Chemotherapy-Induced Diarrhea Evaluation Table 2023: Traditional Chinese Medicine

Systematic Review

Citation	Design/Method Sample/Setting	Variables and Intervention	Outcome Measures	Results/Analysis	Limitations	Quality and Nursing Implications
Chen G. (2018). Effects of Shenfu injection on chemotherapy-induced adverse effects and quality of life in patients with advanced non-small cell lung cancer: A systematic review and meta-analysis. *Journal of Cancer Research and Therapeutics, 14*,(Supplement), S549–S555. https://doi.org/10.4103/0973-1482.187299	**Design:** Systematic review and meta-analysis **Method:** Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA). A search of Cochrane Library, PubMed®, Embase®, CNKI, Chinese Biomedical Database, VIP Chinese Science Journals Database, and Wanfang Database for randomized controlled trials comparing chemotherapy alone to chemotherapy with Shenfu injection (SFI). Data extraction and quality assessment completed. **Sample:** Sixteen randomized controlled trials with a total of 948 participants with lung cancer **Setting:** Patients in active anticancer treatment with chemotherapy in the adjuvant setting for non-small cell lung cancer (NSCLC).	**Independent Variable(s):** Chemotherapy plus SFI 50 mg to 100 mg used at the start of chemotherapy **Dependent Variable(s):** World Health Organization (WHO) Hematologic Toxicity, Karnofsky Performance Status score, and grading of diarrhea **Intervention:** Shenfu is a product of Traditional Chinese Medicine (TCM) that contains ginseng and black aconite. Participants received injections of 50 mg to 100 mg at the start of chemotherapy.	Effects of SFI on chemotherapy-induced side effects for patients with NSCLC. Unclear symptom grading scale used. WHO Hematologic Toxicity Karnofsky Performance Status score	Five trials reported grades 3 and 4 chemotherapy-induced diarrhea results. SFI plus chemotherapy was associated with significantly lower risk of diarrhea when compared with chemotherapy alone (risk ratio (RR) 0.21, 95% CI [0.07, 0.63]).	Authors note risk of publication bias The meta-analysis for diarrhea outcome only includes 2 trials. Chemotherapy regimens varied in trials and included: cisplatin/vinorelbine, cisplatin/gemcitabine, and cisplatin/docetaxel Studies were classified as low-quality, with unclear risk of bias.	Studies were classified as low quality, with unclear risk of bias limiting the reliability of the results. Only 2 studies within the meta-analysis focused on the outcome of diarrhea. SFI had favorable results on diarrhea risk when administered with chemotherapy compared with chemotherapy alone.

McCulloch, M., Ly, H., Broffman, M., See, C., Clemons, J., & Chang, R. (2016). Chinese herbal medicine and fluorouracil-based chemotherapy for colorectal cancer: A quality-adjusted meta-analysis of randomized controlled trials. *Integrative Cancer Therapies, 15*(3), 285–307. https://doi.org/10.1177/1534735416638738	**Design:** Quality adjusted meta-analysis **Method:** Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA**).** Database search of TCMLARS, PubMed®, and Cochrane Library. Data extraction and quality assessment using Cochrane Risk of Bias criteria. **Sample:** For the 3 studies that qualified with low risk of bias, 268 patients. For the 36 before exclusions, 2593 patients. Adult patients with colorectal cancer (CRC) receiving 5-fluorouracil (5-FU) **Setting:** Unspecified, patients receiving 5-FU for CRC.	**Independent Variable(s):** Chinese Herbal Medicine plus 5-FU chemotherapy versus 5-FU chemotherapy alone **Dependent Variable(s):** Diarrhea, neurological toxicity, white blood cell toxicity, platelet toxicity, vomiting, tumor response; survival; performance status **Intervention:** Use of Chinese Herbal Medicine plus 5-FU chemotherapy compared with 5-FU chemotherapy alone	WHO scale for diarrhea WHO scale for neurologic toxicity, WBC toxicity, platelet toxicity, and vomiting Tumor response—partial or complete Survival outcomes Karnofsky Performance Status score	Diarrhea was reduced by 57% in the intervention group though this was not statistically significant (RR = 0.43; 95% CI [0.19, 1.01]; $p = 0.05$; $I^2 = 0\%$) Reduction of neurological toxicity was not statistically significant ($p = 0.27$). Reduction of platelet toxicity was not statistically significant ($p = 0.64$). Reduction of vomiting toxicity was not statistically significant ($p = 0.64$). There was a 66% reduction of WBC toxicity which was statistically significant ($p < 0.01$). Reduction in tumor response was not statistically significant ($p = 0.38$).	Only two studies were reported that had low risk of bias.	A subgroup analysis of studies with low risk of bias in this meta-analysis do not support the use of Chinese herbal medicine with 5-FU therapy among patients with CRC to decrease the toxicity of chemotherapy. Studies supporting the use of Chinese herbal medicine with 5-FU therapies among CRC patients, appear to have a high risk of bias and should be interpreted with caution.

