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**Evaluation of prognostic factors, symptoms
and consequences of dehydration
in patients with cancer based
on retrospective data analysis of 102 patients treated
in the Department of Palliative Medicine
at the University Hospital in Cracow —
preliminary report**

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Abstract: **Introduction:** Dehydration is a common problem in patients with terminal cancer patients. It worsens the quality of life and increases the amount of complications. Factors associated with dehydration need further exploration. The aim of our study was to determine the predictors of dehydration. **Patients and methods:** 102 terminal cancer patients admitted to Palliative Care Unit were retrospectively analyzed. Detailed physical examination, medical history including history taken from

family and care givers was taken upon admission. Laboratory parameters including morphology, sodium, potassium, total and ionized calcium, LDH were taken on admission. We used univariate and multivariate logistic regression analysis to determine factors associated with dehydration.

Results: On admission 39% of patients were diagnosed with dehydration. Multivariate logistic regression analysis after adjustment for possible confounders revealed that lack of family care ($p = 0.006$; OR = 0.147; CI 95% = 0.038–0.577), higher level of PS ($p = 0.0426$; OR = 1.65; CI 95% = 1.017–2.667), lack of prior opioid use ($p = 0.0233$; OR = 0.386; CI 95% = 0.17–0.897), occurrence of nausea and vomiting at admission ($p = 0.0077$; OR = 3.297; CI 95% = 1.372–7.922), occurrence of dyselectrolytemia ($p = 0.0012$; OR = 4.462; CI 95% = 1.81–10.997), lack of prior GKS use ($p = 0.0362$; OR = 0.339; CI 95% = 0.123–0.933); lack of prior NSAID use ($p = 0.0255$; OR = 0.265; CI 95% = 0.082–0.849) remained independently associated with dehydration.

Conclusion: Lack of family care, lack of prior opioid use, higher level of PS, occurrence of nausea and vomiting at admission, occurrence of dyselectrolytemia, lack of prior GKS use and lack of prior NSAID use in patients with terminal cancer are factors associated with dehydration.

Key words: dehydration; cancer patients.

Introduction

Dehydration is a frequent problem among patients suffering from neoplasia. It increases the risk of complications and can worsen a patient's prognosis and quality of life [1–4]. In the majority of patients with late-stage neoplastic disease, we can observe a decrease in oral fluid intake, which may result from weakness, anorexia, dysphagia, infection of the oral cavity, nausea, vomiting, bowel obstruction, or as a result of medical treatment [5, 6]. Particularly in cases of acute dehydration, it is worthwhile to consider parenteral hydration [7]. In such situations, artificial hydration can additionally increase a patient's comfort, as well as decrease pain and fatigue [8]. We must remember, however, to ensure that the potential benefits of hydration outweigh the risks of acute fluid retention [9]. Therefore, our decision to administer parenteral hydration should be made on an individual basis [10–12]. The risk factors associated with dehydration require studies involving larger groups of patients [13, 14]. The aim of this study was to determine the prognostic factors, symptoms and consequences of dehydration in patients suffering from neoplastic disease.

Patients and methods

We retrospectively analyzed the records of 102 patients admitted to the University Hospital Palliative Medicine Department in Krakow, Poland. On admission, a thorough patient history (from patients and/or their families or caregivers) and physical examination were performed. Additionally, laboratory tests were ordered including: complete blood count, electrolytes (sodium, potassium, total and ionized

calcium), and serum lactate dehydrogenase activity (LDH). Of the 102 patients analyzed, 57 were male and 45 were female. The presence of dehydration was assessed on the basis of a structured patient history and the results of the physical examination. As part of the history, special attention was paid to the patient's level of thirst and amount of urine. During physical examination, dryness of oral and lingual mucosa was assessed, as well as skin turgor. Our study received ethic approval from the Jagiellonian University Bioethical Committee (nr 122.6120.169.2016) on June 23, 2016.

Statistical methods

Univariate and multivariate logistic regression analysis was performed to determine the prognostic factors, symptoms and effects of dehydration. After checking normality of the data, we subsequently analyzed the data using the student's t-test (for independent samples) or the Mann-Whitney test in order to better visualize the results. Results with $p < 0.05$ were considered statistically significant. All statistical analysis was performed using Statistica v. 12 for Windows (Statsoft Polska).

