evidence mapping of interactions on concomitant use of Chinese medicine and platinum-based chemotherapy: a scoping review protocol

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ABSTRACT

Background: The utilization of Chinese herbal medicine (CHM) has gained popularity and acceptance worldwide. Increasing use of CHM either as a stand-alone or an adjunctive treatment for cancers has given rise to increasing concern on potential herbal-drug reactions. Possible combinatory effects are important to be explored in evaluating the rationality of integrating CHM and chemotherapy in clinical practice. This study aims to update the current knowledge on herbal-drug interactions (HDI) of the commonly used platinum-based chemotherapy (PtC) in cancer patients.
Methods: Systemic searches will perform on online databases (English and Chinese) to identify papers from inception until December 2019 for inclusion into the review. The search strategy will be following PRISMA Scoping Reviews Checklist as a quality assurance step. All records retrieved will be screened by 2 independent reviewers. The preclinical studies and clinical studies that involve in assessing the concurrent use of CHM and PtC will be considered. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses will be used as scoping review framework.
Discussion: This scoping review will explore the compatibility or combination rule of CHM-PtC and assist in understanding HDI in CHM-PtC co-treatment. Identification of active properties in CHM's HDI and understanding pharmacokinetics and pharmacodynamic of the CHM alone or as co-treatment are essential for patients' safety profile. It will provide a new insight for future practice in cancer treatment.
Study registration: This protocol has been registered in the Research Register (https://www.researchregistry.com/) with an unique registration number: reviewregistry790.

1. Introduction

The utilization of Chinese herbal medicine (CHM), a form of Chinese medicine (CM) has gained popularity and acceptance worldwide.[1] Eighty percent of people in developing countries use herbal medicine as a complementary and alternative medicine (CAM) for illnesses ranging from common cold to chronic diseases. In Asia, the rate of CAM use among cancer patients was 55.0%.[2] Despite the increased popularity of CHM among cancer patients, a vast majority of oncologists believed that CAM were ineffective for treating cancer.[3] However, CHM, is used increasingly, either from patient request or as recommended by the physician, either as a stand-alone or an adjunct in cancer treatment. This has created interest in medical professions to evaluate the effectiveness and safety of CHM as the combination treatment of conventional medicine may give rise to potential harmful herb-drug interactions. To date, a number of in silico, in vitro, and animal studies have been reported to predict or identify the drug interactions with herbal remedies. Clinical studies and case reports have also identified a number of herbal-drug interactions as a consequence of concurrent drug-herb use.[4] However, reports on understanding the clinical rationality of these combinations are yet available. As clinical consequences of herbal-drug interactions varies from well-tolerated

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to severely adverse reactions, early identification is imperative to prevent fatal outcome.[4] The overall viewpoint and pragmatic idea of the possible combination are important in evaluating the rationality of clinical CHM and chemotherapy combinations in extensive clinical practice. Therefore, this scoping review seeks to update our knowledge on herb-drug interactions (HDI) with an emphasis of the commonly used platinum-based chemotherapy in cancer patients.

The main objective of this scoping review is to identify the literature of observational studies on prevalence, patterns on adverse events and experimental on safety issues and other factors associated with concurrent prescription of CHM and platinum-based chemotherapy (PtC) in cancer patients. The secondary objective of this review was to identify the type of CHM-chemotherapy interactions in pre-clinical studies in cotreatment of CHM and PtC.

2. Methods

2.1. Protocol and registration

The method foundation of this review is draws from Arksey and O' Malley's seminal framework[5] for scoping reviews and more recent advancements to the methodology.[6–8] The reporting method for this review will be developed in accordance to the recommendations from the PRISMA extension for scoping reviews (PRISMA-ScR).[9] This protocol has been registered in the Research Register (https://www.researchregistry.com/) and its unique registration number is reviewregistry790.

2.2. Eligibility criteria

We will engage in an interactive process to refine the inclusion and exclusion criteria. We will include studies up to December 2019 from preclinical studies to clinical studies that involves in assessing the concurrent use of CHM and PtC. Studies in which research subjects were prescribed with at least one prescription medicine and concurrently used one or more CHM will also be considered. Studies without full text and protocols or using other forms of Chinese Medicine beside herbal medicine (such as acupuncture, cupping, etc.) will be excluded.

2.3. Information sources

We will search for literature from the following electronic databases: PubMed, EBSCOhost (MEDLINE with full text, Academic Search Complete, MEDLINE), Science Direct, Scopus, Web of science, Cochrane Library and China National Knowledge Database (CNKI).

2.4. Identifying relevant studies (search strategy)

In order to get a comprehensive scoping process, we decided to use a thorough search on English and Chinese online databases. Duplicate records will be removed and two independent authors (AC and SY) will screen through the title and abstracts based on the study eligibility criteria. Due to the heterogeneity of the field in terms of disciplines and terminology, our search strategy may not be able to capture some relevant studies. We will try to minimize the risk by conducting a preliminary review of the literature to evaluate both our search strategy and study selection criteria.

The employed keywords are "Chinese herbal medicine" OR "Traditional Chinese Medicine" OR "Chinese Traditional Herbal" OR "Herbal Medicine" OR "KAMPO Medicine" AND "platinum- based chemotherapy" OR "carboplatin" OR "cisplatin" OR "Oxaliplatin" OR öxaliplatinÄND "interactions".

