



RESEARCH UPDATES FEBRUARY 2013

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FOR THE LATEST IN WORLDWIDE INTEGRATIVE CANCER CARE

IN THIS ISSUE: Torres-Mejia et al. found that moderate-intensity exercise can reduce the risk of breast cancer in diabetic women. Chen and colleagues reported that higher magnesium intake can reduce the risk of colorectal cancer. Meyerhardt and associates found that higher dietary glycemic load and total carbohydrate intake were associated with an increased risk of recurrence and mortality in stage III colon cancer patients. Walentowicz et al. analyzed the association between vitamin D status and overall survival in ovarian cancer patients. Segal and colleagues found that vitamin D deficiency is common in oncology patients with bone metastasis treated with bisphosphonates and may increase bone damage and hypocalcemia. Paskett and associates found that patients with abnormal screening test results who received patient navigation had their diagnostic evaluation completed faster than patients who did not receive patient navigation assistance. De Valois and colleagues found that ear acupuncture was helpful for managing hot flashes and night sweats in breast cancer patients. Nekuzad and associates concluded that external use of sesame oil helped to prevent infusion phlebitis in colon cancer patients receiving chemotherapy. Panahi et al. found that ginger helped to reduce post-chemotherapy nausea in women with breast cancer. In our study of the month, Ravasco and colleagues concluded that nutrition can improve the long-term prognosis of patients with colorectal cancer and that nutritional counseling and education was beneficial for patients during radiotherapy.

BREAST CANCER

Torres-Mejia, G, A. Angeles-Llerenas, C. Ortega-Olvera, et al.

Moderate-Intensity Physical Activity Ameliorates the Breast Cancer Risk in Diabetic Women.

Diabetes Care. 2012 December 2012; 35(12): 2500-2502.

OBJECTIVE: To evaluate the association between self-reported diabetes and the risk of breast cancer (BC) and its interaction with moderate-intensity physical activity in pre- and postmenopausal Mexican women. **RESEARCH DESIGN AND METHODS:** A population-based case-control study was conducted using 1,000 incident case subjects and 1,074 control subjects. Blood samples and information on health, diet, physical activity, and anthropometric measurements were obtained. **RESULTS:** The association between diabetes and BC risk decreased with increasing tertiles of moderate-intensity physical activity (odds ratio [OR] = 4.9 [95% CI 2.3-10.8]; 3.0 [1.3-6.9]; and 1.0 [0.1-9.2], respectively, for each tertile) (test for interaction = 0.04). Compared with the women in the lowest tertiles, increased risk was observed in those premenopausal women with the highest serum C-peptide, IGF-1, and IGF-1 binding protein 3 levels. **CONCLUSIONS:** Moderate-intensity physical activity can substantially ameliorate the increased BC risk in diabetic women.

INSPIREHEALTH'S INTERPRETATION: This observational study suggests that moderate-intensity exercise can reduce the risk of breast cancer in diabetic women.

COLORECTAL CANCER

Chen, G-, Z. Pang and Q. -F Liu.

Magnesium Intake and Risk of Colorectal Cancer: A Meta-Analysis of Prospective Studies.

Eur J Clin Nutr. 2012 November 2012; 66(11): 1182-1186.

BACKGROUND: Epidemiologic studies have suggested that magnesium intake may be associated with a decreased risk of colorectal cancer (CRC), but the findings have been inconsistent. We aimed to assess this association by conducting a meta-analysis of prospective studies. **METHODS:** We performed a literature search on PubMed database through July 2012 to identify prospective studies of magnesium intake in relation to CRC risk. Reference lists of the retrieved articles were also

reviewed. A random-effects model was used to compute the summary risk estimates. Eight prospective studies containing 338979 participants and 8000 CRC cases met the inclusion criteria. **RESULTS:** The summary relative risk (RR) for the highest vs lowest category of magnesium intake for CRC was 0.89 (95% CI, 0.79-1.00), with little evidence of heterogeneity. Restricting the analysis to six studies that have adjusted for calcium intake yielded a similar result. For colon and rectal cancer, the pooled RR was 0.81 (95% CI, 0.70-0.93) and 0.94 (95% CI, 0.72-1.24), respectively. In the dose-response analyses, the summary RRs for an increment of magnesium intake of 50 mg/day for colorectal, colon and rectal cancer were, respectively, 0.95 (95% CI, 0.89-1.00), 0.93 (95% CI, 0.88-0.99) and 0.93 (95% CI, 0.83-1.04), and there was some evidence of heterogeneity; omitting one study that substantially contributed to the heterogeneity yielded generally similar results, but with low heterogeneity. We detected no indication of publication bias. **CONCLUSION:** On the basis of the findings of this meta-analysis, a higher magnesium intake seems to be associated with a modest reduction in the risk of CRC, in particular, colon cancer.

