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Trabajo Original

Otros

# Clinical effects of hydration, supplementary vitamins, and trace elements during end-of-life care for cancer patients

## *Efecto de la hidratación endovenosa suplementaria con vitaminas y oligoelementos sobre los síntomas clínicos y los parámetros bioquímicos en pacientes paliativos*

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## Abstract

**Introduction:** current data regarding the decision on rehydration of patients with terminal-stage cancer remain controversial.

**Objective:** the present study was to evaluate the effect of intravenous hydration and supplementary vitamins and trace elements on clinical symptoms and biochemical parameters in palliative cancer patients.

**Methods:** a randomized clinical trial including 72 palliative cancer patients aged 18 years and older was performed at the National Cancer Institute in Mexico. Patients were divided into two groups: intervention and control, both receiving intravenous saline solution weekly for 4 weeks, but the former was also supplemented with vitamins and trace elements. Symptoms were assessed at baseline and 4 weeks after with the Edmonton Symptom Assessment Scale. Same measurements applied to biochemical parameters.

**Results:** the mean age of the patients was 58.75 years. The most frequent cancer diagnoses were gastrointestinal (32 %). In the between-groups analysis significant improvements were found for the intervention group in anorexia ($p = 0.024$), pain ($p = 0.030$), chloride ($p = 0.043$), phosphorus ($p = 0.001$), potassium ($p = 0.006$), and total proteins ($< 0.0001$).

**Conclusion:** we highlight the improvement in the control of most symptoms and some biochemical parameters in the intervention group receiving vitamins and oligoelements along with intravenous hydration. Further studies are needed.

**Keywords:**

Hydration. Palliative. Pain. Cancer. Mexico.

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## Resumen

**Introducción:** los datos actuales sobre la decisión de rehidratación de pacientes con cáncer en fase terminal siguen siendo controvertidos.

**Objetivo:** el presente estudio fue evaluar el efecto de la hidratación intravenosa y la suplementación con vitaminas y oligoelementos sobre los síntomas clínicos y parámetros bioquímicos en pacientes con cáncer paliativo.

**Métodos:** en el Instituto Nacional del Cáncer de México se realizó un ensayo clínico aleatorizado que incluyó a 72 pacientes con cáncer paliativo de 18 años o más. Los pacientes se dividieron en dos grupos: intervención y control, ambos recibieron solución salina intravenosa semanalmente durante 4 semanas, pero el primero también se complementó con vitaminas y oligoelementos. Los síntomas se evaluaron al inicio del estudio y 4 semanas después con la escala de evaluación de síntomas de Edmonton. Mismas medidas aplicadas a los parámetros bioquímicos.

**Resultados:** la edad media de los pacientes fue de 58,75 años. El diagnóstico de cáncer más frecuente fue el gastrointestinal (32 %). En el análisis entre grupos se encontraron mejoras significativas para el grupo de intervención en anorexia ($p = 0,024$), dolor ($p = 0,030$), cloro ($p = 0,043$), fósforo ($p = 0,001$), potasio ($p = 0,006$) y proteínas totales ($< 0,0001$). **Conclusión:** destacamos la mejoría en el control de la mayoría de los síntomas y algunos parámetros bioquímicos en el grupo de intervención que recibió vitaminas y oligoelementos junto con hidratación endovenosa. Se necesitan más estudios.


**Palabras clave:**

Hidratación. Paliativos. Dolor. Cáncer. México.

## INTRODUCTION

Palliative cancer patients commonly develop physical and psychosocial distress during their last weeks or days of life (1). Also, it is known that patients admitted to referral palliative care units are more likely to present severe symptoms compared with those admitted to hospice or acute care hospital beds; however, symptoms are a burden among all groups, and the availability of care facilities varies from one country to another. Thus, the concept of effective treatment should successfully alleviate or even eliminate the most common symptoms among these patients, such as pain, dyspnea, nausea, vomiting, and fatigue, thereby providing maximum comfort at the end of life. On the other hand, the possibility that dehydration may contribute to suffering in palliative patients has generated strong debates with controversial arguments regarding parenteral fluid administration (2,3). The etiology of fluid deficit in palliative patients is multifactorial and the administration of hydration in this context differs greatly among different care settings. For instance, it is common that cancer patients who die in acute care hospitals will receive hydration until death and, on the contrary, most patients dying in a hospice or at home will receive no fluids (4). The existence of analyses addressing the appropriateness of offering artificial hydration have provided ethical arguments for and against using artificial hydration, affirming the importance of respecting patient preferences (5-7). Moreover, multiple studies have demonstrated that routine hydration generally does not improve all outcomes for patients near the end of life (8-12). In fact, the most commonly mentioned benefits of hydration are thirst alleviation and reduction of the risk of terminal restlessness or delirium (13). Hence, to date, uncertainty remains regarding whether or not hydration improves significant symptoms or quality of life at the end of life (14). Further, there are studies reporting that "non-essential" medications, including vitamins, continue to be administered to palliative patients and that discontinuation of those medications should be facilitated by interventions that enhance recognition and consideration of the patient actively dying status (15,16); additionally, it has been reported that there is not enough solid evidence for the use of minerals, vitamins, proteins, or other supplements in cachexia and cancer (17). Conversely, palliative patients often show deficiency in at least one of the most frequently measured vitamins (18) and, in this context, the correction of those deficiencies, such as vitamin D deficiency, has been associated with positive effects on fatigue (19). Consequently, as both, hydration and supplementation remain debatable and these approaches change by centers and regions, the aim of the present study was to evaluate the effect of intravenous hydration and supplementary vitamins and trace elements on clinical symptoms and biochemical parameters in palliative cancer patients at Mexico's National Cancer Institute.