Yang, J., Zhu, X., Yuan, P., Liu, J., Wang, B., & Wang, G. (2020). Efficacy of traditional Chinese Medicine combined with chemotherapy in patients with non-small cell lung cancer (NSCLC): A meta-analysis of randomized clinical trials. *Supportive Care in Cancer, 28*(8), 3571–3579. https://doi.org/10.1007/s00520-020-05433-w	**Design:** Meta-analysis **Method:** Database search China National Knowledge Infrastructure (CNKI) database, Wanfang Database, PubMed®, Baidu Academic for randomized controlled trials comparing Traditional Chinese Medicine and chemotherapy with chemotherapy alone in patients with NSCLC from January 2005 to October 2019. Data extraction and quality assessment of studies were done by dual investigators. **Sample:** 20 RCTs representing 1669 cases (N = 845 in the intervention group and N = 824 in the control group). Sample of patients with NSCLC. **Setting:** China (unspecified care settings)	**Independent Variable(s):** Traditional Chinese medicine (TCM) **Dependent Variable(s):** Quality of Life (QOL), Karnofsky Performance Status (KPS), efficacy, adverse drug reactions (ADRs) **Intervention:** Yiqi yangyin huatan jiedu recipe, bufei xiaoji recipe, jianpi yishen recipe, yiqi fuzheng recipe, yiwen yang recipe, buqi jianpi xuan fei llitan recipe, ziyin runfei qingre san recipe, liqi huoxue huayu huatan recipe, buqi yangxue fuzheng pei recipe,	QOL KPS Efficacy ADRs	QOL: Odds ratio (OR) = 2.79, 95% CI [1.87, 4.16]; $p < 0.00001$ Clinical efficacy: OR = 2.88, 95% CI [2.32, 3.58]; $p < 0.00001$ KPS score: OR = 2.88, 95% CI [1.79, 4.62]; $p < 0.0001$ Diarrhea results were reported in 3 studies (n = 168 in the intervention group and n = 159 in the control group): OR = 0.21, 95% CI [0.12, 0.37]; $p < 0.00001$, $I^2 = 0\%$) Leukopenia: OR = 0.21, 95% CI [0.12, 0.37]; $p < 0.0001$ Thrombocytopenia: OR = 0.23, 95% CI [0.13, 0.40]; $p < 0.00001$ Hemoglobin reduction: OR = 0.17, 95% CI [0.10, 0.30]; $p < 0.00001$ Myelosuppression: OR = 0.24, 95% CI [0.10, 0.58]; $p < 0.001$ Nausea and vomiting: OR = 0.16, 95% CI [0.11, 0.22]; $p < 0.00001$ Liver damage: OR = 0.17, 95% CI [0.10, 0.27)]; $p < 0.00001$ Kidney damage: OR = 0.30, 95% CI [0.10, 0.90]; $p = 0.03$	Potential bias and exaggeration of the efficacy of the treatment group as not all trials elaborated how they handled concealment and blinding Low sample sizes Studies were only conducted in China; which may make results non-generalizable and complex ingredients in intervention not easily feasible. Possible publication bias	The methodology was valid. Results of the study were reliable because of use of meta-analysis of high quality randomized controlled trials. Although the articles report that TCM combined with chemotherapy can improve clinical efficacy, Karnofsky Performance Status score, and QOL, and reduce ADRs, descriptions of TCM interventions were not included and it is therefore uncertain whether interventions would be feasible for the nursing/care team to offer.

