Dehydration in Cancer Patients: To Treat or Not To Treat

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Abstract Many patients in the terminal phase of their illness experience reduced oral intake before death, due to causes related to their cancer or its treatment. When oral intake is not adequate, dehydration and malnutrition are the obvious results. But these terminally ill patients present a challenge to healthcare providers: to rehydrate these patients or not and, if so, how? Adequate hydration levels are much lower in terminal patients with cancer than in normal adults. Healthcare professionals should assess the patient's hydration needs through personal history, physical examination, and laboratory evaluation before considering the advantages and disadvantages of rehydration, as well as the wishes of the patient and his or her family. In doubtful cases, a short trial of hydration may be appropriate. If hydration is considered, there are a number of methods to consider based on the needs of the patient, including intravenous administration, hypodermoclysis, and proctoclysis. The subcutaneous route is an excellent alternative due to its simplicity, low cost, and feasibility in the home setting.

The great majority of patients in the terminal phase of their illness experience severely reduced oral intake before death, due to a variety of causes related to their cancer or its treatment [1]. The typical causes include anorexia, nausea and vomiting, delayed gastric emptying, bowel obstruction, dysphagia, early satiety, cognitive impairment, and depression [2–5]. The period of reduced intake prompted by any one or more of these causes varies from a few hours to a few weeks—even to months. When oral intake is not adequate, dehydration and malnutrition are the obvious results.

Let us consider two cases for further illustration of the issues relating to dehydration.

Case One: Mrs. Smith, a 66-year-old female, was diagnosed 6 months prior with metastatic colon cancer involving the liver and bone. She has received systemic chemotherapy with progression of her disease. She has recently completed palliative radiation therapy to her lumbar spine and right hip to ameliorate painful metastatic lesions. Despite improvement in her pain symptoms, she continues to require methadone (20 mg/d) with occasional use of morphine for breakthrough pain.

In the past 3 days, she has experienced increasing nausea and vomiting and has not been able to keep down most of her oral medications. In the past 24 hours, she has been unable to get out of bed because of profound weakness and drowsiness. Her daughter, who moved in 1 month ago to help, is concerned about the sudden decline in functional status and seeks medical advice.

Case Two: Mr. Adam is a 52-year-old gentleman with recently diagnosed inoperable pancreatic cancer. His disease has progressed despite his completing two courses of systemic chemotherapy. His abdominal pain has been controlled with sustained-release morphine sulfate (60 mg twice daily). He has profound anorexia and chronic nausea and recently experienced decreased oral intake. Although on disability from work, he continues to enjoy life: going to church, gardening, and watching home improvement shows on TV. He is looking forward to his daughter's graduation from school and is planning a surprise party for her 16th birthday. However, in the past week, he has had increasing nausea, dryness in his mouth, and a daily fluid intake of less than 16 oz. His wife is greatly distressed and calls for advice.

These two cases are examples of what is typically seen in terminally ill cancer patients who have reduced oral intake for the variety of reasons mentioned previously. More pertinent, these terminally ill cancer patients present a challenge to the healthcare profession with regard to the best approaches for their medical care. Both cases have been chosen to highlight that there is no argument that both patients have terminal cancer, both are dehydrated, and both are eventually going to die.

When either patient arrives in the emergency room of a traditional hospital system, irrespective of underlying etiology of the dehydration and cancer status, he or she will receive intravenous fluid

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therapy and will possibly undergo a laboratory workup and imaging studies. When oral intake is insufficient in maintaining adequate hydration, most terminally ill patients in the traditional hospital system receive parenteral fluids, a fact that is well established [1, 6]. Almost all patients admitted to hospitals in the United States have intravenous access, regardless of diagnosis or reason of admission, and a great majority of these patients receive intravenous fluids. Without a need for intravenous therapy, the rules make it more difficult for a hospital to justify billing for inpatient treatment to a patient.

In contrast, if either of these two patients was assessed at this point by a hospice program, in the overwhelming majority of cases, the patient would be provided with mouth care, occasional sips of fluids, symptom control, and patient and family counseling, with no attempt to rehydrate using parenteral fluids. Here, at the other end of the spectrum from hospital care, terminally ill cancer patients may be treated in hospice healthcare without receiving any parenteral fluids [7–9]. Specialists in hospice care argue against parenteral fluids and for a less aggressive approach. Further, the per diem hospice funding mechanism makes the administration of parenteral fluids difficult to finance.

This divergence in approach begs the question: which medical approach is correct? We are not aware of many other areas of medical care where such a divergence in approach exists among healthcare professionals as in the choice of hydration for terminal cancer patients.

The purpose of this review is to discuss the pathophysiology of fluid deficits, the assessment of hydration status in terminally ill cancer patients, the process of decision making regarding rehydration, and the optimal means of fluid administration in those patients for whom a careful evaluation has led to its indication.

Maintaining Fluid Balance

Fluid homeostasis depends on the maintenance of a relatively constant and stable composition of body fluids. It is achieved in normal individuals by matching daily water intake to fluid losses from the body. In normal, healthy adults, water constitutes approximately 60% of total body weight (TBW) in men and 55% in women. This amount declines with aging, with shifts in body composition resulting in a 10%–15% loss of total body water. By the age of 80 years, water constitutes only 45% of TBW.

Water in the body is in a constant state of motion, shifting between the various fluid compartments of the body. Two thirds of the total body water is present in tissue cells and is collectively called intracellular fluid. The remaining third is present as extracellular fluid and is divided between the plasma (intravascular compartment) and interstitial compartment. Additionally, small amounts of extracellular water are distributed in small, contained fluid spaces and include the cerebrospinal, pleural, synovial, intraocular, and peritoneal fluids. Collectively, they are termed "transcellular fluid." The amount of these fluids is highly variable, and these compartments are generally ignored when considering body fluids. However, they may become important in cases of terminal cancer, when patients may present with third-space accumulations, such as in the peritoneal or pleural spaces, contributing to intravascular fluid depletion. The loss of body water in the elderly is mostly limited to the intracellular compartment, whereas extracellular fluid volumes are usually well maintained [10].

The average amount of water lost and consumed per day in healthy adults is around 2.5 L [11]. Maintaining the correct proportions of extracellular and intracellular fluids is vital to proper bodily function. Approximately 90% of the body's water intake is supplied through the gastrointestinal (GI) tract, whereas the remaining 10% is produced internally as a result of cell metabolism [11]. The most important means by which the body loses water is via the kidneys as urine. Hormonally controlled mechanisms maintain water balance by controlling the rate of excretion of water (and electrolytes) in urine. The other sources of fluid loss are the skin, lungs, and GI tract. The kidneys excrete approximately 1–2 L of urine daily. Approximately 900 mL of this amount is obligatory water excretion that eliminates solutes and is constant from day to day. The remainder is excreted according to the fluctuating needs of the body and the changing renal tubular reabsorption rate.