INSPIREHEALTH'S INTERPRETATION: This review of eight different prospective studies suggests that higher magnesium intake can reduce the risk of colorectal cancer, particularly colon cancer. Good sources of dietary magnesium include fruit, vegetables, beans, cereals, nuts and lentils.

Meyerhardt, JA, K. Sato, D. Niedzwiecki, et al.

Dietary Glycemic Load and Cancer Recurrence and Survival in Patients with Stage III Colon Cancer: Findings from CALGB 89803.

J Natl Cancer Inst. 2012 21 Nov 2012; 10422: 1702-1711.

BACKGROUND: The influence of glycemic load and related measures on survival among colon cancer patients remains largely unknown. **METHODS:** We conducted a prospective, observational study of 1011 stage III colon cancer patients reporting dietary intake during and 6 months after participation in an adjuvant chemotherapy trial. We examined the influence of glycemic load, glycemic index, fructose, and carbohydrate intakes on cancer recurrence and mortality using Cox proportional hazards regression; all tests of statistical significance were two-sided. **RESULTS:** Stage III colon cancer patients in the highest quintile of dietary glycemic load experienced an adjusted hazard ratio (HR) for disease-free survival of 1.79 (95% confidence interval [CI] = 1.29 to 2.48), compared with those in the lowest quintile (P (trend) across quintiles <.001). Increased glycemic load was associated with similar detriments in recurrence-free (P (trend) across quintiles <.001) and overall survival (P (trend) across quintiles <.001). These associations differed statistically significant by body mass index (BMI) (P (interaction) =.01). Whereas glycemic load was not associated with disease-free survival in patients with BMI < 25kg/m², higher glycemic load was statistically significant associated with worse disease-free survival among overweight or obese participants (BMI ≥ 25kg/m²); HR = 2.26; 95% CI = 1.53 to 3.32; P (trend) across quintiles <.001). Increasing total carbohydrate intake was similarly associated with inferior disease-free, recurrence-free, and overall survival (P (trend) across quintiles <.001). **CONCLUSION:** Higher dietary glycemic load and total carbohydrate intake were statistically significant associated with an increased risk of recurrence and mortality in stage III colon cancer patients. These findings support the role of energy balance factors in colon cancer progression and may offer potential opportunities to improve patient survival.

INSPIREHEALTH'S INTERPRETATION: Intake of foods that raise blood glucose is associated with an increased risk of recurrence and mortality in stage III colon cancer patients during, and 6 months after, participation in an adjuvant chemotherapy trial.

OVARIAN CANCER

Walentowicz-Sadlecka, M, M. Grabiec, P. Sadlecki, et al.

25(OH)D3 in Patients with Ovarian Cancer and its Correlation with Survival.

Clin Biochem. 2012 December 2012; 4518: 1568-1572.

OBJECTIVES: The aim of this study was to examine vitamin 25(OH)D3 concentration in ovarian cancer patients in relation to a pathological subtype of the tumor, FIGO stage, grading, menopause status and overall 5-year survival. **DESIGN AND METHODS:** 72 epithelial ovarian cancer patients aged 37-79, who undergone optimal cytoreductive surgery were enrolled to the study group. Serum 25(OH)D3 concentration was measured using an electrochemiluminescence immunoassay before surgery. Serum concentration of 25(OH)D3 was also measured in a group of 65 healthy non-obese women aged 35-65years. **RESULTS:** In patients with ovarian cancer serum concentration of 25(OH)D3 was lower than in the reference group (12.5±7.75ng/mL vs 22.4±6.5ng/mL). No significant correlation was found between serum 25(OH)D3 concentration and histological subtype, grading, FIGO stage and menopausal status. The study group was divided into two subgroups and the survival curves were analyzed. Overall 5-year survival rate was significantly higher in the subgroup of patients with 25(OH)D3 concentration over 10ng/mL compared to women with concentration below 10ng/mL. **CONCLUSIONS:** Low 25(OH)D3 concentration associated with lower overall survival rate might suggest for the important role of severe deficiency in more aggressive course of ovarian cancer. Testing for 25(OH)D in the standard procedure could help to find ovarian cancer patients with worse prognosis, who would benefit of special attention and supplementation.

