Original Paper

Acta Haematol

Acta Haematol 2003;109:163–168
DOI: 10.1159/000070964

Received: June 28, 2002
Accepted after revision: November 21, 2002

Monitoring Hyperhydration during High-Dose Chemotherapy: Body Weight or Fluid Balance?

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Key Words

Hyperhydration · Nephrotoxicity · Congestive heart failure · Fluid balance · Fluid overload · Body weight · Chemotherapy protocols · Nursing protocols

Abstract

Body weight and fluid input/output are usually monitored for checking fluid balance in case of intravenous hyperhydration during nephrotoxic chemotherapy. The reliability of measuring fluid input/output is uncertain. Moreover, this measurement is redundant, complex, labour-intensive and represents an occupational hazard for nurses and other health-care workers handling fluids or body excreta. In a prospective cohort study, we determined the concordance between body weight and fluid intake/output. We also examined the clinical consequences with respect to the safety of selecting only body weight measurement as a parameter for fluid overload. A total of 591 combined observations of fluid balances and body weights were collected. We observed a higher increase in body weight than in fluid balance. The Pearson correlation between fluid balance and body weight was relatively low (r = 0.28). With regard to the safety of measuring body weight only, we found 4 cases (0.6%) who might not have received furosemide if the fluid input/output had not been measured, without clinical consequences, however. After standardization, body weight can safely be used as the only parameter for monitoring fluid retention in case of hyperhydration during chemotherapy.

Introduction

Registration of both body weight and fluid input/output in order to prevent fluid overload during intravenous hyperhydration in the course of high-dose chemotherapy seems to be a 'ritual' act. There is no scientific basis for it and no effectiveness rationale.

Hyperhydration with large amounts of fluid like saline is mainly used in nephrotoxic cytostatic treatments with e.g. cisplatin and methotrexate which cause immediate damage to the proximal and distal tubular cells of the kidneys [1, 2]. Cyclophosphamide and ifosfamide may cause haemorrhagic cystitis [3]. This nephrotoxicity and bladder damage can be prevented by forced diuresis with 4–5 litres of saline administered intravenously every 24 h in order to achieve a minimal diuresis of 100 ml/h [4–7]. Even in patients with a normal cardiac and renal function, accumulation of water and salt in the interstitial fluid compartment will occur with hyperhydration. Because of the risk of fluid overload and pulmonary oedema, it is clear that careful monitoring of the fluid balance is necessary.

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In oncology it is customary to register fluid input/output as well as body weight simultaneously in order to monitor fluid balance. These controls preferably take place several times within each 24-hour period in order to be able to timely observe unwanted changes in fluid balance and to be able to intervene, if necessary. Fluid input/output and body weight are registered cumulatively during the entire period of hyperhydration. Above a certain cut-off value a diuretic as furosemide is administered.

There are several objections to this labour-intensive registration. First, it is very likely that these cut-off values are based on experience and opinion since there is no evidence in the literature to support them. Secondly, it is not clear how (possibly) divergent fluid balance and body weight values should be interpreted. Thirdly, the validity of the measurements is also under discussion: there are different views with regard to the registration of fluid input/output [8]. It is not clear, for instance, whether and how the intake of soup, fruit, ice cubes, or the occurrence of diarrhoea and vomiting should be registered. Finally, there are doubts about the reliability: measurements of fluid input/output are not always performed accurately. Fluid balance charts are often incomplete and inaccurate [9].Volumes, for instance, frequently need to be estimated and cannot be measured. Since both fluid input/output and body weight are registered cumulatively, the size of the error can increase with time.

Another argument for critically looking at fluid output is that handling cytotoxic urine of cancer patients is an occupational hazard for nurses. Studies showed an association between handling cytotoxic drugs and fetal loss and/or systemic drug absorption by the health care provider [10, 11]. Therefore, every possibility to avoid handling of fluids and body excreta is welcome.

Body weight measurement also has inherent difficulties, but to a lesser degree. The variation in execution, such as time of measurement, type of scales used, clothing worn by the patient and whether or not the patient has urinated prior to the measurement are aspects that need to be considered using logistical changes and protocols [12]. A quality assurance project analysed the routine practice of chemotherapy and the role performance of nurses. One of the conclusions was the need for standardization of procedures of measuring body weight [13].