Results

Among the analyzed patients, 39% had clinical features of dehydration on admission. The average patient age was 66.64 years and the average length of stay on the ward was 15 days. One-third of patients from the study group were admitted to the Palliative Medicine Department from the Emergency Department as an emergent admission. Nearly half of the analyzed (50 patients) were eventually discharged home. Hospitalization resulted in death for the remaining patients. The most common type of neoplasia in the study group was lung cancer (26.47%). The next most frequent types of neoplasia were pancreatic (10.78%), breast (9.8%), colorectal (8.82%), and prostate (7.84%). Distant metastasis was confirmed in 92 of the patients, including 19 patients with metastasis to the central nervous system and 37 with metastasis to bone.

Upon univariate logistic regression analysis, the statistically significant prognostic factors were found to be (Table 1): family care ($p = 0.002$; OR = 0.147; CI 95% = 0.038–0.577), lack of NSAID use prior to hospitalization ($p = 0.019$; OR = 0.265; CI 95% = 0.082–0.849), lack of GCS use prior to hospitalization ($p = 0.032$; OR = 0.339; CI 95% = 0.123–0.933), and lack of opioid use prior to hospitalization ($p = 0.022$; OR = 0.386; CI 95% = 0.17–0.879). Patients in a worse physical state (higher score in PS scale) had a greater chance of being dehydrated ($p = 0.039$; OR = 1.65; CI 95% = 1.017–2.667). After checking normality, the data was analyzed using the student's t-test (for independent samples) or the U Mann-

Whitney test. We found that properly hydrated patients were being cared for by family members in 95.16% of cases, whereas dehydrated patients were receiving such care in only 74.35% of cases. Analysis of patients who had received treatment before admission revealed that 30.16% of properly hydrated patients took NSAIDs for analgesia, while only 10.26% of dehydrated patients had taken them. The second group of drugs which was analyzed were GCS. 34.92% of properly hydrated patients were receiving GCS before admission, while only 15.38% of dehydrated patients were receiving them. The final group of drugs which we analyzed were opioids. 66.67% of well hydrated patients were taking opioids before hospitalization, whereas only 43.59% of dehydrated patients were taking medications from this group.

Table 1. Factors predisposing patients to dehydration.

Risk factor	Properly hydrated patients (n = 63)	Dehydrated patients (n = 39)	p-value
Active cancer treatment	0.238095	0.230769	0.933278
Family care	0.951613	0.743590	0.021130
NSAID use prior to admission	0.301587	0.102564	0.019261
Antidepressant use prior to admission	0.174603	0.256410	0.325544
Anticonvulsant use prior to admission	0.142857	0.179487	0.625163
GCS use prior to admission	0.349206	0.153846	0.031817
Opioid use prior to admission	0.666667	0.435897	0.021709
Hospice or palliative care	0.349206	0.230769	0.210147
PS score	2.825397	3.205128	0.039059

Based on these results, we can infer that the use of NSAIDs and opioids resulted in better pain control among patients. This led to an increase in homeostasis and consequently better hydration. It should be noted, however, that the combined use of GCS and NSAIDs, particularly in dehydrated patients, can increase the risk of adverse effects. GCS are among the most commonly used medications to relieve symptoms in the advanced stage of neoplastic disease. Rapidly progressive dehydration, hypotension, and oliguria may be signs of acute secondary adrenal insufficiency, which may be caused by a sudden withdrawal of long-term GCS treatment. Overlapping symptoms of adrenal insufficiency and neoplastic disease or misinterpretation of laboratory results as renal failure, especially in patients with exacerbated adrenal insufficiency, may lead to misdiagnosis.

Another parameter we evaluated was the degree of physical disability in patients with neoplastic disease. To evaluate this, we used the PS scale. According to this scale,

an increase in PS score indicates a worsening of a cancer patient's general status, which may lead to disturbances in homeostasis and a greater risk of dehydration. The average PS score in our study group was 2.83 for properly hydrated patients. However, it was significantly higher for dehydrated patients, averaging 3.21.