## PATIENTS AND METHODS

### DESIGN AND PARTICIPANTS

An unblinded, single-center, randomized clinical trial was performed at the National Cancer Institute in Mexico City from July 2018 to July 2020. Palliative care patients aged 18 years and older with a diagnosis of cancer were consecutively evaluated. All presented one or more of the following symptoms: pain, fatigue, chronic nausea, depression, anorexia, dyspnea, somnolence, anxiety, insomnia, lack of overall wellbeing; dehydration was diagnosed on physical examination, along with inability to maintain an adequate water intake. Exclusion criteria included: cirrhosis, anasarca, cardiopathies, bowel obstruction, surgical procedures, severe constipation, renal failure, death, and unwillingness to participate. Seventy-two patients were included in the trial and assigned in the intervention or the control group using a random allocation software (Fig. 1). The protocol was approved by the Institutional Review Boards under the number CI/423/17.

### INTERVENTION

Patients were classified in two groups: 1) intervention group: hydration and supplementation or 2) control group: only hydration. For both, 500 mL of intravenous saline solution was used daily for 4 weeks. The intervention group was also supplemented with one ampule of multivitamins (ascorbic acid 100 mg, folic acid 0.4 mg, biotin 0.06 mg, cyanocobalamin 0.005 mg, pantothenic acid 15 mg, riboflavin 3.6 mg, nicotinamide 40 mg, pyridoxine 4 mg,

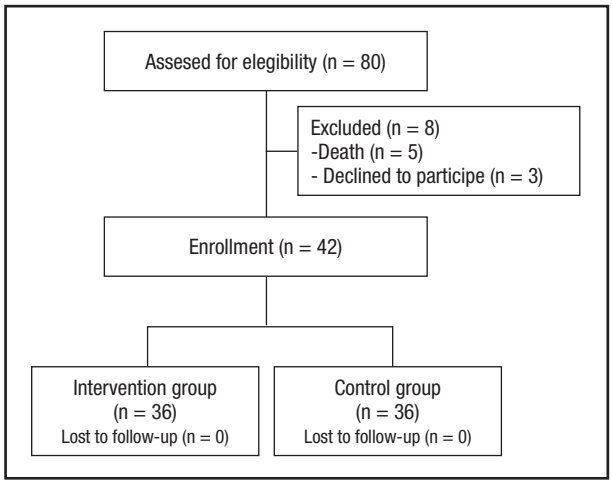


**Figure 1.**
Flow diagram of participant enrollment and group assignment.

thiamine 3 mg, retinol 3.3 g , cholecalciferol 200 IU, vitamin E 10 IU, and injectable water 5 mL), (MVI, for its acronym in Spanish), one ampule of trace elements (zinc 0.1614 mEq; copper 0.0271 mEq; manganese 0.0902 mEq; chlorides 0.7223 mEq; sodium 4.5493 mEq, sulfate 0.11 mEq, iodine 0.0017 mEq, fluoride 0.66 mEq) and 2 grams of vitamin C during the same amount of time. None of the participants within both groups received any medications according to institutional guidelines.

## DATA, ENDPOINTS, AND DEFINITIONS

Data were obtained from the electronic medical records (INCanet) and included, demographics (age and gender) and clinical data (diagnosis, symptoms, biochemical parameters, and survival). All symptoms were evaluated using the Edmonton Symptom Assessment Scale (ESAS). The main endpoint was assessment of pain. Additional endpoints were assessment of fatigue, chronic nausea, depression, anorexia, dyspnea, somnolence, anxiety, insomnia, and lack of overall wellbeing. Chronic nausea was defined as nausea present for 4 weeks or more. Additionally, biochemical parameters (complete blood count (CBC) and comprehensive metabolic panel (CMP)) were quantified. Laboratory parameters were obtained and evaluated according to institutional guidelines. In all the cases, the assessment of symptoms and laboratory parameters was carried out when randomized (at baseline) and 4 weeks after.