The process by which the body loses water through the skin and lungs is called insensible water loss. Approximately 350 mL of water is excreted by diffusion through the skin, whereas another 100 mL is lost through normal perspiration. Heavy perspiration may cause greater water loss. Water loss through respiration amounts to about 350 mL per day but varies with climate and increases with tachypnea. Insensible fluid losses thus account

for approximately 800–850 mL per day. Another 150–200 mL is lost through the feces.

The tonicity or osmolality of extracellular fluids relates to its solute concentration and is predominately determined by sodium. The plasma osmolality is maintained in a relatively narrow range (280–295 mOsm/kg) under normal circumstances [12]. A net gain or loss of water will cause shifts affecting both the intracellular and extracellular fluids due to osmosis. When plasma osmolality rises as a consequence of dehydration, osmoreceptors in the hypothalamus are stimulated to induce thirst and increase antidiuretic hormone (ADH) levels. ADH increases the absorption of water in the distal convoluted tubules and collecting ducts of the nephrons, thereby decreasing urine output. ADH is also stimulated by non-osmotic mechanisms. When the effective circulatory volume of plasma falls below a critical level, baroreceptors present in the carotid sinus, aortic arch, and atria are stimulated to maintain an effective circulatory volume, at the expense of perfusion to other organs, such as the kidneys. This process also increases sympathetic tone.

WATER HOMEOSTASIS IN TERMINALLY ILL CANCER PATIENTS

In some studies [6], adequate hydration has been achieved in terminally ill cancer patients with much lower fluid volumes than those needed by the average medical or surgical patient. The lower water requirement in this population is related to a combination of factors, which include age, body weight, decreased insensible losses, and decreased clearance of free water.

Most patients with advanced cancer are elderly. As discussed earlier, shifts in body composition with age decrease the total body water content by 10%–15% compared with that of younger adults. In addition, cancer-related cachexia and weight loss decrease the water requirement further, even when caregivers follow the 30 mL/kg body weight recommendation. Hyponatremia associated with decreased water clearance is common in cancer patients and may be independent of hydration status [6, 13]. Hyponatremia in association with volume depletion occurs when sodium loss exceeds that of water or when patients with baseline hyponatremia experience both water and sodium loss. The latter scenario is common in patients taking diuretics, often prescribed in terminally ill patients to treat third-space fluid losses or leg edema.

Chronic nausea and the use of morphine for pain control further stimulate ADH release [14]. Some cancer patients, especially those with small cell lung cancer, develop a syndrome of inappropriate ADH secretion (SIADH), but it is not associated with fluid deficits. Further, in the elderly, there is a resetting of the osmostat. ADH release is not impaired with aging, but ADH levels are increased for any given plasma osmolality level, indicating a failure of the normal responsiveness of the kidneys to ADH. Probably because of these mechanisms, the normal baseline concentration of sodium in serum shifts to 125–137 mmol/L. In 100 consecutive cancer patients admitted to the Edmonton acute palliative care unit [6], the average plasma sodium level was 132 ± 18 mmol/L, with normal urea and creatinine levels.

Although the daily water requirement of a 70-kg man might be about 2,100 mL, a loss of 30 kg in body weight would result in a daily requirement of 1,200 mL. Insensible losses from the skin and lungs approximating 850 mL in healthy adults are usually lower in terminally ill patients who are less physically active or are bedridden. This calculation should further subtract for decreased insensible losses, which—although variable and dependent on climate, level of activity, presence of fever, and tachypnea—are usually less than those in healthy adults, leading to a water requirement in the range of 800–1,000 mL/d.

Ironically, although the fluid requirements in terminal cancer patients may be less, they are at an increased risk of fluid deficits, often precipitated by minor variations in fluid intake, infections, and other conditions. Many patients with cancer are elderly, in whom renal and neurohormonal functions, important in maintaining water balance and hydration status and deteriorated by age, are not as effective as in younger individuals [15–19]. The thirst mechanism diminishes with age, which significantly impairs the ability of the elderly to maintain homeostasis and increases their risk for dehydration. An age-related decrease in maximal urinary concentrating ability further increases the risk for dehydration.

Assessment of Hydration Status

HISTORY

A history of decreased oral intake and/or increased fluid losses in the form of vomiting or diarrhea provides the most useful information regarding

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Peer viewpoints on this article by Drs. Pedro E. Huertas, J. Andrew Billings, and Robin L. Fainsinger appear on pages 483 and 485.

Table 1

The Hydration Debate

Arguments for hydration
Provides a basic human need
Provides comfort and prevents uncomfortable symptoms: confusion, agitation, and neuromuscular irritability
Prevents complications (eg, neurotoxicity with high-dose narcotics)
Relieves thirst, recognized as a sign of fluid needs
Does not prolong life to any meaningful degree
Allows providers to continue their efforts to find ways to improve comfort and life quality, despite the perception of a poor quality of life
Provides minimum standards of care; not doing so would break a bond with the patient
May set a precedent to withhold therapies from other patients who are compromised
Arguments against hydration
Interferes with acceptance of the terminal condition
Intravenous therapy is painful and intrusive
Prolongs suffering and the dying process
Unnecessary since unconscious patients do not experience uncomfortable symptoms, such as pain or thirst
Less urine output means less need for bed pan, urinal, commode, or catheter
Less fluid in the GI tract and less vomiting
Less pulmonary secretions and less cough, choking, and congestion
Minimizes edema and ascites
Ketones and other metabolic by-products in dehydration act as natural anesthetics for the central nervous system, causing decreased levels of consciousness and decreased suffering

any patient's hydration status and may be obtained from the patient, family, or caregivers. Associated changes in comfort level, cognition, and behavior, along with a detailed review of systems, should be part of the initial history taking and help to formulate treatment goals and plans. Assessment of fluid losses should include an evaluation of urine output, loss in feces, vomiting, and an estimation of insensible fluid losses. This assessment would be crude in most settings unless the patient is specifically monitored, as is the case in hospitals or nursing homes. In patients with urinary incontinence, the number and frequency of wet diapers may provide helpful information. Patients may have internal bleeding or third-space fluid losses in which a history may not be clear, and a high index of suspicion must be maintained about patients who may be at risk. A thorough assessment should also include a medication history and the presence of comorbidities, which will provide useful information on predisposing factors potentially leading to dehydration.

Many of the symptoms experienced by healthy individuals as a consequence of dehydration, such as thirst, dry mouth, fatigue, nausea, anorexia, drowsiness, and confusion, are prevalent in cancer patients, even in the absence of dehydration [20, 21]. Although a sensation of thirst and dry mouth are commonly reported as the most distressing symptoms for dehydrated terminally ill patients, these symptoms may be present due to other factors, such as medications, radiation, mouth breathing, or thrush [21]. Fluid deficits may cause cognitive impairment, altered behavior, a decrease in energy level, confusion, delirium, fainting, or syncope. These problems may result in further reduced intake of fluids. Impaired access to water may also be secondary to immobility, mood disturbances, or dementia. Patients at risk for aspiration or pulmonary edema may be deliberately restricting oral intake. Hyperglycemia secondary to diabetes or hypercalcemia can result in increased urine losses, potentially resulting in negative fluid balance. Presence of fever may increase fluid losses through evaporative skin losses. A review of medications must be undertaken, as many patients may be on diuretics and may continue to take them despite decreased fluid intake.