Further univariate logistic regression analysis of the occurrence of certain symptoms in patients was performed (Table 2). We found that nausea and vomiting at admission was a statistically significant symptom of dehydration ($p = 0.0061$; OR = 3.297; CI 95% = 1.372–7.922) (Fig. 1). While 20.63% of well hydrated patients reported nausea and vomiting at admission, the rate for dehydrated patients was more than two times higher, measuring 46.15%.

Table 2. Symptoms of dehydration.

Symptom at admission	Properly hydrated patients (n = 63)	Dehydrated patients (n = 39)	p-value
Anxiety	0.380952	0.333333	0.630952
Constipation	0.349206	0.384615	0.721003
Nausea/vomiting	0.206349	0.461538	0.006136

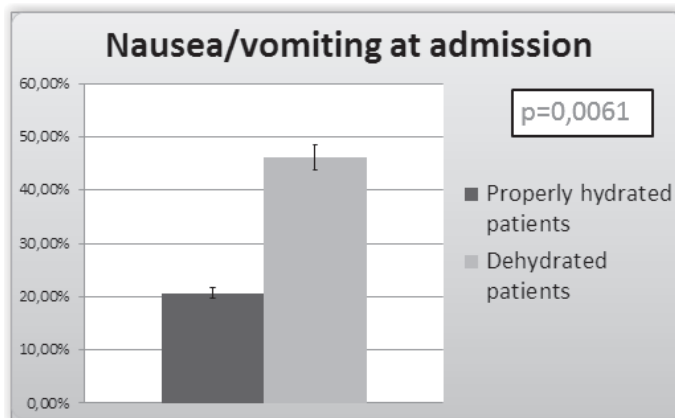
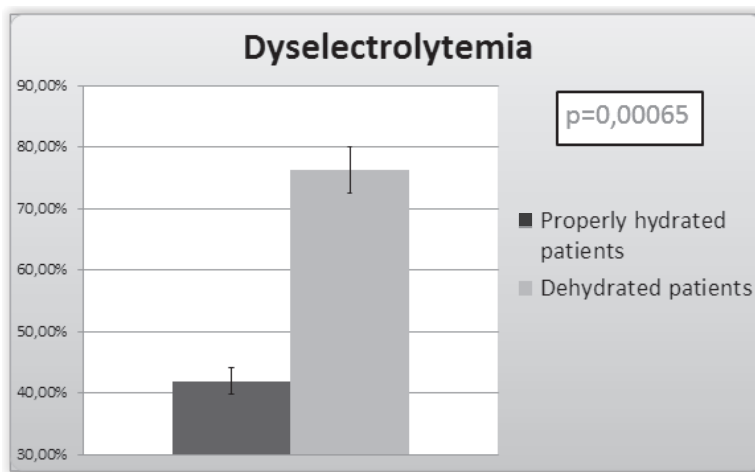


Fig. 1. Correlation between nausea/vomiting at admission and dehydration among patients.

The next univariate logistic regression analysis was performed in regards to the effects of dehydration (Table 3). It was revealed that dyselectrolytemia is a statistically significant effect of dehydration ($p = 0.000646$; OR = 4.462; CI 95% = 1.81–10.997) (Fig. 2). Dyselectrolytemia was diagnosed in 41.94% of patients who were properly hydrated, but was markedly more frequent among dehydrated patients, being diagnosed in 76.32%.

Table 3. Effects of dehydration.