General Evidence

Citation	Design/Method Sample/Setting	Variables and Intervention	Outcome Measures	Results/Analysis	Limitations	Quality and Nursing Implications
Xing, H., Zhang, L., Ma, J., Liu, Z., Song, C., & Liu, Y. (2018). *Fructus mume* extracts alleviate diarrhea in breast cancer patients receiving the combination therapy of lapatinib and capecitabine. *Frontiers in Pharmacology, 9*, 516. https://doi.org/10.3389/fphar.2018.00516	**Design:** Randomized controlled trial **Method:** The intervention group received 100 mg of *Fructus mume* extract (EFM) daily for 6 weeks; the control group took placebo. Gastrointestinal (GI) symptoms and QOL outcomes were measured during the 6 weeks of intervention and for 4 weeks following the intervention. **Sample:** N = 208 (104 in the intervention group, 104 in the control group) **Setting:** China (unspecified)	**Independent Variable(s)**: EFM **Dependent Variable(s):** Diarrhea and other GI symptoms, anxiety and depression, QOL **Intervention: The intervention** group received 100 mg of EFM daily for 6 weeks; the control group took placebo. GI and QOL outcomes were measured for during the 6 weeks of intervention and for 4 weeks following intervention.	Diarrhea: Measure of three fecal volumes and three fecal consistencies. Daily scores were calculated on all stools. GI symptoms, including abdominal pain, bloating, straining, mucus, incomplete evacuation, urgency, wind, hard stool, loose stool, frequency of motions, and nausea, were measured using a seven-point Likert-type scale. Overall QOL was measured using the SF-36® questionnaire. Hospital Anxiety and Depression (HADS) score Components of the EFM were measured in different batches repeatedly and determined to be stable, thereby not affecting therapeutic results.	Baseline differences in GI symptoms were not statistically significant. Diarrhea symptoms in EFM group (12.97, SD = 6.62) compared with the control group (13.11, SD = 7.53) did not differ at baseline ($p > 0.05$). After 6 weeks of therapy, diarrhea symptoms were reduced in the EFM group over the control group (8.47, SD = 4.62 vs. 14.29 SD = 8.15; $p < 0.001$). After an additional 4 weeks following treatment, diarrhea symptom scores were reduced in the EFM group compared with the control group (9.25, SD = 4.63 vs. 13.01, SD = 6.24; $p < 0.001$). There were no significant differences in QOL between the EFM and control groups at baseline ($p > 0.05$). After 6 weeks of intervention and 4 weeks after intervention, the EFM group had significant improvement of quality of life and decrease in HADS scores compared with the control group ($p < 0.05$).	Authors explicitly stated that they did not include safety aspects such as dose intensity, rash, mucositis, and drug interactions in this work. Potential safety implications of the intervention are important to note when planning symptom management interventions. Although patients were randomized and a placebo control group was included, there was no discussion of blinding of participants or of the researchers, which is a potential source of bias. In addition, EFM batch differences were measured for this study, which may not be feasible in practice.	Methodology was sound; results reporting are interpreted with caution considering risk of bias and lack of potential safety implications, which may indicate selective reporting. More research is needed on the utility of EFM for treatment of lapatinib- and capecitabine–related diarrhea in patients with metastatic breast cancer. Diarrhea scoring measures were not fully described, leading to difficulty in interpretation and effect size.

Xu, M., Wang, Y., & Wang, H. C. (2021). Adjuvant concomitant treatment with traditional Chinese medicines in patients receiving chemotherapy for HER2-positive breast cancer: A pilot randomized controlled trial. *Complementary therapies in Clinical Practice, 43*, 101373. https://doi.org/10.1016/j.ctcp.2021.101373	**Design:** Randomized controlled trial **Method:** Patients were allocated to paclitaxel and trastuzumab plus traditional Chinese medicine (TCM) or to paclitaxel/trastuzumab alone. **Sample:** N = 80 (40 in control group and 40 in intervention group) average age 60.5 (SD= 6.6) years **Setting:** Inpatient postmastectomy	**Independent Variable(s)**: TCM **Dependent Variable(s):** Cardiac function, complete blood count, hepatic and renal function, symptom dimensions of pain, diarrhea, hair loss, nausea, asthenia, insomnia, loss of appetite, vomiting **Intervention:** TCM regimen containing the following ingredients: Poria cocos, 10 g; atractylodes, 10 g; ginger pinellia, 10 g; Thunberg fritillary bulb, 10 g; radix curcumae aromaticae, 10 g; *Scutellaria*, 10 g; zedoary, 10 g; orange fruit, 10 g; dried tangerine peel, 10 g; solanum lyrate, 10 g; chicken gizzard membrane, 10 g; turtle carapace, 10 g; licorice root, 10 g; and centipede, 10 g.. Participants took the boiled Chinese herbal medicine in 50 milliliters twice daily for 6 months. Adjustments were made based on patient's reaction to treatment.	Cardiac function, complete blood count, hepatic and renal function, symptom dimensions of pain, diarrhea, hair loss, nausea/asthenia, insomnia, loss of appetite, vomiting	Scores of symptom dimensions for pain, diarrhea, and hair loss were better in the experimental group than in the control group after chemotherapy ($P < 0.01$). Diarrhea in the experimental group symptom dimension scores was 17.11 (SD = 3.11) versus 21.91 (SD = 3.12) in the control group ($p = 0.003$). The left ventricular global longitudinal strain was better in the experimental group (–18.01, SD = 0.64 vs. –16.22, SD = 0.52; $p < 0.01$). The reduction in white blood cells was more significant in the control group (5.04×10^9/L, SD = 2.32×10^9/L) than in the intervention group (2.57×10^9/L, SD = 2.11×10^9/L; $p < 0.01$). Hepatic function in the experimental group was better than that in control group after chemotherapy measured by serum glutamic-oxaloacetic transaminase and serum glutamic-pyruvic transaminase ratio and bilirubin levels ($p < 0.01$). No significant differences in renal function were observed between the two groups.	Small sample Unclear assessment tools for symptom outcomes	Results of the study were reported with reliability. However, further research is needed in a large-scale trial before application to other populations. Feasibility concerns with multicomponent intervention and possibly unavailable components of the TCM compound. TCM in combination with chemotherapy showed promise in improving myelosuppression, hepatic and renal function, as well as symptom dimensions of pain, diarrhea, and hair loss. Further research is needed to develop specific nursing implications for use with TCM.