The effect of intravenous fluid infusion on blood and urine parameters of hydration and on state of consciousness in terminal cancer patients

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Abstract

The purpose of the present study was to assess retrospectively the state of hydration of terminal cancer patients in the last 48 hours of their lives, with or without IV fluid infusion and to correlate parameters of hydration with the state of consciousness (SOC). We studied the parameters of hydration in plasma and urine of 68 consecutive patients 48 hours or less before death. Thirteen patients were treated by IV fluids. We found a state of dehydration in all investigated patients as reflected by biochemical parameters. Patients with IV fluids were not better hydrated and did not show better SOC. SOC correlated significantly with plasma sodium ($p < 0.001$) and urine osmolality ($p < 0.02$). In light of the present findings, the decision-making process regarding treatment with IV fluids should be guided by the preferences of the dying patient and his family.

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Introduction

IV fluids are widely administered to terminal cancer patients in general medical wards and this is considered routine treatment. The arguments pro and con have already been mentioned in the literature,[1-3] but very little is known about these patients' actual state of hydration immediately prior to death.[4-5] This is due, in part, to ethical limitations associated with conducting clinical trials on such populations. More-

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Table 1. Biochemical blood parameters in the study population						
Parameter	**Normal values**			**Patients**		
Urea (mg%)	30.0	±	15.0	142.0	±	88.0
Creatinine (mg%)	1.05	±	0.35	2.3	±	1.5
NA+ (mEq/L)	142.0	±	6.0	141.0	±	8.6
Uric acid (mg%)	6.2	±	2.2	12.0	±	5.5
Osmolality (mOsm/kg)	300.0	±	20.0	314.0	±	26.8

over, the hospice movement favors restraint in the use of invasive treatments on terminal cancer patients and has reservations about the widespread use of intravenous fluids in these patients. Oliver's report[4] on terminal dehydration concluded that in patients venopunctured near to death, the electrolytes' balance and state of hydration were essentially normal or only moderately impaired, without the use

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of intravenous fluids. However, the study was based on a small number of cases and did not cover either the various parameters of hydration or the correlation with the SOC.

We previously presented some of our experiences on this issue in a letter to *The Lancet*[6] and concluded that most of the patients do present severe dehydration and electrolyte imbalance, including those with IV fluids. We, herein, present details of our study, concerning a relatively large number of terminal cancer patients, in which we tried to answer the following questions:

- Were these patients dehydrated when close to death?
- Is there any impact of IV fluids on their parameters of hydration and level of consciousness?

Patients and methods

The study population comprised consecutive patients admitted for palliative care. The majority were referred from nearby hospitals and others by their general practitioners. Since we were interested in near-to-death state of hydration, we examined the blood and urine collected only 48 hours or less before death. A complete CBC and a 12-channel SMA were performed, and urine samples were tested for osmolality and electrolytes. At time of venopuncture, patients were assessed for their SOC according to a local alertness scale:

- Patient fully conscious.
- Patient responsive to visual or vocal stimuli.
- Patient responsive to painful stimuli.

Table 2. Effect of infusion on blood and urine parameters.

	Urea (mg%)	NA+ (mEq/L)	Osmolality (mOsm/kg)	Urine (mOsm/kg) ratio	Urine/ plasma osmolality	BUN Creatinine, ratio
Without infusion						
Mean ± SD	140.6 ± 84.4	139.0 ± 7.3	310.0 ± 24.0	470.5 ± 141.0	1.53 ± 0.5	33.5 ± 14.0
N	55	54	50	32	32	55
With infusion						
Mean ± SD	150.5 ± 105.0	148.5 ± 10.0	330.7 ± 31.0	520.0 ± 117.0	1.6 ± 0.34	33.0 ± 13.4
N	13	13	13	11	11	13
(t-test)	NS	0.01	0.02	NS	NS	NS

Table 3. The interaction between state of consciousness and blood and urine parameters.

	Urea (mg%)	NA+* (mEq/L)	Serum** Osmolality (mOsm/kg)	Urine Osmolality (mOsm/kg)
1. Fully conscious				
Mean ± SD	129.3 ± 90.0	136.0 ± 8.5	301.3 ± 25.0	410.0 ± 141.0
N	12	12	12	7
2. Responsive to stimuli				
Mean ± SD	330.7 ± 31.0	520.0 ± 117.0	1.6 ± 0.34	33.0 ± 13.4
3. Responsive to painful stimuli				
Mean ± SD	113.0 ± 53.0	141.4 ± 8.7	312.5 ± 24.0	508.4 ± 147.60
N	28	28	26	1
4. Coma				
Mean ± SD	188.0 ± 119.0	143.0 ± 7.0	336.6 ± 32.6	540.0 ± 127.0
N	12	11	10	8

* Pearson correlation ($p < 0.001$)
** Pearson correlation ($p < 0.02$)

- Patient completely unconscious, and the metabolic parameters correlated to SOC.