Effect	Properly hydrated patients (n = 63)	Dehydrated patients (n = 39)	p-value
Weightloss >30%	0.322581	0.512821	0.057860
Dyselectrolytemia	0.419355	0.763158	0.000646
Neuropsychiatric symptoms during hospitalization	0.428571	0.481790	0.567713
Neuropsychiatric symptoms at discharge	0.333333	0.333333	1.000000

**Fig. 2.** Correlation between the occurrence of dyselectrolytemia and dehydration among patients.

The final phase of our analysis consisted of multivariate logistic regression analysis (Table 4). In this phase, we analyzed factors interacting with each other in complex model and having an influence on dehydration, as well as those independent from other factors. Our results showed that the independent prognostic factors associated with dehydration are: family care ($p = 0.006$; OR = 0.147; CI 95% = 0.038–0.577), NSAID use before hospitalization ($p = 0.0255$; OR = 0.265; CI 95% = 0.082–0.849); GCS use before hospitalization ($p = 0.0362$; OR = 0.339; CI 95% = 0.123–0.933), opioid use before hospitalization ($p = 0.0233$; OR = 0.386; CI 95% = 0.17–0.897), and PS score ($p = 0.0426$; OR = 1.65; CI 95% = 1.017–2.667). Family care reduces the chance of dehydration by 6.8 times. Medication use before hospitalization also reduces the risk of dehydration (NSAIDs by 3.8x, GCS by 3x, opioids by about 2.6x). An increase of 1 unit on the PS scale results in a 1.7 times greater chance for the presence of dehydration. Nausea and vomiting at admission is the only symptom independently associated with dehydration ($p = 0.0077$; OR = 3.297; CI 95% = 1.372–7.922),

occurring 3.3 times more frequently among dehydrated patients. Dyselectrolytemia is an independently associated effect of dehydration ($p = 0.0012$; OR = 4.462; CI 95% = 1.81–10.997) and occurs 4.5 times more frequently in patients suffering from dehydration.

Table 4. Multivariate regression analysis of factors associated with dehydration.

Factor	p-value	OR	95% CI	Rate	
Family care	0.0060	0.147	0.038–0.577	6.8x ↓	Prognostic factors
NSAID use prior to admission	0.0255	0.265	0.082–0.849	3.8x ↓	
GCS use prior to admission	0.0362	0.339	0.123–0.933	3.0x ↓	
Opioid use prior to admission	0.0233	0.386	0.170–0.897	2.6x ↓	
PS score	0.0426	1.650	1.017–2.677	1.7x ↑	
Nausea/ vomiting at admission	0.0077	3.297	1.372–7.922	3.3x ↑	Symptom
Dyselectrolytemia	0.0012	4.462	1.810–10.997	4.5x ↑	Consequence

The above analyses indicate that the factors contributing to dehydration in advanced cancer patients admitted to a hospital ward as an emergency admission are: lack of family care at home, lack of medication usage (GCS, NSAIDs, opioids), higher score on the PS scale, occurrence of nausea and vomiting, and laboratory-confirmed dyselectrolytemia.

Discussion

Patients in the terminal phase of neoplastic disease are at high risk of dehydration [1]. Effective symptom control and optimization of therapy and clinical status in this phase of disease can result in many benefits, including proper maintenance of a patient's fluid-electrolyte balance [8, 14]. Our results appear to be clinically useful, as they allow us to identify factors which can potentially lower the risk of dehydration in patients suffering from advanced neoplasia. The results indicate a need for the optimization of pain control in patients receiving outpatient palliative care. In the treatment of this pain, we should use drugs ranging from non-opioid analgesics to strong opioids, depending on pain severity, in accordance with the recommendations of the World Health Organization and European Association of Palliative Care.

GCS are medications administered via several routes, including parenteral, for a variety of specific and non-specific indications. In palliative medicine, they are most frequently used for non-specific indications. Therefore, one must plan to administer them for approximately 3–4 weeks. These drugs limit inflammation, thus promoting

homeostasis and reducing the risk of dehydration. However, it is important to remember that in many patients, after an initial improvement, the therapeutic effect of GCS decreases despite continued administration, and the risk of adverse effects quickly increases, due to long-term disruption of the hypothalamic-pituitary axis. As the results of our study show, the problem of dehydration in patients admitted to the hospital is also related to care from family members in the outpatient setting. It is therefore worthwhile to discuss with family members the important role their care plays in limiting the risk of dehydration. Nausea and vomiting are also important risk factors of dehydration in patients with cancer, who are not receiving chemotherapy. However, in patients receiving this therapy, they are the most frequent side effects and we should, therefore, bring this to the attention of the family. Thus, proper oral hydration in the outpatient setting can potentially decrease the risk of rapid deterioration of a patient's general status.