The sparse literature on this subject does not indicate whether it is really necessary to register both fluid balance parameters, and which parameter would be best in terms of measurement error sensitivity and execution simplicity. In 1979, Plaum [14] investigated the concordance between fluid balance and body weight, but failed to find a correlation. Because of a lack of published data, the Dutch Institute for Healthcare Improvement has based its guidelines 'Sense and Nonsense of the Fluid Balance' on consensus and only recommends the use of fluid input/output measurements if it is supported by strong arguments [15].

In light of the uncertainty regarding the policy to be pursued, we determined the concordance between body weight and fluid balance as parameters of fluid overload to indicate that body weight and fluid balance are exchangeable. Next, we determined the clinical consequences with respect to the safety of selecting the simplest and most reliable parameter, body weight measurement.

Patients and Methods

Between March and June 2000, all patients treated with cytostatics and in whom hyperhydration was used were included in a prospective cohort study. Patients undergoing high-dose chemotherapy were screened for comorbidity in the out-patient clinic before starting this intensive treatment. Patients were recruited at the Academic Medical Centre (AMC) Amsterdam in the departments of pulmonary disease, gynaecology, and haematology/oncology. Consent from the medical ethics committee was not necessary and informed consent was not required since no changes in the current policy were implemented.

Present Situation

The AMC employs international and national treatment protocols. The duration of administration in these protocols varies from 1 to 5 days and each treatment course is followed by the next with a resting period of at least 1 week. Fluid input/output and body weights are registered during hyperhydration (4 to 5 litres of fluid in each 24-hour period) and measured simultaneously 3 times per 24 h. In case of a cumulative fluid balance >2 litres and/or a cumulative body weight increase >2 kg from the start of treatment 5 mg of furosemide is administered.

Standardization

In order for these measurements to be performed as precisely and reliably as possible, standardization of 'body weight measurement' and 'fluid balance measurement' took place prior to data collection. Special attention was paid to standardization of the weight scales (type and use) and standardization of the circumstances under which the body weight measurements were performed, e.g. time point and frequency, clothing and shoes worn and prior urination. The results of a recently completed investigation into body weight measurement policy have led to a relatively new standardized protocol [16]. Standardization of the fluid balance measurement, e.g. agreement on parameters that should or should not be considered relevant, was done with the co-operation of dieticians and nutritionists.

Data Collection

During the study period, all fluid input/output and body weight measurements registered took place in patients who had been admit-

ted for a course of treatment with cytostatics involving hyperhydration. Both medical and nursing patient files were used and data collection was performed per patient and per course of treatment.

At the start of each course of treatment, sex, age, diagnosis, comorbidity and data on the treatment (type of cytostatics, treatment duration, etc.) were registered. Every 8 h both body weight and fluid input/output were registered and the cumulative fluid balance and cumulative increase or decrease in body weight were measured. If necessary, intervening administration of furosemide was also recorded. Possible calculation errors were checked afterwards. Increased body temperature (>37.5°C) or fever (>38.0°C), vomiting, and diarrhoea were registered as well.

Analysis

The agreement, or concordance, between fluid balance and body weight was determined using the Pearson correlation coefficient for the entire cohort [17]. This designates the magnitude of the relationship between these variables. In addition, the Pearson correlation coefficient of the individual first, second, third and fourth fluid balance and its corresponding body weight was determined in order to be able to trace specific trends in a possible discordance.

To analyse whether the discordance between fluid balance and body weight increases with the increase in body weight, a Bland-Altman analysis was performed [18]. In this analysis the mean scores of difference in body weight minus the mean scores of difference in fluid input/output are plotted against the mean scores of difference in weight alone. In the Bland-Altman analysis, the difference in body weight has been used as a reference value, since this is considered to be the most reliable parameter if data are clustered near the zero line, no differences in concordance occur in case of an increase in weight.

The clinical consequence, in terms of safety, of using only one parameter (body weight) for registration of the fluid balance instead of both body weight and fluid input/output was analysed in a 2 × 2 table, depicting (dis)agreement between body weight and fluid balance. This way it can be determined how often interventions with diuretics had to be applied. In case they had to be applied, whether this was based on fluid input/output or body weight or both. It gives insight into how many cases with a fluid imbalance one would have potentially missed if only body weight had been registered.