We isolated a subgroup of patients who were treated by IV fluids and compared their data to those not infused. Though our policy is to avoid unnecessary intravenous fluids, we had patients with IV fluids due to requests of family members and to the fact that many were transferred to us from other wards with infusions. Total IV fluid administered ranged between one to two litres daily, and was intended to maintain a reasonable fluid intake rather than to correct biochemical parameters. Statistical analysis of data was performed by using the Systat package.

Results

A total of 68 patients was selected for the purpose of the study, of whom 55 patients were hydrated orally, and 13 had received IV fluids. The results of the main biochemical parameters are presented in Table 1. Mean values for urea, creatinine, uric acid, and osmolality were elevated. Mean sodium levels were within normal ranges. The increased urea/creatinine ratio (> 30) indicated

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that a pre-renal azotemia occurred, as does the increased urine/plasma osmolality ration (> 1.2). Considering a serum urea level of 72 mg/dl or more as indicating significant dehydration, we found 59 patients to be dehydrated (mean 141.6 ± 27.6 mg/dl). Only nine patients had lower urea levels (mean 52.8 mg/dl). Urea levels in those with or without IV fluids were not significantly different when tested by two tail t tests (305.4 ± 183 vs 327 ± 228.6 mg/dl). However, serum sodium level showed significant difference between the groups ($p < 0.02$, 139 ± 7.3 vs 148.5 ± 10 mEq/L). Potassium levels were found to be higher than 5.5 mEq/L in 31/68 patients (mean 7.25 ± 1.67 mEq/L).

The possible effects of infusion on blood and urine parameters are shown in Table 2. It is evident that patients with IV fluids did not show better biochemical parameters. On the contrary, these patients had significantly abnormal values of sodium and serum osmolality.

A significant correlation was found between state of consciousness and serum sodium levels ($p < 0.001$), and also with urine osmolality ($p < 0.001$), but not with potassium levels (not shown). There was also a trend of correlation with plasma osmolality ($p < 0.02$) (see Table 3). Moreover, SOC did not correlate with the use or non-use of

Table 4. The interaction between IV infusion and consciousness.

Consciousness*	1 (%)	2 (%)	3 (%)	4 (%)
No infusion	18.2	27.3	38.2	16.4
Infusion	15.4	7.7	53.8	23.1

* 1 = Fully conscious
2 = Responsive to stimuli
3 = Responsive to painful stimuli
4 = Coma

No significant difference between the groups
Pearson Chi-Square = 2.65, p = 0.448

IV fluids ($p = 0.448$) (see Table 4).

Discussion

The results of the present study are important regarding the following points:

- We found a state of dehydration in 59/68 of the patients, as reflected by blood and urine parameters.
- Those treated with IV fluids did not have better biochemical parameters when close to death, though overall, they were as seriously ill as those non-infused.
- The state of consciousness did correlate significantly with serum sodium and urine osmolality.
- Patients treated by IV fluids did not show a better state of consciousness than those not treated.

The clinical implications of these results further support the view that IV fluids are medically unnecessary in terminal cancer patients, and perhaps even worsen the condition of these patients with multi-organ failure, since direct challenge of fluids might precipitate terminal pulmonary congestion and promote death. Many hospice physicians feel that avoiding intravenous fluids infusion may suppress alertness of patients, increase pain threshold by increasing the sensorial clouding of terminal uremia, thereby diminishing the awareness of tragic circumstances which the patient and his family experience. However, this is not support by our results which show no correlation of IV fluids to SOC. On the other hand, the present results indirectly support and explain in part, the observation that there is no difference in survival of terminal cancer patients whether they stay in a hospice facility or in a general medical ward,[7] where it is routine policy to administer IV fluid.

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The present article may be criticized with regard to the lack of randomization between the two groups, but perhaps in this situation, this is not possible. Also, the small population of patients precludes meaningful subdivision of the various variables. One would, therefore, wonder whether rather than consider IV fluids' effect on the blood and urine parameters, it would be appropriate as well to interpret results on the decision to administer fluids being influenced by the state of the patients.

Despite these difficulties, we believe that in advanced cancer patients there is no place for IV fluids. This may create problems both for the family, for whom intravenous fluid infusion is interpreted as the continuation of the medical care, and the physician for whom it symbolizes the realization of the commitment to continue medical care until the patient's death.

In light of the present data showing the inefficiency of MIFI, we suggest that the decision making process regarding MIFI treatment should be guided only by the preference of the dying patient and his family.

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