Our observations demonstrating a clear correlation between number of nausea/vomiting states and dehydration in our study group was confirmed in six other studies [5, 14]. In patients who display clinical signs of dehydration (dryness of mucous membranes, oliguria, decreased skin turgor, etc.), electrolyte levels should be measured. According to our results, dyselectrolytemia occurs almost 5 times more frequently in dehydrated individuals. Several other investigators also noted the need to monitor electrolytes in dehydrated patients [6, 15]. It should be noted that electrolyte disturbances must be corrected slowly. In clinical practice, correcting sodium levels too quickly can result in severe neurologic consequences (central pontine myelinolysis), and a sudden rise in potassium can lead to cardiac arrest [15].

Insufficient fluid intake associated with weakness, coexisting renal insufficiency, potential for diarrhea, and increased hyperventilation in febrile patients promotes the development of dehydration and a decreased amount of water in the intra- and extracellular space. These conditions may lead to hyperosmolarity with the following clinical manifestations: nausea, lassitude, muscle weakness, disturbances of consciousness [15, 16]. Plasma hyperosmolarity leads to stimulation of osmoreceptors in the hypothalamus and secretion of anti-diuretic hormone (ADH) [17]. ADH increases the reabsorption of water leading to a reduction in plasma osmolarity and, consequently, to hyponatremia, which significantly increases the risk of death [1]. The fluid deficit observed in our patients also promotes the development of symptoms of confusion. In previously published studies, the authors of three independent papers recognized that dehydration and the administration of large doses of opioids were the two main causes of qualitative disturbances of consciousness [6, 12, 18, 19]. It is believed that hydration is a potential method for reversing this undesirable condition in these patients [1, 20].

Finally, it is worth noting that hydration is a controversial topic in palliative medicine and is associated with quite divergent opinions. Research on this topic

is mixed. We must take clinical and socio-cultural conditions into account when determining our approach. Preferences of the patient and family should be respected. In emergency cases of dehydration (vomiting, diarrhea), physicians should weigh the benefits of parenteral hydration. When deciding on the route of hydration, one should consider the fact that intravenous fluid administration may be inconvenient and unpleasant for patients. It is worth remembering that subcutaneous infusion remains a good alternative method of hydration in terminal cancer patients. Hydration can be beneficial, but the decision to begin this treatment should be made on an individual basis. It is also recommended that properly hydrated patients in the terminal phase should receive reduced doses of medications, to reduce the risk of adverse effects [7].

In conclusion, analysis of our data indicates that the factors contributing to dehydration in patients with advanced neoplastic disease, admitted to a hospital ward as an emergency admission, are: lack of family care at home, lack of medication usage before hospitalization (GCS, NSAIDs, opioids), higher PS score, presence of nausea and vomiting, and laboratory-confirmed dyselectrolytemia.

Conflict of interest

None declared.

Abbreviations

- NSAID — non-steroidal anti-inflammatory drug
GCS — glucocorticosteroids
PS — ECOG (Eastern Cooperative Oncology Group) Performance Status scale (attempts to determine the general status and quality of life in patients with neoplastic disease)
OR — odds ratio

References

1. Price K.A.R.: Hydration in cancer patients. *Curr Opin Support Palliat Care*. 2010 Dec; 4 (4): 276–280.
2. Fortes M.B., Owen J.A., Raymond-Barker P., Bishop C., Elghenzai S., Oliver S.J., et al.: Is this elderly patient dehydrated? Diagnostic accuracy of hydration assessment using physical signs, urine, and saliva markers. *J Am Med Dir Assoc*. 2015 Mar; 16 (3): 221–228.
3. El-Sharkawy A.M., Watson P., Neal K.R., Ljungqvist O., Maughan R.J., Sahota O., et al.: Hydration and outcome in older patients admitted to hospital (The HOOP prospective cohort study). *Age Ageing*. 2015 Nov; 44 (6): 943–947.
4. Teno J.M., Gozalo P., Mitchell S.L., Tyler D., Mor V.: Survival after multiple hospitalizations for infections and dehydration in nursing home residents with advanced cognitive impairment. *JAMA*. 2013 Jul 17; 310 (3): 319–320.