PHYSICAL EXAMINATION

Physical examination by itself has a low sensitivity and specificity for determining fluid status in cancer patients. Classic signs of fluid deficit, such as dry mucous membranes, reduced skin turgor, sunken eyes, lack of axillary moisture, postural hypotension, and tachycardia, are less reliable in patients with advanced cancer, since these signs may also be present in patients who are not volume depleted.

Skin turgor as a measurement of skin elasticity and interstitial fluid is tested by lightly pinching the skin to form a "tent." If the skin returns to its original shape, skin turgor is good; if it stays "tented," turgor is poor. A pinched facial expression and sunken eyes are other signs suggestive of poor skin turgor. Other skin signs include pallor, decreased capillary refill time (greater than 2 seconds), cyanosis, mottling, and reticulation. Delayed capillary refill may also be secondary to anemia, cigarette smoking, a cold environmental tem-

perature, decreased cardiac output, or peripheral vasoconstriction. Examination of the oral cavity may reveal dry mouth, absent saliva, and tongue furrows. Dry mouth, present in 70% of cancer patients, may be secondary to other causative factors. Resting tachycardia or postural orthostasis is also nonspecific and may be secondary to autonomic neuropathies common in some malignancies [22]. Increased body temperature can be both a cause and a symptom of fluid deficit. Weight loss may occur secondary to negative fluid balance. Recording the patient's weight daily may be easier to measure than recording fluid intake and output.

One should note that although physical signs and symptoms are unhelpful in isolation, a combination of findings in a patient with a history of decreased oral intake or increased fluid loss will be highly suggestive of dehydration.

LABORATORY EVALUATION

The classic findings in volume-depleted patients include increased plasma protein, hematocrit, sodium, blood urea nitrogen, and serum creatinine levels. Isolated laboratory results usually are not helpful in patients with advanced cancer and must be interpreted with caution. Baseline serum creatinine levels are often found to be low due to decreased muscle mass but may be elevated in the presence of chronic or acute renal failure. Hematocrit is usually low due to chronic anemia but may be within the normal range in a setting of volume depletion. Blood urea nitrogen may be elevated in the presence of liver failure or GI bleeding. Hyponatremia is a frequent finding in cancer patients, and its measured value may be difficult to interpret in a setting of suspected dehydration. Plasma and urine osmolality measurements may be helpful in some situations. Low plasma protein concentrations are also associated with advanced cancer, and their level must be considered in context. Comparison of a series of values may be more useful, but these interventions are uncomfortable for the patient, may not add much value to treatment, and are usually unnecessary when the goal of care is providing comfort. When hypokalemia or hypercalcemia is suspected, these tests may be added to guide treatment.

The Decision-Making Process

In recent years, there has been a strong debate concerning the consequences of dehydration for terminally ill patients, with arguments being made for and against fluid administration. The arguments for both sides of the debate on the issue of hydration are presented in Table 1. Understandably, much controversy surrounds this issue, but, unfortunately, the debate is clouded by the fact that there is no evidence-based research to illuminate one approach or the other to the determination of how best to proceed.

Table 2

Considerations in the Decision-Making Process Regarding Hydration

Is the patient dehydrated?
What are the symptoms caused and/or aggravated by dehydration?
What are the expected advantages of re-hydration?
What are the disadvantages of hydration?
What are the views of the patient and family?
What are the individualized goals of care?

The process of decision making should take into consideration a number of factors, as shown in Table 2.

IS THE PATIENT DEHYDRATED?

In most cases, a careful history and physical examination will help identify clinically dehydrated patients. Occasionally, obtaining laboratory data, if acceptable to the patient or surrogate, may guide interventions, as in the case of mental status changes with dehydration and suspected hypercalcemia.

WHAT ARE THE SYMPTOMS CAUSED AND/OR AGGRAVATED BY DEHYDRATION?

Fluid deficits, as mentioned earlier, may cause cognitive impairment, altered behavior, decreased energy level, confusion, delirium, fainting, or syncope. A confused patient may hurt himself, be at risk for falls, and/or have aberrant behavior with paranoid delusions or hallucinations. A patient may experience discomfort or appear distressed to the patient's family or caregiver. As mentioned previously, other symptoms, such as thirst and dry mouth, may be present and cause significant discomfort. Many studies, although noting a high prevalence of thirst and dry mouth in patients with advanced cancer, have failed to show an association between these symptoms and biochemical markers of fluid deficit or dehydration [7, 20, 23, 24] In these studies, dry mouth symptoms were relieved by simple measures, such as oral

care, imbibing small sips of water, and lubrication. Conversely, once symptoms of delirium are present, they may be difficult to manage in the home setting.

Delirium, present in 70%–90% of patients with terminal cancer, is often multifactorial in etiology and may be secondary to hypoxia, infections, hypercalcemia, fever, dehydration, or medications such as opioids [25–30]. Studies in elderly patients with cancer have consistently demonstrated that although dehydration is a risk factor for delirium [19, 31, 32], changes in cognition or frank delirium may also predispose the patient to dehydration. Symptoms of opioid-induced toxicity include tactile hallucinations, agitation, myoclonus, allodynia, hyperalgesia, and seizures. Some researchers have postulated that this toxic state relates to the accumulation of the parent opioid compound or its metabolites when renal clearance is reduced, as in the case of pre-renal failure precipitated by dehydration [30, 33].

Fluid therapy has also been reported anecdotally to worsen edema and increase respiratory tract secretions, although these outcomes are not strongly supported by research. Most of these cases have been secondary to the use of a large volume of fluids administered intravenously in the hospital setting. Reports of improvement in these symptoms after fluids were withdrawn lent support to the position that fluids were not beneficial and possibly harmful in terminal patients.

WHAT ARE THE EXPECTED ADVANTAGES OF RE-HYDRATION?

One of the goals of hydration is to prevent or potentially reverse distressful symptoms attributed to dehydration. One of the most critical arguments relating to the hydration controversy in terminal patients concerns the relationship between delirium and symptoms of opioid-induced neurotoxicity with hydration status.

Many investigators have shown that the incidence of delirium in hospitalized patients may be substantially reduced by administration of fluids. The adoption of a vigorous hydration stance in a palliative care unit in Canada was partly responsible for the diminished incidence of delirium noted in the years since the hydration policy was started, when compared with prior years [34]. Other studies have demonstrated that therapeutic interventions can reverse many episodes of delirium or at least result in improvement in 30%–70% of cases [26, 35–38]. In these studies, opioids, other psychoactive medications, and dehydration were the most frequent causes of reversible delirium. Other common etiologies of delirium include toxic accumulation of drug metabolites and hypercalcemia, both of which can improve rapidly with replacement of fluids. Although the prevention of delirium in patients with cancer has not been systematically examined, studies in patients with advanced cancer and in the elderly have found that hydration of these patients can prevent the development of delirium [18, 34, 39]. Hepatic and renal function deteriorate with advanced illness or as the time of death approaches, and patients become more vulnerable to delirium. Small changes in fluid balance can tip the patient into delirium, mostly precipitated by worsening renal function. Accumulation of opioids or their metabolites may reach levels toxic enough to induce symptoms. Interventions in the form of dose reduction or opioid switching in association with assisted hydration allows for clearing of the offending opioid or its metabolites.