INSPIREHEALTH'S INTERPRETATION: Vitamin D is an important nutrient for cancer patients. In this small study, compared to healthy women, ovarian cancer patients showed lower mean serum vitamin D levels, which could impact survival. Such women may benefit from vitamin D supplementation.

VITAMIN D

Segal, E, S. Felder, N. Haim, et al.

Vitamin D Deficiency in Oncology Patients—an Ignored Condition: Impact on Hypocalcemia and Quality of Life.

Israel Medical Association Journal: Imaj. 2012 Oct; 1410: 607-612.

BACKGROUND: Vitamin D status is not evaluated routinely in cancer patients with bone metastasis who are treated with bisphosphonates. **OBJECTIVES:** To assess the effect of vitamin D status on risk of hypocalcemia and quality of life in these patients. **METHODS:** We performed laboratory tests for routine serum biochemistry, 25(OH)D, plasma parathyroid hormone (PTH) and bone turnover markers (CTX, P1NP) in 54 patients aged 57.5 +/- 13 years treated with intravenous bisphosphonates. **RESULTS:** Most of the patients (n = 44, 77.8%) did not receive calcium and vitamin D supplementation. Their mean serum 25(OH)D levels (12.83 +/- 6.86 ng/ml) correlated with vitamin D daily intake (P = 0.002). In 53 patients (98.1%) 25(OH) D levels were suboptimal (< 30 ng/ml). Albumin-corrected calcium levels correlated with plasma PTH (P = 0.001). No correlation was observed between daily calcium intake and serum calcium (P = 0.45). Hypocalcemia was observed in one patient. Mean plasma PTH was 88.5 - 65 ng/L. Plasma PTH correlated negatively with 25(OH)D serum levels (P = 0.003) and positively with P1NP (P = 0.004). Albumin-corrected calcium correlated negatively with P1NP (mean 126.9 +/- 191 ng/ml) but not with CTX levels (mean 0.265 +/- 0.1 ng/ml) (P < 0.001). There was no correlation among quality of life parameters, yearly sun exposure and 25(OH)D levels (P = 0.99). **CONCLUSIONS:** Vitamin D deficiency is frequent in oncology patients with bone metastasis treated with bisphosphonates and might increase bone damage. Our results indicate a minor risk for the development of severe hypocalcemia in vitamin D-deficient patients receiving bisphosphonate therapy. Although vitamin D deficiency might have some effect on the quality of life in these patients, it was not proven significant.

INSPIREHEALTH'S INTERPRETATION: Vitamin D deficiency is common in cancer patients with bone metastasis who are being treated with bisphosphonates, and may increase the risk of bone damage and low blood calcium. Supplementation with calcium and vitamin D, as well as monitoring of serum levels is important to such patients.

PATIENT NAVIGATION

Paskett, ED, M. L. Katz, D. M. Post, et al.

The Ohio Patient Navigation Research Program: Does the American Cancer Society Patient Navigation Model Improve Time to Resolution in Patients with Abnormal Screening Tests?

Cancer Epidemiol Biomarkers Prev. 2012 Oct; 2110: 1620-1628.

BACKGROUND: Patient navigation (PN) has been suggested as a way to reduce cancer health disparities; however, many models of PN exist and most have not been carefully evaluated. The goal of this study was to test the Ohio American Cancer Society model of PN as it relates to reducing time to diagnostic resolution among persons with abnormal breast, cervical, or colorectal cancer screening tests or symptoms. **METHODS:** A total of 862 patients from 18 clinics participated in this group-randomized trial. Chart review documented the date of the abnormality and the date of resolution. The primary analysis used shared frailty models to test for the effect of PN on time to resolution. Crude HR were reported as there was no evidence of confounding. **RESULTS:** HRs became significant at 6 months; conditional on the random clinic effect, the resolution rate at 15 months was 65% higher in the PN arm (P = 0.012 for difference in resolution rate across arms; P = 0.009 for an increase in the HR over time). **CONCLUSIONS:** Participants with abnormal cancer screening tests or symptoms resolved faster if assigned to PN compared with those not assigned to PN. The effect of PN became apparent beginning six months after detection of the abnormality. **IMPACT:** PN may help address health disparities by reducing time to resolution after an abnormal cancer screening test.