Finally frequencies of occurrence have been calculated for the following factors: vomiting, diarrhoea, fever, calculation errors and performed interventions.

All data were analysed with the statistical package SPSS, version 9.0.

Results

Of 43 patients, 279 person-days were observed. The mean age of these patients (58.1% men) was 45 years (range 18–73). In 91% (39/43) no comorbidity was found. The patients underwent a total of 84 first and follow-up courses of treatment, in which a total of 591 combined observations of both fluid balance and body weight (cases) were collected. The number of combined cases with more than 11 consecutive fluid balances (courses >4 days) was 70% (416/591). Short courses of treatment (1 or 2 days) with fewer than 7 consecutive observations were performed in 24% (143/591). Treatment with cisplatin was most frequently administered, namely in 78% (460/591) (table 1).

Table 1. Basic characteristics

Patients	43
Male	25 (58.1%)
Female	18 (41.9%)
Age, years, mean (range)	45 (18–73)
Fluid balance/weight registrations	591
Courses/patient (range)	84 (1–6)
Fluid balance/weight registrations/course of treatment (range)	7 (2–18)
Speciality	
Oncology	16
Haematology	11
Pulmonary oncology	6
Gynaecology	10
Comorbidity	
None	39
Congestive heart failure	2
Hypothyroidism	1
Tumour lysis	1
Duration of course of treatment	
Short 1–2 days, fluid balance <7	143 (24.2%)
Middle 3–4 days, fluid balance 7–10	32 (5.4%)
Long >4 days, fluid balance >11	416 (70.4%)
Type of course of treatment	
Fluid balance/weight – cisplatin	460 (77.8%)
Fluid balance/weight – cyclo-/ifosfamide	131 (22.2%)

No cases of clinically manifest left- or right-sided congestive heart failure were observed. In 1 case, furosemide was administered based on physical findings – the occurrence of oedematous ankles – but it is unclear whether this incidence actually involved congestive heart failure.

In general, there was a higher increase in body weight than in fluid balance; with a mean difference of 728 mg. The Pearson correlation between fluid balance and body weight of *all* 591 fluid balances and weight measurements was r = 0.28. At the start, the Pearson correlation between all *first* fluid balances and body weight measurements was r = 0.57 (84/591). At the *second* measurement, r was 0.57(83/591), at the *third* r was 0.40 (58/591) and at the *fourth* r was 0.46 (42/591).

The Bland-Altman plot (fig. 1) shows that the discordance between fluid balance and body weight also increases as the difference in weight measurements increases. This means that if a patient had gained only a