## STATISTICAL ANALYSIS

Quantitative variables were tested for normality using Shapiro-Wilk test, and described accordingly. Descriptive statistics included central tendency measurements: mean and standard deviation, and median and minimum and maximum ranges for quantitative variables and frequencies and percentages for categorical variables. Continuous and ordinal variables were analyzed using Student's t-test, Mann-Whitney U-test or Wilcoxon's sign-rank test where appropriate according to the distribution. Fisher's exact test was used to analyze dichotomous and nominal categorical variables. Analysis of repeated measures on generalized linear models (GLM) were performed to compare baseline and 4-week assessments in both the intervention and control groups. Kaplan-Meier was used to estimate long term survival and comparisons were made using log rank. A two-tailed p-value $< 0.05$ was considered significant. SPSS v.23 was used to collect data and to perform the analysis.

## RESULTS

Thirty six of the 72 patients included in the study were part of the intervention group. The mean age among all the patients was 58.75 years (± 13.76). Most were males (n = 41, 57 %). The most frequent cancer diagnoses were gastrointestinal (n = 23, 32 %), gynecological (n = 15, 21 %), urological (n = 10, 14 %), and head and neck (n = 9, 12 %) tumors. In both groups, some patients presented more than one symptom. Anorexia, fatigue, and lack of overall wellbeing were the most common symptoms among all patients. Overall demographics and clinical characteristics by group are shown in table I. Participants in the intervention group were older (mean age, 61.47 years) compared to those in the control group (mean age, 56.03 years); however, this difference was not statistically significant (p = 0.094). There were more males in the control group in comparison with the intervention group, 64 % and 50 %, respectively, without statistical significance (p = 0.341). Regarding cancer diagnoses, the most common among both groups were gastrointestinal tumors, followed by gynecological tumors, without showing statistical significance (p = 0.229). No differences were observed within the symptoms between the two groups. There were differences in phosphorus and total proteins among the two groups (p = 0.042 and p = 0.010, respectively), but not in the rest of the laboratory parameters.

The changes within symptoms between baseline and 4 weeks in the two groups are shown in table II, with no significant changes within groups in anxiety, lack of overall wellbeing or somnolence. Depression and dyspnea were not significant within the intervention group, contrary to the control group where these showed statistically significant differences (p = 0.003 and p = 0.004, respectively). Significant changes within groups were observed in both for anorexia, chronic nausea, fatigue, insomnia, and pain.

In the between-groups analysis significant differences were found for anorexia and pain. The intervention group showed an improved after 4 weeks for both symptoms (p = 0.024 and p = 0.030, respectively) and the control group did not improve in these symptoms but worsened (p = 0.005 and p = 0.009, respectively) as shown in figure 2.

Table III shows the within and between group changes of the biochemical parameters from baseline to 4 weeks of assessment. As observed, significant changes within groups were observed in both for hemoglobin, hematocrit, and phosphorus. In the between groups analysis significant differences were found for chloride, phosphorus, potassium, and total proteins.

Regarding the survival analysis, the median survival for the intervention and the control groups were 12.9 and 9.2 months, respectively, without statistical significance (Fig. 3).