Hydration is not usually required for relief of symptoms such as dry mouth and thirst, since they are not associated with fluid status; therefore, parenteral fluids are unlikely to alleviate thirst [7]. Dry mouth is common, but it is not improved by tube feeding or intravenous hydration; conscientious mouth care and offering small amounts of fluid and ice chips effectively relieve dry mouth [8, 23, 40].

The beneficial effects of holding fluids in terminally ill patients with respect to vomiting, pulmonary congestion, and secretions are not well established, and many of the complications related to fluid overload may be prevented by judiciously using fluids in patients at risk.

WHAT ARE THE DISADVANTAGES OF HYDRATION?

The common disadvantages of hydration are related to complications of intravenous fluid administration. They include symptoms of fluid overload and local and systemic complications (Table 1). Notably, the main argument set forth by hospice personnel for not hydrating terminally ill cancer patients is about the complexity and discomfort associated with the administration of intravenous fluids. Hospice personnel also highlight the patient's need for hospitalization and the time spent away from home. This argument may no longer be valid if hypodermoclysis, a safe and simple method of parenteral hydration, is adopted in

the home setting. Hypodermoclysis, by way of its simple technique, low cost, and feasibility in the home setting, is an attractive option for patients who can receive hydration, and it avoids the need for hospitalization. However, this method of fluid administration is dependent on the availability of the patient's family or caregivers who have to be willing or able to learn the skills required for this technique. In some instances, patients may have poor social support, making home clyses unfeasible. In such situations, in accordance with the patient's wishes, a decision for hospitalization or placement may be warranted.

WHAT ARE THE VIEWS OF THE PATIENT AND FAMILY?

Promoting early discussions with the patient and family about the goals of care and treatment choices, including the expected benefits and burdens, based on the best available evidence, of possible end-of-life interventions including hydration [41], is ethically appropriate, respects patient and family autonomy, and facilitates informed decision making. Such discussions should be conducted early, prior to treatment initiation, refusal, or withdrawal. Otherwise, impaired cognition, frequently found in terminal stages, would hinder effective communication among the patient, family, and healthcare provider, thereby compromising active patient participation in the therapeutic decision-making process. Emotional issues of family members, stemming from concerns of seeing their loved one suffering from starvation and dehydration, must be acknowledged and addressed. Watching for sudden changes in behavior and the appearance of distress without understanding the etiology is difficult on family and patient caregivers [38, 42].

These discussions should include simple explanations of commonly found symptoms associated with the dying process, including the frequency of delirium and its potential causes. Goals of care discussed should be reasonable, practical, and in accordance with the family wishes. These goals need to change as the patient's condition changes. To continue with a treatment that was appropriate at first but no longer has clinical meaning makes little clinical or ethical sense. Patients, families, friends, and caregivers should know that hydration can be ethically withheld and withdrawn.

Current practice of hydration decisions is largely influenced by physician attitudes towards hydration near the end of life based on anecdotal reports, small studies, and experience. In many circumstances, patients agree to what their doctor tells them to do. This fact is highlighted in a study from Canada where 100 patients from a palliative care unit, where hydration was routinely practiced, were compared with a group of 100 patients from another facility, where physicians and nurses did not provide regular hydration [1]. All patients in the first group agreed to receive hydration, whereas none of the patients in the second group did. Unfortunately, this type of practice may continue until there are results from randomized controlled trials addressing the impact of hydration or no hydration on symptoms and function in the terminally ill.

A study was recently presented at the 40th annual meeting pf the American Society of Clinical Oncology regarding this very issue [43]. Terminally ill cancer patients (n = 51) with clinical evidence of mild-to-moderate dehydration and a daily oral intake of less than 1,000 mL were randomized to receive parenteral hydration with 1,000 mL of normal saline (subcutaneously [SC] or intravenously [IV]) versus placebo (100 mL of normal saline SC or IV) over 4 hours on days 1 and 2. Patients were evaluated for target symptoms, including hallucinations, myoclonus, fatigue, sedation, and global well-being at baseline and on day 2 of the study using numerical scales ranging from 0 to 10.

Of the 49 patients who were evaluable, 27 patients randomized to receive parenteral hydration showed improvement in 73% of the evaluable target symptoms, versus 49% in the 22 patients who received placebo ($P = 0.005$). Improvement in myoclonus and sedation after hydration was noted in 83% of patients each, versus 47% and 33% in the placebo group, respectively. Patients assessed hydration as effective in 63% of cases and placebo effective in 41% of cases. Overall, investigators found hydration to be effective in 20 of 27 cases (74%) and placebo in 12 of 22 (54%) cases ($P = 0.15$). The investigators concluded that parenteral hydration improves symptoms in terminally ill cancer patients with decreased fluid intake, setting the stage for ongoing studies in this area with longer follow-up.

WHAT ARE THE INDIVIDUALIZED GOALS OF CARE?

Until more research is made available to guide decisions regarding hydration for cancer patients near the end of life, to have a blanket policy of hydration or no hydration would be unreason-

Table 3

Modalities of Re-hydration in Terminal Cancer Patients

MODALITY	ADMINISTRATION	COMMENTS
Subcutaneous	Continuous 24-hour infusion, overnight 12-hour infusion, or several 1-hour bolus clyses	First choice when oral intake is severely restricted
Intravenous	Via peripheral or central line	Recommended only if subcutaneous route is contraindicated or if intravenous line is clearly needed or present for another purpose
Enteral	Nasogastric tube (short-term use only) or gastrostomy	When present for nutrition and hydration in dysphagic patients with head and neck cancer
Proctoclysis	Given as intermittent infusions of tap water or normal saline	When other routes of hydration are not possible or are impractical

Dehydration

able. The current reluctance of hospice personnel to provide hydration could potentially translate into other policies under which all hospice patients are not likely to receive hydration in most instances. This reluctance has the potential to lead to withdrawal of care in other avenues or earlier in the trajectory of illness, depending on when the patient is referred to hospice. Conversely, instituting a "hospital" philosophy of hydrating all, with the potential problems of fluid overload and other complications, would be incorrect as well.

Rather than force one approach on the other, a more productive solution might be to consider a "middle road." Here, one may combine compassionate care philosophies of the hospice model with the traditional approach of the US hospital system without controversy. Such a consensus approach has a growing number of supporters, and given the wide spectrum of patients now treated by hospice and palliative care teams, a middle road between universal treatment and universal non-treatment will help foster the most effective decision making in regard to hydration [44, 45]. The contention is that until more results of better research on hydration for terminally ill cancer patients are available, the decision to administer fluids should remain highly individualized and based on a careful assessment of the clinical presentation, should consider the potential advantages of parenteral fluids, and should take into account the patient's and family's wishes [46–48].