5. *Raijmakers N.J.H., van Zuylem L., Costantini M., Caraceni A., Clark J., Lundquist G., et al.*: Artificial nutrition and hydration in the last week of life in cancer patients. A systematic literature review of practices and effects. *Ann Oncol Off J Eur Soc Med Oncol ESMO*. 2011 Jul; 22 (7): 1478–1486.
6. *Dalal S., Bruera E.*: Dehydration in cancer patients: to treat or not to treat. *J Support Oncol*. 2004 Dec; 2 (6): 467–479, 483.
7. *Bruera E.*: Textbook of palliative medicine and supportive care. 2016.
8. *Cohen M.Z., Torres-Vigil I., Burbach B.E., de la Rosa A., Bruera E.*: The meaning of parenteral hydration to family caregivers and patients with advanced cancer receiving hospice care. *J Pain Symptom Manage*. 2012 May; 43 (5): 855–865.
9. *Nakajima N., Hata Y., Kusumoto K.*: A clinical study on the influence of hydration volume on the signs of terminally ill cancer patients with abdominal malignancies. *J Palliat Med*. 2013 Feb; 16 (2): 185–189.
10. *Torres-Vigil I., Mendoza T.R., Alonso-Babarro A., De Lima L., Cárdenas-Turanzas M., Hernandez M., et al.*: Practice patterns and perceptions about parenteral hydration in the last weeks of life: a survey of palliative care physicians in Latin America. *J Pain Symptom Manage*. 2012 Jan; 43 (1): 47–58.
11. *Nakajima N., Satake N., Nakaho T.*: Indications and practice of artificial hydration for terminally ill cancer patients. *Curr Opin Support Palliat Care*. 2014 Dec; 8 (4): 358–363.
12. *Dev R., Dalal S., Bruera E.*: Is there a role for parenteral nutrition or hydration at the end of life? *Curr Opin Support Palliat Care*. 2012 Sep; 6 (3): 365–370.
13. *Hui D., Dev R., Bruera E.*: The last days of life: symptom burden and impact on nutrition and hydration in cancer patients. *Curr Opin Support Palliat Care*. 2015 Dec; 9 (4): 346–354.
14. *Nakajima N., Takahashi Y., Ishitani K.*: The volume of hydration in terminally ill cancer patients with hydration-related symptoms: a prospective study. *J Palliat Med*. 2014 Sep; 17 (9): 1037–1041.
15. *Sarhill N., Walsh D., Nelson K., Davis M.*: Evaluation and treatment of cancer-related fluid deficits: volume depletion and dehydration. *Support Care Cancer Off J Multinatl Assoc Support Care Cancer*. 2001 Sep; 9 (6): 408–419.
16. *Morita T., Tei Y., Tsunoda J., Inoue S., Chihara S.*: Underlying pathologies and their associations with clinical features in terminal delirium of cancer patients. *J Pain Symptom Manage*. 2001 Dec; 22 (6): 997–1006.
17. *Nwosu A.C., Mayland C.R., Mason S.R., Khodabukus A.F., Varro A., Ellershaw J.E.*: Hydration in advanced cancer: can bioelectrical impedance analysis improve the evidence base? A systematic review of the literature. *J Pain Symptom Manage*. 2013 Sep; 46 (3): 433–46.e6.
18. *Galanakis C., Mayo N.E., Gagnon B.*: Assessing the role of hydration in delirium at the end of life. *Curr Opin Support Palliat Care*. 2011 Jun; 5 (2): 169–173.
19. *Lawlor P.G.*: Delirium and dehydration: some fluid for thought? *Support Care Cancer Off J Multinatl Assoc Support Care Cancer*. 2002 Sep; 10 (6): 445–454.
20. *Lawlor P.G., Gagnon B., Mancini I.L., Pereira J.L., Hanson J., Suarez-Almazor M.E., et al.*: Occurrence, causes, and outcome of delirium in patients with advanced cancer: a prospective study. *Arch Intern Med*. 2000 Mar 27; 160 (6): 786–794.