**Table I.** Demographics and clinical characteristics of the patients in the two groups

| Characteristics | Intervention group (n = 36) | Control group (n = 36) | Total (n = 72) | p-value |
|---|---|---|---|---|
| | **mean (SD)** | **mean (SD)** | **mean (SD)** | |
| Age (years) | 61.47 (± 10.91) | 56.03 (± 15.80) | 58.75 (± 13.76) | 0.094[a] |
| | **n (%)** | **n (%)** | **n (%)** | |
| *Gender* | | | | |
| Female | 18 (50) | 13 (36) | 31 (43) | *0.341*[b] |
| Male | 18 (50) | 23 (64) | 41 (57) | |
| *Cancer diagnosis* | | | | |
| Breast | 5 (14) | 1 (3) | 6 (8) | |
| Gastrointestinal | 10 (28) | 13 (36) | 23 (32) | |
| Gynecological | 8 (22) | 7 (19) | 15 (21) | |
| Head and neck | 4 (11) | 5 (14) | 9 (12) | *0.229*[b] |
| Hematological | 1 (3) | 1 (3) | 2 (3) | |
| Lung | 1 (3) | 2 (6) | 3 (4) | |
| Skin and soft tissue | 0 | 4 (11) | 4 (6) | |
| Urological | 7 (19) | 3 (8) | 10 (14) | |
| *Baseline symptoms* | | | | |
| Anorexia | 28 (78) | 32 (89) | 60 (83) | 0.565[c] |
| Anxiety | 14 (39) | 15 (42) | 29 (40) | 0.838[c] |
| Chronic nausea | 17 (47) | 17 (47) | 34 (47) | 0.742[c] |
| Depression | 20 (56) | 21 (58) | 41 (57) | 0.741[c] |
| Dyspnea | 9 (25) | 8 (22) | 17 (24) | 0.479[c] |
| Fatigue | 29 (81) | 31 (86) | 60 (83) | 0.351[c] |
| Insomnia | 17 (47) | 22 (61) | 39 (54) | 0.946[c] |
| Lack of overall wellbeing | 28 (78) | 30 (83) | 58 (81) | 0.961[c] |
| Pain | 19 (53) | 12 (61) | 41 (57) | 0.864[c] |
| Somnolence | 23 (64) | 24 (67) | 47 (65) | 0.525[c] |
| *Baseline laboratory parameters* | | | | |
| Albumin | 3.11 (± 0.72) | 3.18 (± 0.50) | 3.14 (± 0.62) | 0.635[a] |
| Blood urea nitrogen | 13.60 (± 6.79) | 11.81 (± 4.36) | 12.71 (± 5.74) | 0.189[a] |
| Chloride | 97.61 (± 6.16) | 96.17 (± 7.74) | 96.89 (± 6.98) | 0.384[a] |
| Creatinine | 0.91 (± 0.71) | 0.83 (± 0.23) | 0.87 (± 0.54) | 0.545[a] |
| Glucose | 105.72 (± 36.18) | 100.44 (± 16.66) | 103.08 (± 28.09) | 0.429[a] |
| Hemoglobin | 11.59 (± 1.91) | 11.27 (± 2.00) | 11.43 (± 1.95) | 0.491[a] |
| Hematocrit | 35.81 (± 5.48) | 34.07 (± 6.17) | 34.94 (± 5.86) | 0.210[a] |
| Magnesium | 1.74 (± 0.38) | 1.74 (± 0.36) | 1.74 (± 0.37) | 0.939[a] |
| Phosphorus | 3.74 (± 1.04) | 3.32 (± 0.62) | 3.53 (± 0.88) | 0.042[a]* |
| Potassium | 4.14 (± 0.74) | 3.86 (± 0.59) | 4.00 (± 0.68) | 0.081[a] |
| Total protein | 6.58 (± 1.09) | 6.03 (± 0.57) | 6.31 (± 0.91) | 0.010[a]* |
| Sodium | 160.39 (± 165.26) | 130.36 (± 6.97) | 145.37 (± 117.12) | 0.280[a] |
| Urea | 27.51 (± 11.88) | 23.84 (± 10.06) | 26.68 (± 11.09) | 0.162[a] |

*SD: standard deviation. [a]Student's t-test; [b]Fisher's exact test; [c]Mann-Whitney U-test; *Statistically significant.*

**Table II.** Mean changes in symptoms between baseline and week 4 (n = 72)

| Variable | Intervention group (n = 36) | | | Control group (n = 36) | | | |
|---|---|---|---|---|---|---|---|
| | Baseline | Week 4 | p-value[a] | Baseline | Week 4 | p-value[a] | Between groups p-value[b] |
| Anorexia | 4.31 (± 3.26) | 2.94 (± 3.10) | 0.024* | 4.72 (± 2.41) | 5.86 (± 2.63) | 0.001* | 0.005* |
| Anxiety | 2.08 (± 3.22) | 0.83 (± 1.73) | 0.013 | 1.47 (± 2.12) | 1.97 (± 2.65) | 0.074 | 0.604 |
| Chronic nausea | 2.44 (± 3.34) | 0.92 (± 2.06) | 0.005* | 1.89 (± 2.47) | 2.78 (± 3.33) | 0.011* | 0.272 |
| Depression | 2.78 (± 3.30) | 1.89 (± 2.42) | 0.063 | 2.25 (± 2.54) | 2.89 (± 2.92) | 0.003* | 0.703 |
| Dyspnea | 1.19 (± 2.25) | 0.92 (± 1.99) | 0.551 | 0.53 (± 1.05) | 1.06 (± 1.80) | 0.004* | 0.447 |
| Fatigue | 4.81 (± 3.36) | 3.17 (± 3.26) | 0.003* | 4.06 (± 2.73) | 5.58 (± 2.59) | < 0.0001* | 0.203 |
| Insomnia | 2.83 (± 3.53) | 1.39 (± 2.37) | 0.003* | 2.19 (± 2.40) | 2.94 (± 2.94) | 0.007* | 0.451 |
| Lack of overall wellbeing | 4.33 (± 3.27) | 3.72 (± 3.09) | 0.294 | 4.42 (± 2.53) | 4.97 (± 3.06) | 0.095 | 0.274 |
| Pain | 2.36 (± 2.59) | 1.31 (± 2.01) | 0.030* | 2.14 (± 2.00) | 3.94 (± 2.38) | < 0.0001* | 0.009* |
| Somnolence | 3.39 (± 3.41) | 2.61 (± 2.67) | 0.191 | 2.64 (± 2.45) | 3.14 (± 2.94) | 0.060 | 0.852 |