Methods of Fluid Administration

If a decision is made to consider hydration by the healthcare team in accordance with the wishes of the patient or the patient's proxy, there are a number of modalities for fluid administration (Table 3).

INTRAVENOUS ROUTE

For the past five decades, artificial hydration has traditionally been given by the IV route and usually via a peripheral line. The peripheral IV route for hydration may be problematic for terminal cancer patients and poses a potential problem in the home-care setting. The disadvantages are listed in Table 4.

In some situations, fluids may be administered via central venous access devices (CVADs). These devices differ in several ways, including where and how they are inserted and how long they can stay in place. Non-tunneled CVADs, inserted via the subclavian or the jugular vein, are temporary lines and are usually left in place for days to weeks. In contrast, tunneled catheters are made of durable silicone and can be left in place for months or years. They are inserted through the subclavian vein; the other end is then tunneled under the skin and exits on the chest. Peripherally inserted central catheters (PICCs) are inserted through an antecubital or upper arm vein and then threaded up to the superior vena cava. They can remain in place for weeks to years. PICCs are ideal for chronically ill patients who need to receive long-term IV therapy and for patients who are active. An implanted vascular access port (VAP) is a central catheter attached to a reservoir and placed beneath the skin in the chest. VAPs are most often placed for cancer patients who require infrequent central access, such as once-a-month chemotherapy, for several months or years. When it is needed, the reservoir is accessed using a special non-coring needle.

Although vital to the administration of numerous lifesaving therapies, CVADs are associated with an increased risk of complications. The incidence of catheter-related infections is high. In a prospective study assessing 57 catheterization periods in 51 patients in a general intensive care unit [49], the frequency of local infections was 21% and for catheter-associated bacteremia, 8.7%. Occlusion is the most common non-infectious complication and has been found to occur in up to 36% of catheters [50].

Another prospective study [51] assessed the major complications related to catheter insertion in 1,303 central venous cannulations performed

in intensive care units or operating theaters. The incidence of arterial puncture was 5%; arrhythmia, 1.6%; cardiopulmonary arrest, 0.1%; pneumothorax, 0.5%; and incorrect location of the tip of the catheter, 11%.

For these reasons, in patients for whom there is an indication for parenteral hydration, the IV route should be limited to situations where SC administration of fluids is contraindicated. These situations include patients who have generalized edema, major coagulation disorders, or an IV line or CVAD in place for other purposes.

ENTERAL ROUTE

The enteral route for nutrition is indicated in any malnourished patient with a functional GI tract who is unable to ingest sufficient nutrients orally as long as enteral access can be achieved safely. The route is preferred over parenteral nutrition because it is simpler, safer, more physiologic, and less costly. Common indications for enteral nutrition include dysphagia due to head and neck cancer, esophageal obstruction, gastric outlet obstruction, or critical illness requiring prolonged mechanical ventilation. Home enteral nutrition allows many patients to receive outpatient treatment. The outcome of these patients is dependent on the underlying cancer.

The choice of enteral access device is based on anticipated duration of use, the underlying pathophysiology and anatomy, patient preference, and local expertise. Tubes may be placed through the nose or percutaneously, and the tips terminate in the stomach or small intestine. Nasogastric tubes are best suited when the anticipated duration of enteral support is less than 30 days [52]. Placement of a percutaneous feeding tube is indicated in patients who will require enteral nutrition for more than 4 weeks. Surgical, radiologic, and endoscopic methods of placement have been developed and used successfully. The percutaneous gastrostomy tube (PEG) is usually preferred and allows the use of hypertonic nutrient formulas and bolus infusions. Jejunal feeding is indicated in the presence of gastric outlet obstruction, gastroparesis, proximal fistula or leak, or suspicion of aspiration of gastric contents. Direct delivery of nutrients into the jejunum is accomplished via either a tube passed from the PEG through the pylorus or one passed directly through the skin into the jejunum. Bolus feedings are contraindicated with jejunostomy. However, infusion rates as high as 180 mL/hr have been safely tolerated.

Table 4

Disadvantages of Intravenous Route for Hydration in Terminal Cancer Patients

Pain associated with needle insertion
Need for frequent site changes
Difficulty in finding venous access
Need for immobilization of arm
Impediments to mobility
Risk of increasing agitation and accidental catheter removal in patients with delirium
Need for hospitalization
High cost
Need for specific training in surveillance and care
Complications such as thrombophlebitis and infections

HYPODERMOCLYSIS

Although hypodermoclysis was initially used to describe the infusion of fluids into the SC space, it also comprises the delivery of medications. This method of parenteral fluid administration was widely accepted in clinical practice until the 1940s and 1950s [53, 54], but it subsequently fell out of favor due to several reports of adverse reactions and was replaced by IV fluid therapy. Most of the adverse reactions were related to the misuse of electrolyte-free or hypertonic solutions [55, 56]. Recently, there has been a renewed interest in this method as an alternative to the IV route, with several studies and clinical experience in the past two decades demonstrating its safety and practical advantages over the IV route [46, 57–61]. Initial research was focused on elderly patients, but subsequent studies on terminally ill cancer patients have helped establish the safety, efficacy, and tolerability of hypodermoclysis in this patient group [46, 62, 63].

Although hypodermoclysis is suitable for fluid administration in a variety of clinical settings (hospital or home), its current use is primarily restricted to the geriatric or palliative care setting, where parenteral fluid administration is often considered for providing hydration or comfort for ill-defined or indefinite periods. Despite the advantages of hypodermoclysis over IV access (Table 5), current practices in the United States and worldwide have not adopted its widespread use, and most physi-

Table 5

Advantages and Disadvantages of Hypodermoclysis

Advantages
Low cost
Minimal training required for initiation or maintenance of site and infusion
Less need for supervision
Ability to maintain site for 5–7 days
Less distressful needle insertion; more comfortable than intravenous access
Ideal for home use or long-term care facilities, avoiding the need for hospitalization
No thrombophlebitis, a lower incidence of local adverse reactions than with intravenous access
Preferable in agitated patients, with a lower incidence of agitation and need for restraints and reinsertions of access site compared with intravenous route
Disadvantages
Unsuitable for large-volume rapid infusion needs; maximum administration of 3 L in 24 hours when two subcutaneous sites are used simultaneously
Possible edema and local skin reactions at infusion site
Risk of bleeding prevents use for patients who have clotting disorders
Lack of education regarding subcutaneous route among US nurses and physicians

cians and nurses are unfamiliar with its safety and administration technique. Some of the arguments against hydration for terminally ill patients are made in reference to IV fluid therapy and, therefore, may not be applicable when hydration is considered via the SC route. Frequently, patients in acute care settings receive invasive lines, such as those placed in the subclavian or jugular veins, when IV access is found to be difficult. Except in emergency situations, use of hypodermoclysis can obviate the need for these risky procedures.

In addition, studies have also suggested that hypodermoclysis may be the preferred route in delirious patients, where the presence of IV access has been associated with increased agitation and need for restraints.