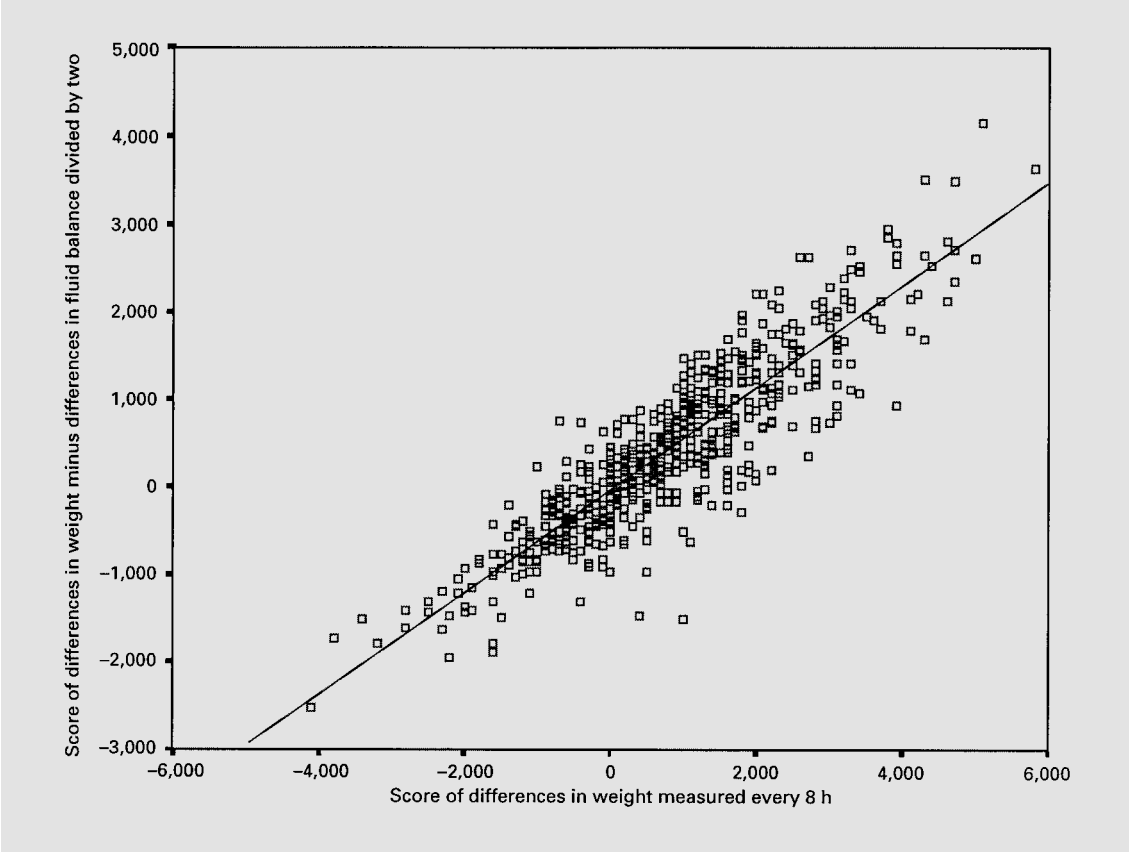

Fig. 1. Bland-Altman plot showing that when the discordance between fluid balance and body weight increases, the difference in weight measurements increases as well.

little weight, his fluid balance was more or less in agreement with his weight, whereas if his body weight had strongly increased, the discrepancy between fluid balance and body weight had become much larger.

Next, we investigated the clinical consequence of the concordance between fluid balance and body weight. Of all included cases, 81% (479/591) showed a balance <2 litres and <2 kg, which means that no furosemide was necessary. In 1.5% (9/591) both fluid balance and body weight had increased (>2 liters and >2 kg, respectively); the administration of furosemide was indicated based on both parameters. In 17% (99/591) the weight increased by >2 kg, but the fluid balance remained <2 litres, and an intervention with furosemide was indicated based on weight increase alone. The percentage of cases with a fluid balance increase >2 liters and a body weight increase <2 kg was 0.6% (4/591). In these 4 cases, furosemide would not have been administered if the fluid balance had not been measured (table 2). Upon further analysis of these 4 cases, involving different patients, the registered body weight of one patient appeared to be dramatically different from the previous and subsequent measurement and must have been a registration error. The other 3 cases involved differences between fluid balance and body weight of 230, 350 and 430 ml/g, in which the fluid balance remained just >2 litres and body weight barely <2 kg. All 4 cases concerned the first or second fluid balance/body weight registration. The mean age of these patients did not differ from the whole group (40 years against 45 years) (table 3).

Of the interacting factors, fever, vomiting and calculation errors, all occurred relatively infrequently and therefore required no further analysis (table 4).

Discussion

Considering the fact that there is no gold standard for fluid overload, body weight and fluid balance seem to be logical and practical parameters for monitoring possible

Table 2. Number of cases above and below the cut-off level of 2 litres and/or 2 kg

		ΔWeight >2 kg		
		yes	no	total
ΔFluid balance >2 litres	Yes	9 (1.5%)	4 (0.6%)	13 (2.2%)
	No	99 (17%)	479 (81%)	578 (98%)
	Total	108 (18%)	483 (82%)	591

fluid overload in hyperhydration. In this study we investigated the concordance between body weight and fluid balance as parameters of (possible) fluid overload in treatment courses with cytostatics. We also determined the clinical consequences of only selecting the easiest applicable parameter. We found that body weight appears to change more rapidly than fluid balance as a result of fluid administration. The correlation between body weight and fluid balance is rather weak: the maximum correlation is 0.57 at the first measurement and decreases to 0.28 when all measurements are calculated together. The Bland-Altman analysis confirms that the concordance decreases as body weight increases. A possible cause of this discordance is the cumulative incidence of error which has been taken into account in the calculations. Through standardization and training, the body weight and fluid measurements were assured to be as reliable as possible. It is not expected that more training would have improved the accuracy of the measurements.