*[a]Wilcoxon's sign-rank test; [b]GLM repeated measures; *Statistically significant.*

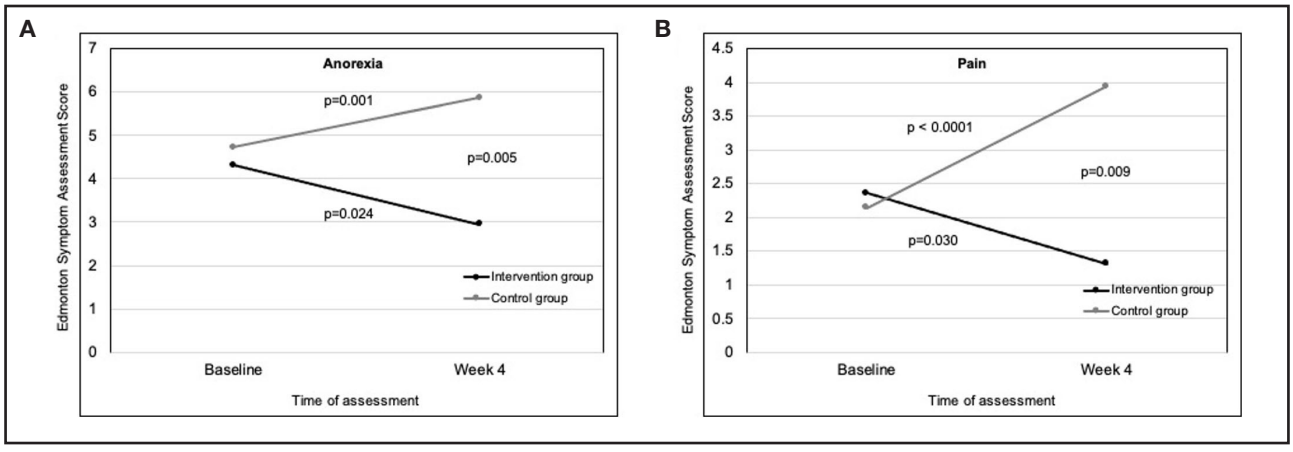


**Figure 2.**

A. Within-group and between-groups comparisons of anorexia at baseline and at 4 weeks. B. Within-group and between-groups comparisons of pain at baseline and at 4 weeks.

**Table III.** Mean changes in biochemical parameters within and between groups from baseline to week 4 (n = 72)

| Variable | Intervention group (n = 36) | | | Control group (n = 36) | | | |
|---|---|---|---|---|---|---|---|
| | Baseline | Week 4 | p-value[a] | Baseline | Week 4 | p-value[a] | Between-groups p-value[b] |
| Albumin | 3.11 (± 0.72) | 3.10 (± 0.87) | 0.260 | 3.18 (± 0.50) | 3.58 (± 4.21) | < 0.0001* | 0.462 |
| Blood urea nitrogen | 13.60 (± 6.80) | 13.90 (± 6.67) | 0.528 | 11.81 (± 4.36) | 12.77 (± 4.79) | 0.009* | 0.274 |
| Chloride | 97.61 (± 7.74) | 98.69 (± 5.45) | 0.110 | 96.17 (± 7.74) | 93.69 (± 7.84) | < 0.0001* | 0.043* |
| Creatinine | 0.91 (± 0.71) | 0.82 (± 0.30) | 0.609 | 0.82 (± 0.29) | 0.87 (± 0.31) | 0.097 | 0.859 |
| Glucose | 105.72 (± 36.17) | 105.81 (± 25.21) | 0.310 | 100.44 (± 16.65) | 105.42 (± 18.40) | 0.005* | 0.617 |
| Hb | 11.59 (± 1.91) | 11.19 (± 2.08) | 0.015* | 11.27 (± 2.01) | 10.74 (± 2.05) | < 0.0001* | 0.406 |
| Hematocrit | 35.81 (± 35.81) | 34.66 (± 34.66) | 0.010* | 34.07 (± 6.17) | 32.92 (± 6.04) | < 0.0001* | 0.199 |
| Magnesium | 1.73 (± 0.36) | 1.58 (± 0.32) | 0.069 | 1.74 (± 0.38) | 1.80 (± 0.41) | < 0.0001* | 0.148 |
| Phosphorus | 3.74 (± 1.04) | 3.81 (± 0.58) | 0.032* | 3.32 (± 0.62) | 3.13 (± 0.66) | 0.001* | 0.001* |
| Potassium | 4.14 (± 0.74) | 4.16 (± 0.63) | 0.597 | 3.86 (± 0.58) | 3.62 (± 0.61) | < 0.0001* | 0.006* |
| Total protein | 6.58 (± 1.09) | 6.57 (± 0.85) | 0.988 | 6.03 (± 0.57) | 5.66 (± 0.52) | < 0.0001* | < 0.0001* |
| Sodium | 160.39 (± 165.26) | 133.83 (± 4.64) | 0.101 | 130.36 (± 6.97) | 127.06 (± 6.47) | < 0.0001* | 0.183 |
| Urea | 27.51 (± 11.88) | 28.94 (± 14.10) | 0.362 | 23.84 (± 10.06) | 24.28 (± 10.43) | 0.539 | 0.119 |