Procedure. Hypodermoclysis involves a simple and minimally distressful procedure of inserting a butterfly needle SC and attaching a line for fluids to be administered via an infusion pump or gravity in the home setting [64]. In ambulatory patients, the abdomen, upper chest, and area above the breast may be used as the SC infusion site. In bedridden patients, preferred sites are the thighs, abdomen, and outer aspects of the upper arm [65, 66]. The same SC site can be used for approximately 5–7 days.

In a prospective study conducted at a palliative care unit, the mean duration of a subcutaneous site for the administration of narcotics was 7 days [67]. In one of the studies, the most common reasons cited for site change included poor absorption (47%), inflammation (37%), and bleeding or bruising (11%) [46]. In another study [68], the duration of a SC site was significantly longer ($P = 0.0009$) with the use of a Teflon cannula at 11.9 ± 1.7 days, versus 5.3 ± 0.5 days for a butterfly needle. Patients' comfort level and acceptance were similar with both types of needles. The cost of Teflon needles is significantly more than butterfly needles, so Teflon needles may be limited to patients who have problems maintaining SC sites.

Volume and rate of infusion. As mentioned previously, terminally ill cancer patients in most situations have lower fluid needs than healthy adults. There are several reports of terminal cancer patients suffering from respiratory distress due to pulmonary edema while receiving parenteral fluids; these patients received exceeding high volumes of fluids relative to their diminished needs [6]. Keeping the lower fluid needs in mind and identifying those with a history of congestive heart failure would avoid situations of fluid overload in these patients.

In most circumstances, approximately 1 L of fluid is sufficient for a 24-hour period and allows for normal urine output and adequate clinical hydration. In the home setting, fluids can be administered by gravity at a rate of 1–2 mL per minute at one site, allowing 1.5 L to be delivered in a 24-hour period. If the fluid requirement is higher, up to 3 L can be administered in 24 hours by using two separate sites simultaneously. In most situations, when fluids have been replaced and the goal is maintenance therapy, the patient can receive overnight infusions or several 1-hour boluses, which will allow for mobility and freedom from tubings for the remaining periods of the day (Table 6) [69].

Types of fluids. Commonly administered electrolyte fluid solutions via the IV route, such as normal (0.9%) and 0.5N (0.45%) saline, saline-dextrose combinations such as one-third saline with two-thirds glucose (5%), or 5% glucose with normal or 0.5N saline have been used in studies involving hypodermoclysis and can be safely administered SC [57, 60, 61, 67]. In addition,

salt-free solutions, such as 5% dextrose, have also been found to be safe for administration [61]. Use of other non-electrolyte solutions is not recommended for hypodermoclysis.

As mentioned previously, many of the complications related to hypodermoclysis prior to the 1950s were due to the use of non-electrolyte solutions. There is evidence that non-electrolyte solutions draw fluid into interstitial spaces and thereby form a "third space." These solutions can also cause the sloughing of tissue, mostly in pediatric patients. Rapid or large-volume SC infusions of electrolyte-free solutions can cause circulatory collapse [56, 70]. Since pure water loss is extremely rare, the rationale of such therapy is not justifiable [1]. Colloidal and hyperosmolar solutions should not be given via the SC route. There is evidence that potassium chloride, 20–40 mmol/L, can be safely added to fluids administered via this route [55, 57, 71, 72]. Potassium chloride may be considered for patients with symptomatic hypokalemia or who have conditions in which potassium loss can be anticipated, such as vomiting, diarrhea, or fistulas, and who cannot be supplemented by the oral route.

The decision must always be based on a careful evaluation of the risks and benefits for the individual patient and must be regularly reassessed [63]. Although there are reports of adding opioids to the fluid bag in patients who received 24-hour hydration [73], in most cases separating hydration from medications allows for better treatment flexibility and increased mobility. The patient can receive overnight or 1-hour bolus clysis, thereby avoiding the need to carry a bag continuously, and medications can be given via a light, portable pump [61].

Adverse effects. The risks of hypodermoclysis are minimal when administered in conformity with accepted indications and guidelines. Adverse effects in several studies have been found to be infrequent and are easily avoided. In a study of 270 patients receiving hypodermoclysis, local edema was the only noted complication and was found in just 4 patients (1.5%). The local and systemic adverse effects of hypodermoclysis are summarized in Table 7.

Contraindications. There are few contraindications to hypodermoclysis. Patients with generalized edema or clotting disorders should not be given hypodermoclysis. Similar to the use of IV access, caution should be maintained when administering fluid to patients at increased risk of pulmonary edema, such as those with known congestive heart failure, to prevent respiratory distress from fluid overload. Hypodermoclysis should not be used in emergency situations, such as managing patients with circulatory collapse or major electrolyte imbalances, where a large volume of fluids and electrolytes needs to be replaced rapidly.

Table 6

Methods of Fluid Administration in Hypodermoclysis

TYPE OF INFUSION	RATE	COMMENTS
Continuous 24-hour infusion	40–60 mL/h	• Limits mobility since patient has to be connected to the line and bag • Two sites can be used simultaneously • No more than 3 L should be administered in 24 hours
Overnight infusion	80 mL/h	• More convenient for patients and caregivers, with patient not being hooked up to tubing during daytime hours
One-hour bolus infusions	500 mL given 2 or 3 times a day	• Well tolerated and ideal for active patients • If local, repeated edema is noted,150 U of hyaluronidase may be given prior to the first infusion

Dalal Bruera

PROCTOCLYSIS

Proctoclysis refers to the rectal administration of fluids. This method is an alternative for patients who require hydration but are unable to receive it by another route, such as parenterally or enterally, because of contraindications or lack of necessary technical resources. Although there have been some earlier reports of its use in the literature [74, 75], hydration via the rectal route has several advantages (Table 3) and has only recently been recognized as a suitable option for use in terminal cancer patients.

In a prospective, open, multicenter study [76], 78 terminally ill, dehydrated adult patients who were unable to receive hypodermoclysis underwent proctoclysis. The procedure involved the insertion of a 22 French nasogastric catheter about 40 cm into the rectum. Fluids were administered as saline or tap water at rates of 250 ± 63 mL/h for 15 ± 8 days. Hydration via this route was continued at home until death in 60 patients, whereas 4 patients discontinued therapy secondary to pain. Hydration was discontinued in the remaining patients secondary to return to oral hydration (n = 6) or a decision to discontinue hydration (n = 8). The main adverse reactions were an enema effect seen with maximal rates of infusion (n = 9), leakage of fluids (n = 4), pain during infusion

Table 7

Local and Systemic Adverse Effects of Hypodermoclysis

Local edema	• Most common • Minimized or resolved with massage • Occasionally, hyaluronidase is required to increase absorption
Local catheter-related reactions	• Less common than with intravenous routes
Pain or discomfort at infusion site	• Less common than with intravenous routes • Minimize with reduced rate of infusion
Inadvertent puncture of blood vessels	• If blood returns in the needle, withdraw and re-insert at another site
Side effects of hyaluronidase (local edema, local erythema, local itching, chills, nausea, dizziness, tachycardia, hypotension)	• Rare • Routine infusions do not require hyaluronidase • Reserve for use if rapid, large infusions are needed and patient is experiencing pain and/or swelling at local sites

Dehydration

(n = 6), and pain during insertion of the catheter (n = 5). Patients reported their discomfort after each proctoclysis on a visual analog scale ranging from 0 (no discomfort) to 100 (worst possible discomfort); the mean level of reported discomfort was 19 ± 14.