2.5. Screening

Following the two-part study selection process. In the first stage, researchers (working in pairs) independently screened the titles and abstracts of all resources based on the inclusion criteria and search terms. Duplicate will be removed and irrelevant articles will be excluded. The search results will be imported into Microsoft Excel for further analysis. Full text will be retrieved. In the second step, two reviewers will independently evaluate the full-text articles to decide if they meet the inclusion/exclusion criteria. In case of any disagreement about inclusion, full-text articles will be reviewed again by both reviewers (AC and SY) and if an agreement cannot be reached, this will be resolved by a consolidation with an independent third reviewer/expert (RJ).

2.6. Data extraction/charting

A charting form will be developed and standardized by team to allow the investigator to chart the data. A data extraction form will be developed and refined by the reviewers (AC and SY) to help in deciding the relevance of the study. The form will be piloted on 10–15 articles by two reviewers independently. Final feedback on form will be solicited prior to the charting process. The form will be revised if it is necessary.

During this stage, key information about the selected articles will be collected and summarized (Supplementary tables 1–4) according to article type (in vivo, in vitro, randomized control trial, clinical trial and reviews). Both reviewers (AC and SY) will separately extract data from a sample of included articles. Subject to the outcome of this data extraction and the volume of included papers, the team will determine whether complete independent extraction is necessary or if it can be performed separately. A third reviewer/expert (RJ) will perform a third check on the included studies.

2.7. Synthesis results

As a scoping review, our purpose of the study is to aggregate the findings and present an overview of the reported herbal-drug interactions rather than to evaluate the quality of the individual studies. The emerging themes will be analysed. The relationship of the emerging themes to the research question will be critically examined. Hence, the overall assessment of the evidence will therefore be a narrative approach rather than a quantitative or qualitative method. The findings will be reported based on reviewers' experiences with scoping review methodology and any suggestions for improvement that might develop.

2.8. Collating, summarising and reporting results

These articles will not be assessed for quality appraisal in this review. The search results will be presented through the use of the adapted PRISMA-P chart. The themes will be reported to highlight the similarities, differences, patterns and outliers found in the literature. Bubble plot will be used to show an estimate of the evidence base for the systematic reviews and reviews articles. All studies will be present in table forms.

3. Discussion

CHM has been used for cancer- and treatment- related symptom alleviation, quality of life improvement, metastasis and recurrence prevention and to prolong survival time. Cotreatment chemotherapy and CHM provide a new insight for future practice in cancer treatment. Therefore, this scoping review is to explore the compatibility or combination rule of CHM-PtC and understand HDI in

CHM-PtC cotreatment as identification active properties in CHM, HDI interactions and understanding pharmacokinetics and pharmacodynamic of the CHM alone or cotreatment are essential for patients' safety profile.

We recognise that our defined scope, decision-making by researches, may exclude other important aspects of the possible included studies. However, this definition is in line with the nature of our planned primary research and therefore sufficient for the current study. We hope to extend this review with further work with a broader scope in due course.

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Author contributions

Conception: ACL and SYC. Methodology: ACL, SYC, RJL, and NML. Investigation: ACL, SYC, RJL, and WNNN. Formal Analysis: SYC, ACL, and SMH. Writing – original draft: SYC and ACL. Writing – review & editing: RJL, WNNN, and NML. Supervision: ACL.

Conflict of interest

The authors declare no conflict of interest.

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None.

Ethical statement

As it is a scoping review, it was exempted from Medical Research and Ethics Committee (MREC), Ministry of Health, Malaysia review.

Data availability

Data associated with this article will be provided upon request. All data used for this study are from previous studies which are included in References.

Supplementary material

Supplementary Table S1. Data Charting domains and elaboration of subdomains of randomized control trial and clinical trial can be found in the online version at doi:10.1016/j.imr.2020.01.014.

References

1. Hsiao WL, Liu L. The role of traditional Chinese herbal medicines in cancer therapy–from TCM theory to mechanistic insights. *Planta Med* 2010;76:1118–31.
2. Chow WH, Chang P, Lee SC, Wong A, Shen H-M, Verkooijen HM. Complementary and alternative medicine among Singapore cancer patients. *Ann Acad Med Singap* 2010;39:129–35.
3. Hyodo I, Eguchi K, Nishina T, Endo H, Tanimizu M, Mikami I, et al. Perceptions and attitudes of clinical oncologists on complementary and alternative medicine. *Cancer* 2003;97:2861–8.
4. Chen XW, Serag ES, Sneed KB, Liang J, Chew H, Pan SY, et al. Clinical herbal interactions with conventional drugs: from molecules to maladies. *Curr Med Chem* 2011;18:4836–50.
5. Arksey H, O'Malley L. Scoping studies: Towards a methodological framework. *Int J Soc Res Methodol* 2005;8:19–32.
6. Levac D, Colquhoun H, O'Brien KK. Scoping studies: advancing the methodology. *Implement Sci* 2010;5:69.
7. Colquhoun HL, Levac D, O'Brien KK, Straus S, Tricco AC, Perrier L, et al. Scoping reviews: Time for clarity in definition, methods, and reporting. *J Clin Epidemiol* 2014;67:1291–4.
8. Daudt HML, van Mossel C, Scott SJ. Enhancing the scoping study methodology: A large, inter-professional team's experience with Arksey and O'Malley's framework. *BMC Med Res Methodol* 2013;13:48.
9. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. Prisma extension for scoping reviews (prisma-scr): Checklist and explanation. *Ann Intern Med* 2018;169:467–73.