*Hb: hemoglobin. [a]Wilcoxon's sign-rank test; [b]GLM repeated measures. ± standard deviation. *Statistically significant.*

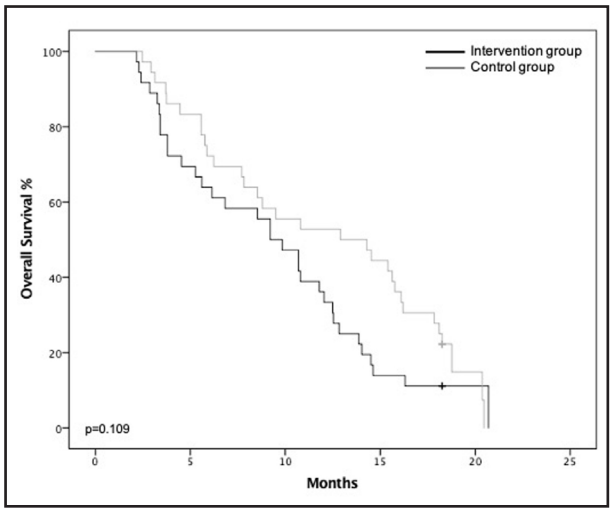


**Figure 3.**

Overall survival by group (intervention versus control) (p = 0.109).

## DISCUSSION

Palliative care patients commonly present with several intense symptoms. They present extreme fatigue and distress. Thus, a number of simplified tools are available to allow repeated symptom assessment to acknowledge the intensity of the different symptoms (21). The most frequently used scale is ESAS. In this context, periodic reassessment adds value for the identification or modification of treatment goals and to monitor the response to specific interventions.

This randomized trial evaluated the effect of hydration and supplementary vitamins and oligoelements in controlling the symptoms, especially pain, occurring during the end-of-life care of cancer patients. There is a scarcity of clinical trials evaluating the administration of artificial hydration and results are controversial. Overall, artificial nutrition and hydration are not recognized as interventions to prolong survival or improve clinical symptoms of terminally ill cancer patients. Nonetheless, little is known about the effect of artificial hydration alone on patients' survival, symptoms or quality of dying. Deciding whether or not to provide artificial nutrition and hydration at the end of life may cause concerns in patients and caregivers but there is scarce evidence regarding their preferences (21,22). Moreover, studies have focused on parenteral nutrition rather than vitamin and oligoelements supplementation. Thus, our study is the first one reporting the effect of both, hydration and vitamin and trace elements supplementation in terminal-stage cancer patients. The main finding was that the intervention group had an improvement in pain and anorexia from baseline to 4 weeks after. Therefore, as it is known that pain is the most distressing and feared symptom in end-stage cancer patients and their families, affecting up to 80 % of cancer patients before death (23,24), it is important to achieve a good pain control. In general, pain is best considered as a domain within the broader context of palliative care.

Moreover, loss of appetite or anorexia and weight loss are common among patients with an advanced serious life-threatening illness, for instance, cancer. Sometimes, simple starvation, which is characterized by a caloric deficiency can be reversed with appropriate feeding, while cachexia cannot be reversed by the supplementation of calories. Hence the importance of addressing the problem of anorexia among palliative cancer patients.

Different international studies have addressed the importance of interventions including hydration during the end of life of cancer patients. For instance, Cerchietti et al. (12) performed randomized trial dividing 42 patients into two groups. Both groups received subcutaneous haloperidol and/or metoclopramide. The intervention group also received 5 % dextrose and sodium chloride. The authors reported that both groups showed significant and equal improvements in relief of thirst and chronic nausea at 24 hours, more importantly, after 48 hours, this improvement was maintained only for the relief of chronic nausea in the group that received hydration. Delirium did not improve significantly in either group during the 48-hour trial period. They concluded that the decision on rehydration of patients with terminal-phase cancer should be mainly based on the comfort of the patient rather than on providing optimal hydration per se (12). A study performed in Italy (25) reported the outcomes of 125 patients, 89 with home parenteral nutrition (HPN) and 36 only with artificial hydration. The survival of the two groups showed a significant difference favoring patients receiving HPN. Cotogni et al. concluded that their data supported the guidelines recommendation that HPN should be considered when malnutrition represents the overriding threat for the survival of palliative cancer patients.