The tolerance of proctoclysis is probably better in patients who have previously received frequent enemas and suppositories. The results of this study suggest that proctoclysis may be a suitable alternative in the home setting for hydrating terminally ill patients who do not have tumor involvement of the colon and who are unable to tolerate hypodermoclysis secondary to generalized edema.

Procedure and preparation. The procedure is simple and may be performed by the patient's family or caregiver at the bedside. In most situations, the caregiver may already be responsible for a bathing and bowel routine with administration of enemas or rectal suppositories to the patient. For proctoclysis, a 22 French nasogastric catheter is inserted into the rectum to a depth of about 40 cm, and normal saline or tap water is infused. The catheter does not have to be sterilized. Fluids are administered intermittently, over 4 hours or less, either daily or several times a week. If there is leakage or an enema effect, the rate of infusion should be decreased.

The advantages of proctoclysis, including low cost, ease of administration, no need for sterilization of fluids or equipment (tubing), and the fact that it does not have to be implemented by healthcare workers, make it a valuable option for both medical facilities and patients in developing countries or rural areas where access to expensive equipment, sterilization methods, and healthcare workers may be restricted.

Conclusion

Decreased oral intake is a frequent complication of advanced cancer. In recent years, there has been a strong debate concerning the consequences of dehydration, with a number of arguments for and against artificial hydration. Common symptoms experienced with dehydration, such as cognitive impairment, fatigue, delirium, fainting, syncope, dry mouth, nausea, and constipation, are often difficult to interpret because similar symptoms may be caused by the malignancy itself, its treatment, or the presence of infection. Many studies, however, have found a relationship between the presence of delirium and opioid-induced toxicity with the patient's hydration status. Hydration has been shown to reverse these symptoms in many circumstances.

The maintenance of fluid balance in terminally ill cancer patients, many of whom are elderly, is complex, confounded by unknown variables secondary to the disease process itself and in part related to physiological changes associated with aging. For a variety of reasons, these patients achieve hydration with much lower volumes than recommended for the average medical or surgical patient, due to decreased body weight with a resultant decrease in absolute water requirements, decreased free water clearance due to release of ADH related to chronic nausea and/or use of opioids, and decreased insensible losses from decreased physical activity. The decision to hydrate these patients should be personalized, based on careful assessment of the problems or symptoms related to dehydration, the potential risks and benefits of fluid administration, and the wishes of the patient and his or her family. In cases of doubt, a short trial of hydration may be appropriate. If a decision is made to hydrate the patient, there are several options from which to choose. The SC route (hypodermoclysis) is an excellent alternative due to it simplicity, low cost, and feasibility in the home setting.

Peer viewpoints on this article by Drs. Pedro E. Huertas, J. Andrew Billings, and Robin L. Fainsinger appear on pages 483 and 485.

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PEER VIEWPOINT

Dalal
Bruera

To Hydrate or Not to Hydrate: Is That the Real Question?

Commentary by Pedro E. Huertas, MD, PhD, and J. Andrew Billings, MD

Alleviating discomfort and suffering has been the primary goal of palliative care from the inception of the hospice movement. The value of hydration, especially in the last weeks of life, has an ambiguous status in attaining these goals. The appropriate role of volume repletion in the terminally ill patient is a relatively "data free zone," but we are faced in the United States with entrenched habits of providing parenteral fluids for all hospitalized patients; societal notions that everyone should carry around a bottle of water to avoid dehydration; and a host of ideological, financial, religious, ethical, and biomedical concepts that underpin strongly held positions.

Dalal and Bruera review basic elements of fluid and electrolyte homeostasis in normal humans and terminally ill cancer patients and discuss the role of dehydration and re-hydration in alleviating and/or prompting disagreeable symptoms. They also present various means of fluid supplementation, recognizing that all of these methods have advantages and disadvantages and must be tailored to each patient and to specific circumstances. We especially appreciate their exposition on subcutaneous fluid replacement, a neglected technology appropriate to both home and institutional settings.

Does hydration of the terminally ill patient alleviate or cause discomfort and suffering? Studies, primarily of normal volunteers, have demonstrated an array of distressing and probably self-perpetuating problems from dehydration, including distinctive syndromes of hyponatremic and hypernatremic dehydration [1, 2]. These observations are loosely understood but widely applied in clinical medicine, so that dehydration is commonly cited as a cause of symptoms and an indication for treatment. A glance at the orders in our outpatient chemotherapy infusion unit reveals significant numbers of patients who are receiving hydration to help with fatigue, weakness, and other vague symptoms.

Hospice pioneers observed that dying patients did not seem bothered by dehydration, except for experiencing a dry mouth that could be alleviated with good oral care. Their conclusion, which flew in the face of established practices, has been widely accepted in the hospice movement. However, systematic study of the role of hydration or lack thereof in terminally ill patients has proven difficult. Hospice researchers, as well as other investigators, have been reluctant to subject dying patients to uncomfortable interventions that provide no clear and immediate benefit

PEER VIEWPOINT

but are necessary for understanding the effects of various states of hydration. Moreover, patients in the final phase of life may be difficult to study because of their rapidly changing medical conditions, brief and perhaps unpredictable survival, and depressed levels of consciousness [3].

Withholding of hydration, of course, also commonly raises personal, cultural, religious, and ethical concerns, as well as medical issues. The only somewhat convincing research on the topic, a naturalistic observation study by McCann et al [4], seemed to confirm the initial hospice observations that dehydration in terminal patients is well tolerated.

Discussions in the hospice literature, however, often contrast the ills of overhydration with the benign or beneficial effects of dehydration. These discussions rarely, if ever, compare dehydration or overhydration with a normal fluid status or address the differences among hyper-, hypo-, and normonatremic dehydration.

As reflected in the current paper, Dalal and Bruera have pointed out the extremely high frequency of symptoms near the end of life that might be attributed to dehydration, as well as various alternate explanations for some of these symptoms. Striving to make sense of imperfect information, they have suggested that limited re-hydration (not including well-accepted indications for hydration, such as for hypercalcemia or tumor lysis syndrome) promotes well-being in terminally ill patients, and they have hypothesized that the benefits reflect improved renal metabolism of toxic substances, including opioids and their metabolites. The authors have singled out, in particular, cognitive status as a dimension that may improve with hydration. The evidence for this viewpoint remains unconvincing, though the hypothesis is attractive and reasonable. More rigorous experimental support for their viewpoint would be welcome, presumably utilizing defined and relatively homogeneous populations with a particular pathological fluid status.