With regard to the safety of measuring body weight only we found that 4 cases in this study (0.6%) would not have received furosemide if the fluid input/output had not been registered. Except in 1 case, which was a registration error, the differences between fluid balance and body weight in those 3 cases were so small that they were considered as 'borderline'. It should be realized that the cut-off points are arbitrary and that if the cut-off value had been slightly increased to 2.5 kg/litre these cases would not have been registered at all. The interesting question is whether the current cut-off value for the intervention, i.e. administration of furosemide, is too low and needs to be raised.

Patients in our study were relatively young and had little comorbidity. So it is not surprising that no case of clinically manifest congestive heart failure was observed and our means to prevent fluid overload appeared to be adequate. The question remains whether there is a risk of right-sided congestive heart failure in noncardiac patients treated with hyperhydration. However left-sided congestive heart failure (pulmonary oedema) is a serious complication and should be prevented. All in all, we and many other clinicians would feel uncomfortable if the volume status remained unmonitored. Therefore we focused on a single and effective monitoring parameter.

The sample showed a mix of short and long courses of treatment, performed in accordance with the current protocols and with the usual cytostatics, in particular the nephrotoxic cisplatin. However, the patients were not selected and therefore can be seen as representative for the oncology patient population in our academic hospital. Of course, our results may not be directly extrapolated to other situations involving patients with congestive heart failure, for instance in cardiac, nephrologic patients and especially older patients. But one could also question the

Table 3. Four cases: Δweight <2 kg, Δfluid balance >2 litres

No.	Case	PIN	Age	ΔWeight	ΔFluid balance	Difference
1	190	11	51	−700	2,200	2,900
2	207	12	21	1,800	2,150	350
3	305	18	35	2,000	2,430	430
4	311	19	53	1,800	2,030	230

PIN = Patient identification number.

Table 4. Occurrence of possible interacting variables

	Patients		
	n	%	range
Increased body temperature			
Registrations >37.5 °C	8	1.4	7–43
Registrations >38.0 °C	5	0.8	4–43
Vomiting			
Moderate (<200 cm^3)	24	4.1	13–43
Severe (>200 cm^3)	27	4.6	7–43
Calculation errors	30	5.1	

effectiveness of using similar parameters to monitor fluid overload in those cases. There is one exception to using body weight to control fluid overload: this is when patients are bedridden and cannot be weighed. What remains very important is the clinical evaluation and the identification of physical signs of fluid overload by nurses and physicians.

The underlying rationale to opt for body weight only as parameter for checking fluid balance is that measuring fluid input/output is complex and labour-intensive and it is unsure whether it is a reliable measuring instrument. Inaccurate registration and calculation errors, such as double notation or omission of fluid input or urine production, may cause considerable variation in the measurement of fluid balance. Due to the large number of calculations, calculation errors may easily occur. It seems plausible to assume that fewer errors can occur in body weight measurement and that weight is a more reliable indicator to detect potential fluid overload and congestive heart failure than fluid balance. With respect to time and costs no data were found in the literature on the amount of time used for registering and processing fluid input/output. However, it is clear that omission of fluid balance registration in chemotherapy protocols will save a lot of time. A positive side effect is that the risk of handling cytostatic urine incurred by nurses will be much lower. It has to be said that this is only the case once the weighing procedure has been properly standardized. We found the results based on 591 observations a sufficient basis for a policy change and the implementation of a new guideline.

Conclusion

This study has provided a good argument for only measuring body weight as a parameter for possible flush overload upon hyperhydration in a course of treatment with cytostatics. No longer registering the fluid input/output during such treatments hardly has any clinical consequences and does not affect the patients' safety. Congestive heart failure rarely occurs and clinical parameters other than body weight, such as oedematous ankles and shortness of breath, may also lead to adequate interventions. The weighing method, with the proper standardization of procedures, can and should be performed since it appears to be reliable, safe, simple and time-saving.

Acknowledgement

First we would like to thank the Centre for Clinical Practice Guidelines and the AMC Medical Board for providing financial support, which has enabled the elaboration of this guideline. We also wish to thank all the nurses and other personnel of the participating wards for collecting data or providing support for this project in another way.

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