Moreover, an East-Asian Collaborative Study (26) conducted a multicenter cohort study to assess the effects of parenteral nutrition and hydration on survival in patients with malignant bowel obstruction reporting significant differences in survival rates ($p < 0.001$), with a higher median of 35.5 days in the group receiving the intervention.

Another pilot study of 25 patients performed by Adem and AL-Mouaalamy (27) assessed the effectiveness of hypodermoclysis to close the gap of treatment for home-based palliative patients with cancer, concluding that hypodermoclysis was effective and could enhance the comfort of the patients.

On the contrary, a study from Taiwan (28) observed that artificial hydration did not prolong survival or improved dehydration symptoms of terminally ill cancer patients, but it did influence the quality of dying.

We acknowledge the limitations of the present study: a single center study that did not evaluated the administration of parenteral nutrition or other medications, as well as quality of life, however, as literature within this topic remains disputed, it is important to report the findings, especially in the scenario of a developing country. We highlight the improvement within the control of most symptoms and some biochemical parameters in the intervention group receiving vitamins and oligoelements along with intravenous hydration.

In general, most recommended therapies for cancer pain are within the scope of both specialty and primary care medical

practice and the adequate treatment of cancer pain should be viewed as a best practice for all medical disciplines involved in the care of this population. When the clinical issues are complex, particularly when pain is difficult to control or accompanied by other concerns, experimental interventions proven to diminish this burden may be appropriate. Therefore, further prospective trials at an international level are needed.