Designing controlled studies raises several issues:

- Ethical conflicts arise when provoking and/or maintaining specific physiological states (eg, hyponatremia in severely ill patients whose outcome, death, is known and anticipated) [5]. The clinical principle of equipoise—indifference to a particular course of action because we cannot clinically tell apart the effect of two or more interventions—may not be readily maintained in these situations. We must wonder what constitutes informed consent under these circumstances, and the potential to cause suffering must be assessed carefully.
- Study populations should be defined prospectively, which requires separating out subpopulations for whom re-hydration may have different consequences than anticipated for the "average" cancer patient (eg, patients with congestive heart failure or ascites or with renal failure not due to dehydration; patients not receiving opioids or other medications whose metabolism is likely to be influenced by fluid status; hypernatremic versus hyponatremic dehydration).
- Reliable assessment of fluid and electrolyte status in terminally ill patients may necessitate the use of uncomfortable or cumbersome methods that can be impractical outside the research setting. A successful research program might initially require the use of relatively complex methodologies but ideally can lead to practical clinical techniques, such as physical examination and urinalysis.
- The effect of mild-to-moderate dehydration and/or simple renal failure on the metabolism of the drugs commonly used in palliative care (particularly opioids) could be studied in a variety of populations, not just terminally ill patients. The symptoms that develop with a particular dosage regimen and renal clearance have not been well documented and might be useful in hypothesizing how dehydration affects terminally ill patients who use these drugs.
- Implicit in the above discussion is the need to assess the role of electrolyte status, and not just water imbalance, in terminally ill patients. Just as the dichotomy between dehydration and overhydration is an oversimplification and not the relevant clinical issue for our patients, appropriate therapy for total body fluid loss (or gain) may not involve simply providing (or restricting) fluid but also considering salt replacement or restriction.
- Finally, how do we assess symptoms? Patients may not be able to complete questionnaires, and our clinical evaluation may not be sufficiently sensitive or specific. Regardless of our sophistication in assessing biochemical and physiological markers, the role of sodium, antidiuretic hormone, mineralocorticoids, and total body water is poorly understood in relationship to the perception of thirst. We must develop and use valid measures of symptom improvement.

In the absence of new evidence, we agree with Dalal and Bruera in not advocating a blan-

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ket policy of hydration or no hydration and, of course, to use gentle re-hydration rather than fluid overload. For most terminal patients, we prefer to "do no harm," which means not prescribing fluid replacement without clear indications. The debate in the literature, which seems to reflect ideology or unconvincing suppositions, would best be supplanted with well-done studies.

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Commentary by Robin L. Fainsinger, MBChB, LMCC, CCFP

The comprehensive review by Dalal and Bruera on dehydration in cancer patients provides an excellent overview of the many facets of this often complicated and controversial clinical situation. However, there are some aspects that are worthy of further emphasis, clarification, and discussion.

The current divergent opinions are well illustrated by the following quotes from recent reports:

"Research is limited but suggests that artificial hydration in imminently dying patients influences neither survival nor symptom control. [1]"

"The best available evidence suggests that hydration of advanced cancer patients plays an important role in maintaining cognitive function and is therefore an important factor in the prevention and reversal of delirium in this population. [2]"

Superimposed on these conflicting medical comments are the other complex issues, illustrated by this comment: "Terminal dehydration is a controversial topic, weighted heavily with historic symbolism, and strong religious, societal, and cultural conflicts. [3]"

Some clarity and perspective are brought to this issue by focusing on the three dimensions of research on the use of hydration in palliative care settings [4], namely the association between biochemical findings and hydration status; between biochemical findings and clinical symptoms; and between hydration status and clinical symptoms. Two systematic reviews found it impossible to draw firm conclusions about hydration, given the limitations of available research [5, 6].

Although the terms fluid deficit, hypovolemia, volume depletion, and dehydration have been reasonably well defined in past literature, dehydration is often used incorrectly to include all of this terminology [7]. Dehydration has been defined as total body water deficit with associated hypernatremia. Given the extensive discussion in the report by Dalal and Bruera with regard to hyponatremia, one can conclude that we are discussing clinical issues of overlap with volume depletion and dehydration.

An often misunderstood issue is that we are not all seeing patients in the same trajectory of their illness. Clinical circumstances evolve [8]; a physically independent and cognitively intact patient at an early stage of a palliative illness is likely to be viewed very differently from the same patient a number of months later, who is now cognitively impaired and physically dependent. As a result, the first two authors quoted in this commentary [1, 2] likely had different patient populations in mind when they referred to "advanced cancer patients" and "imminently dying patients."

Physicians and nurses continue to have divergent attitudes toward the provision of parenteral hydration. A report on the attitudes of 584

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Japanese physicians demonstrated that 50%–60% would provide intravenous hydration to patients with a survival measured in weeks [9]. On the other hand, 307 hospice nurses in Oregon responded to a questionnaire indicating that the majority felt that patients who voluntarily choose to refuse fluids usually die a "good" death within 2 weeks [10]. A recent Canadian survey demonstrated the wide range of opinion and practice within one country, with physicians estimating that they ordered parenteral hydration in a median of 6%–10% of patients (range, 0%–100%) [11]. The majority of physicians indicated that they used hypodermoclysis (median = 70%), with the average volume ranging from 200 to 2,400 mL.

Two reports in England and Canada also found divergent results when looking at the current use of parenteral hydration in patients dying in institutional care facilities. Soden et al [1] reported results on 111 patients dying in a general hospital. They found that 65% were hydrated during the last week of life, and only 46% were being hydrated at the time of death. The authors concluded that artificial hydration no longer appears to be routine hospital practice for dying patients in that institution.

Lanuke et al [12] conducted a retrospective chart review of 50 consecutive patients dying in a palliative care unit and in acute wards at a hospital, both while receiving and not receiving consult advice from the palliative care service. The authors found that the majority of patients at all sites received hydration, although the volume of hydration in the palliative care unit was significantly lower. In addition, all of the patients in the palliative care unit received hydration by hypodermoclysis, whereas the majority of the patients in the acute care setting received intravenous hydration.

A report from an Italian palliative care program [13] stated that 82% of palliative care patients will have an intravenous line and receive a range of 1.0–1.5 L of fluid per day. In addition, the authors stated that although hypodermoclysis is often suggested, it has not been demonstrated to be less stressful for palliative care patients and that, in their experience, the patients and relatives preferred the intravenous route.

The reference to an unpublished randomized control trial of parenteral hydration is intriguing [14]. The clinical and practical problems of doing research in palliative care have been well described [15, 16]. Many difficulties come to mind when speculating on how a randomized, double-blind controlled study that meets all of the modern-day ethical constraints could be applied to aspects of the parenteral hydration debate.

One can assume that the information presented to patients and families remains open to both individual literature interpretation and the biases of the healthcare professionals involved. We could perhaps agree that dehydration is a cause of renal failure, and hypodermoclysis is a safe and effective way of providing parenteral hydration. There are also sufficient reports with similar conclusions to recommend that if terminally ill patients are not hydrated, medications such as opioids should be gradually decreased to avoid accumulation and unnecessary side effects. We can also agree that there are inadequate data for final conclusions [17], and individual assessment of the relevance of dehydration to each clinical situation is central. Finally, despite a plethora of research, we still have to define the questions, outcomes, measurement tools, and research populations as we discuss the many possible ways we can move forward in research in this challenging area.

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