INSPIREHEALTH'S INTERPRETATION: Timely completion of diagnostic evaluation can facilitate speedier healthcare for cancer patients. Patient navigation, defined as guiding patients to clinical care services provided by nurses and other healthcare personnel, can reduce the duration of full diagnostic evaluation for cancer patients who received an abnormal cancer screening test result.

E-VERSION EXTRA**COMPLEMENTARY & ALTERNATIVE MEDICINE**

Lo-Fo-Wong, DNN, A. V. Ranchor, H. C. J. M. de Haes, et al.

Complementary and Alternative Medicine use of Women with Breast Cancer: Self-Help CAM Attracts Other Women than Guided CAM Therapies.

Patient Educ Couns. 2012 December 2012; 893: 529-536.

OBJECTIVE: Examine stability of use of complementary and alternative medicine (CAM) of breast cancer patients, reasons for CAM use, and sociodemographic, clinical, and psychological predictors of CAM use. **METHODS:** CAM use was assessed after adjuvant therapy and six months later. Following the CAM Healthcare Model, CAM use was divided into use of provider-directed (guided) and self-directed (self-help) CAM. Stability and reasons for CAM use were examined with McNemar's tests and descriptive statistics. Cross-sectional and longitudinal associations between predictors and CAM use were examined with univariate and multivariate logistical analyses. **RESULTS:** Use of provider-directed and self-directed CAM was stable over time (N=176). Self-directed CAM was more often used to influence the course of cancer than provider-directed CAM. Both were used to influence well-being. Openness to experience predicted use of provider-directed CAM, while clinical distress predicted use of self-directed CAM, after adjusting for other predictors. Perceived control did not predict CAM use. **CONCLUSION:** CAM use is stable over time. It is meaningful to distinguish provider-directed from self-directed CAM. **PRACTICE IMPLICATIONS:** Providers are advised to plan a 'CAM-talk' before adjuvant therapy, and discuss patients' expectations about influence of CAM on the course of cancer. Distressed patients most likely need information about self-directed CAM.

INSPIREHEALTH'S INTERPRETATION: Prior to adjuvant therapy, breast cancer patients should discuss any plans to use self-directed or provider-directed complementary and alternative medicine with their health care providers.

EAR ACUPUNCTURE

De Valois, B, T. E. Young, N. Robinson, et al.

NADA Ear Acupuncture for Breast Cancer Treatment-Related Hot Flashes and Night Sweats: An Observational Study.

Medical Acupuncture. 2012 01 Dec 2012; 244: 256-268.

BACKGROUND: Hot flashes and night sweats (HF&NS) are major side-effects of adjuvant hormonal treatments for breast cancer. **OBJECTIVE:** The aim of this study was to evaluate the feasibility of the National Acupuncture Detoxification Association (NADA) five-point ear acupuncture protocol to reduce HF&NS and improve physical and emotional well-being for women receiving adjuvant treatments for breast cancer. **DESIGN:** This trial was a single-arm observational study that used before-and-after measurements. **SETTING:** The trial was conducted at a National Health Service cancer treatment center in southern England. **PATIENTS:** The subjects included women with early breast cancer, ≥ 35 years old, ≥ 6 months post-active cancer treatment, receiving tamoxifen ≥ 6 months, and self-reporting ≥ 4 HF&NS incidents/24-hours for ≥ 3 months. **INTERVENTION:** Fifty participants completed weekly NADA treatment for 8 weeks in small groups of ≤ 5 patients. **MAIN OUTCOME MEASURES:** The factors examined were changes in scores at end of treatment over baseline for HF&NS frequency, physical, and emotional well-being, and perception of HF&NS as a problem. **RESULTS:** Mean HF&NS frequency was reduced by 35.9% (95% confidence interval: 25.4-45.4, $p < 0.0001$, $n = 47$). Statistical and clinical improvements were recorded for Anxiety/Fears, Depressed Mood, Memory/Concentration, Sleep Problems, Somatic Symptoms, and Vasomotor Symptoms. Perceptions of HF&NS as a problem were reduced by 2.2 points (standard deviation=2.23, $n = 48$, $t = 7.22$, $p < 0.0001$). **CONCLUSIONS:** NADA ear acupuncture may be a simple nonpharmacological method of managing breast-cancer treatment-related HF&NS.