## REFERENCES


1. Blinderman CD, Billings JA. Comfort Care for Patients Dying in the Hospital. N Engl J Med 2015;373:2549-61. DOI: 10.1056/NEJMra1411746
2. Bruera E, Belzile M, Watanabe S, Fainsinger RL. Volume of hydration in terminal cancer patients. Support Care Cancer 1996;4:147-50. DOI: 10.1007/BF01845764
3. Bruera E, Franco JJ, Maltoni M, Watanabe S, Suarez-Almazor M. Changing pattern of agitated impaired mental status in patients with advanced cancer: association with cognitive monitoring, hydration, and opioid rotation. J Pain Symptom Manage 1995;10:287-91. DOI: 10.1016/0885-3924(95)00005-J
4. Lawlor PG, Gagnon B, Mancini IL, Pereira JL, Hanson J, M E Suarez-Almazor, et al. Occurrence, causes, and outcome of delirium in patients with advanced cancer: a prospective study. Arch Intern Med 2000;160:786-94. DOI: 10.1001/archinte.160.6.786
5. Dalal S, Del Fabbro E, Bruera E. Is there a role for hydration at the end of life? Curr Opin Support Palliat Care 2009;3:72-8. DOI: 10.1097/SPC.0b013e32832531a5
6. Dalal S, Bruera E. Dehydration in cancer patients: to treat or not to treat. J Support Oncol 2004;2:467-79.
7. Dunphy K, Finlay I, Rathbone G, Gilbert J, Hicks F. Rehydration in palliative and terminal care: if not--why not? Palliat Med 1995;9:221-8. DOI: 10.1177/026921639500900307
8. Burge FI. Dehydration symptoms of palliative care cancer patients. J Pain Symptom Managem1993;8:454-64. DOI: 10.1016/0885-3924(93)90188-2
9. Morita T, Tei Y, Tsunoda J, Inoue S, Chihara S. Determinants of the sensation of thirst in terminally ill cancer patients. Support Care Cancer 2001;9:177-86. DOI: 10.1007/s005200000205
10. Waller A, Hershkowitz M, Adunsky A. The effect of intravenous fluid infusion on blood and urine parameters of hydration and on state of consciousness in terminal cancer patients. Am J Hosp Palliat Care 1994;11:22-7. DOI: 10.1177/104990919401100607
11. Musgrave CF, Bartal N, Opstad J. The sensation of thirst in dying patients receiving i.v. hydration. J Palliat Care 1995;11:17-21.
12. Cerchietti L, Navigante A, Sauri A, Palazzo F. Hypodermoclysis for control of dehydration in terminal-stage cancer. Int J Palliat Nurs 2000;6:370-4. DOI: 10.12968/ijpn.2000.6.8.9060
13. Lokker ME, van der Heide A, Oldenmenger WH, van der Rijt CCD, van Zuylen L. Hydration and symptoms in the last days of life BMJ Supportive & Palliative Care 2021;11:335-43. DOI: 10.1136/ bmjspcare-2018-001729
14. Bruera E, Hui D, Dalal S, Torres-Vigil I, Trumble J, Roosth J, et al. Parenteral hydration in patients with advanced cancer: a multicenter, double-blind, placebo-controlled randomized trial. J Clin Oncol 2013;31:111-8. DOI: 10.1200/jco.2012.44.6518
15. Williams BR, Amos Bailey F, Kvale E, Steil N, Goode PS, Kennedy RE, et al. Continuation of non-essential medications in actively dying hospitalised patients. BMJ Support Palliat Care 2017;7(4):450-7. DOI: 10.1136/bmjspcare-2016-001229
16. Bailey FA, Williams BR, Woodby LL, Goode PS, Redden DT, Houston TK, et al. Intervention to improve care at life's end in inpatient settings: the BEACON trial. J Gen Intern Med 2014;29(6):836-43. DOI: 10.1007/s11606-013-2724-6
17. Mochamat, Cuhls H, Marinova M, Kaasa S, Stieber C, Conrad R, et al. A systematic review on the role of vitamins, minerals, proteins, and other supplements for the treatment of cachexia in cancer: a European Palliative Care Research Centre cachexia project. J Cachexia Sarcopenia Muscle 2017;8(1):25-39. DOI: 10.1002/jcsm.12127
18. Vollbracht C, Gündling PW, Kraft K, Friesecke I. Blood concentrations of vitamins B1, B6, B12, C and D and folate in palliative care patients: Results of a cross-sectional study. J Int Med Res 2019;47(12):6192-205. DOI: 10.1177/0300060519875370
19. Helde Frankling M, Klasson C, Sandberg C, Nordström M, Warnqvist A, Bergqvist J, et al. 'Palliative-D'-Vitamin D Supplementation to Palliative Cancer Patients: A Double Blind, Randomized Placebo-Controlled Multicenter Trial. Cancers (Basel) 2021;13(15):3707. DOI: 10.3390/cancers13153707
20. Bükki J, Unterpaul T, Nübling G, Jox RJ, Lorenzl S. Decision making at the end of life--cancer patients' and their caregivers' views on artificial nutrition and hydration. Support Care Cancer 2014;22(12):3287-99. DOI: 10.1007/s00520-014-2337-6
21. Bruera E. Patient assessment in palliative cancer care. Cancer Treat Rev 1996;22(Suppl A):3-12. DOI: 10.1016/s0305-7372(96)90058-4
22. Good P, Richard R, Syrmis W, Jenkins-Marsh S, Stephens J. Medically assisted hydration for adult palliative care patients. Cochrane Database of Systematic Reviews 2014;4:CD006273. DOI: 10.1002/14651858.CD006273.pub3
23. Van den Beuken-van Everdingen MH, de Rijke JM, Kessels AG, Schouten HC, van Klef M, Patijn J. High prevalence of pain in patients with cancer in a large population-based study in The Netherlands. Pain 2007;132:312-20. DOI: 10.1016/j.pain.2007.08.022
24. Teunissen SC, Wesker W, Kruitwagen C, de Haes HC, Voest EE, de Graeff A. Symptom prevalence in patients with incurable cancer: a systematic review. J Pain Symptom Manage 2007;34:94-104. DOI: 10.1016/j.jpainsymman.2006.10.015
25. Cotogni P, Ossola M, Passera R, Monge T, Fadda M. De Francesco A, et al. Home parenteral nutrition versus artificial hydration in malnourished patients with cancer in palliative care: a prospective, cohort survival study. BMJ Support Palliat Care 2020;21:bmjspcare-2020-002343. DOI: 10.1136/bmjspcare-2020-002343
26. Arakawa S, Amano K, Oyamada S, Maeda I, Ishiki H, Miura T, et al. East-Asian Collaborative Cross-Cultural Study To Elucidate the Dying Process (EASED) Investigators. Effects of parenteral nutrition and hydration on survival in advanced cancer patients with malignant bowel obstruction: secondary analysis of a multicenter prospective cohort study. Support Care Cancer 2021;29(12):7541-9. DOI: 10.1007/s00520-021-06293-8
27. Adem S, ALMouaalamy N. Effectiveness and Safety of Hypodermoclysis Patients With Cancer: A Single-Center Experience From Saudi Arabia. Cureus 2021;13(3):e13785. DOI: 10.7759/cureus.13785
28. Wu CY, Chen PJ, Ho TL, Lin WY, Cheng SY. To hydrate or not to hydrate? The effect of hydration on survival, symptoms and quality of dying among terminally ill cancer patients. BMC Palliat Care 2021;20(1):13. DOI: 10.1186/s12904-021-00710-9