INSPIREHEALTH'S INTERPRETATION: NADA ear acupuncture is a simple non-pharmacological method for managing treatment symptoms such as hot flashes and night sweats in breast cancer patients.

SESAME OIL

Nekuzad, N, T. A. Torab, F. Mojab, et al.

Effect of External use of Sesame Oil in the Prevention of Chemotherapy-Induced Phlebitis.

Iranian Journal of Pharmaceutical Research. 2012 2012; 114: 1065-1071

BACKGROUND: Intravenous chemotherapy is an important mean for the treatment of cancers. Infusion phlebitis (Ph) is a common and acute complication of chemotherapy. The frequency of Ph is about 70% in patients undergoing chemotherapeutic management. It can induce the pain, increase the risk of thrombophlebitis, lead to incomplete follow-up, and thereby, affect the patient's health status. Respecting the great importance of these issues, it is essential to prevent Ph. **METHODS:** This study conducted to determine the effect of external use of Sesame Oil (SO) in the prevention of Ph. Sixty patients with colon or rectum cancer, who admitted for chemotherapeutic management, enrolled in clinical trial and were randomly divided into two equal

groups: Control and Intervention. Ten drops of SO was applied twice a day for 14 days externally in intervention group, whereas the control group received nothing. Incidence and grade of Ph was measured in both groups. Data was analyzed through independent t-test, X², Fisher's exact test, Mann-Whitney, and Lagrange survival using SPSS 16. **RESULTS:** The incidence of Ph was 10% and 80% in intervention group and control group, respectively. There was a significant difference between two groups ($p < 0.05$). Ph was 8 times more frequent in control group (RR = 8; AR R = 70%). In addition, there was statistically significant difference between the grade and incidence of Ph with SO and control group ($p < 0.05$). **CONCLUSIONS:** According to these results, it seems that external use of SO is effective, safe and well-tolerated for prophylaxis from Ph. Therefore, it can be suggested as a selected prevention method for reducing the complication.

INSPIREHEALTH'S INTERPRETATION: Phlebitis is the inflammation of veins and can be a side effect of intravenous chemotherapy. External application of sesame oil is well tolerated for a period of 14 days and can help prevent chemotherapy-induced phlebitis.

GINGER

Panahi, Y, A. Saadat, A. Sahebkar, et al.

Effect of Ginger on Acute and Delayed Chemotherapy-Induced Nausea and Vomiting: A Pilot, Randomized, Open-Label Clinical Trial.

Integrative Cancer Therapies. 2012 September 2012; 113: 204-211.

BACKGROUND: Nausea and vomiting are among the most prevalent and disturbing side effects of chemotherapy. Therefore, there is a need for additional antiemetic agents that could effectively reduce chemotherapy-induced nausea and vomiting (CINV), whether alone or in combination with current standard therapies. Since clinical data on the effectiveness of ginger in patients with advanced breast cancer is lacking, the present study aimed to evaluate the effects of ginger against both acute and delayed forms of CINV in a population with advanced breast cancer as the main malignancy. **METHODS:** In this pilot, randomized, open-label clinical trial, 100 women (mean age = 51.83 ± 9.18 years) with advanced breast cancer who were initially assigned to standard chemotherapy protocol with docetaxel, epirubicin, and cyclophosphamide (the TEC regimen) were randomized to receive ginger (1.5 g/d in 3 divided doses every 8 hours) plus standard antiemetic regimen (granisetron plus dexamethasone; the ginger group) or standard antiemetic regimen alone (control group). The duration of treatment with ginger was specified to 4 days from the initiation of chemotherapy. Prevalence, score, and severity of nausea, vomiting, and retching were assessed using a simplified form of Rhodes index in the first 6 hours, between 6 to 24 hours, and days 2, 3, and 4 postchemotherapy. **RESULTS:** A significantly lower prevalence of nausea was observed in the ginger group during 6 to 24 hours postchemotherapy. Despite this effect, no other significant additional benefit from ginger (1.5 g/d) was observed against prevalence or severity of nausea, vomiting, and retching in any of the assessed periods. **CONCLUSION:** Addition of ginger (1.5 g/d) to standard antiemetic therapy (granisetron plus dexamethasone) in patients with advanced breast cancer effectively reduces the prevalence of nausea 6 to 24 hours postchemotherapy. However, there is no other additional advantage for ginger in reducing prevalence or severity of acute or delayed CINV.

INSPIREHEALTH'S INTERPRETATION: Together with standard anti-nausea medication, ginger can help to reduce nausea in women with breast cancer receiving chemotherapy.

STUDY OF THE MONTH

Ravasco, P, I. Monteiro-Grillo and M. Camilo.

Individualized Nutrition Intervention is of Major Benefit to Colorectal Cancer Patients: Long-Term Follow-Up of a Randomized Controlled Trial of Nutritional Therapy.

Am J Clin Nutr. 2012 01 Dec 2012; 966: 1346-1353.

BACKGROUND: In our published randomized trial in colorectal cancer, group 1 ($n = 37$) received individualized nutritional counseling and education about regular foods, group 2 ($n = 37$) received dietary supplements and consumed their usual diet of regular foods, and group 3 ($n = 37$) consumed their usual diet of regular foods. Neither group 2 nor group 3 received individualized counseling. Early nutritional counseling during radiotherapy was highly effective at reducing acute radiotherapy toxicity and improving nutritional intake/status and quality of life (QoL). Efficacy persisted for 3 mo after the intervention. **OBJECTIVE:** The objective was to perform long-term follow-up in survivors of that clinical trial to specifically evaluate survival, late toxicity, QoL, and nutritional variables. **DESIGN:** Medical data were collected from patients' records, and prescheduled interviews were conducted by dietitians for individualized evaluations. Analyses and comparisons between groups (adjusted for stage) were performed after a median follow-up of 6.5 (range: 4.9-8.1) y. **RESULTS:** Patients complied with the Radiotherapy Department's follow-up protocol. Nutritional deterioration was higher ($P < 0.001$) in group 3 ($n = 26$) and group 2 ($n = 29$) than in group 1 ($n = 34$). Adequate nutritional status was maintained in 91% of group 1 patients but not in any of the group 3 patients ($P < 0.002$). Intakes in group 1 were similar to reference values, and the patients adhered to the prescribed recommendations.

Intakes in groups 2 and 3 were lower than recommended intakes: group 3 \approx group 2 < group 1 ($P = 0.001$). Median survival in group 3 was 4.9 y (30% died), in group 2 was 6.5 y (22% died), and in group 1 was 7.3 y (only 8% died): group 3 > group 2 > group 1 ($P < 0.01$). Late radiotherapy toxicity was higher in group 3 ($n = 17$; 65%) and group 2 ($n = 17$; 59%) than in group 1 ($n = 3$; 9%): group 3 \approx group 2 > group 1 ($P < 0.001$). QoL was worse in groups 3 and 2 than in group 1: group 3 \approx group 2 < group 1 ($P < 0.002$). Worse radiotherapy toxicity, QoL, and mortality were associated with deteriorated nutritional status and intake ($P < 0.001$). Likewise, depleted intake, nutritional status, and QoL predicted shorter survival and late toxicity (HR: 8.25; 95% CI: 2.74, 1.47; $P < 0.001$). **CONCLUSIONS:** This study conveys novel information about the effectiveness of nutrition at improving long-term prognosis in colorectal cancer. Overall, the data indicate that early individualized nutritional counseling and education during radiotherapy is valuable for patients.

INSPIREHEALTH'S INTERPRETATION: Nutritional counseling to improve nutritional status is beneficial for colorectal cancer patients, not only to reduce radiotherapy-induced toxicity, but also can improve long-term prognosis.

We are grateful to the Prostate Cancer Foundation BC and the Canadian Breast Cancer Foundation (BC/Yukon) for their generous support of *Research Updates*.



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