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Changes in Total Body Water in Infants Receiving Total Intravenous Nutrition

THEODORE Z. POLLEY, JR., M.D., JON W. BENNER, M.D., ANDERS RHODIN, M.D., WILLIAM H. WEINTRAUB, M.D., AND ARNOLD G. CORAN, M.D.[1]

Section of Pediatric Surgery, Mott Children's Hospital and University of Michigan Medical School, Ann Arbor, Michigan 48109

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Using deuterium oxide dilution technique, the total body water changes of five infants maintained on total parenteral nutrition have been determined. While average weight gains of from 14 to 53 g/day were documented, there were decreases in percentage total body water from 13 to 50%. These data taken together support tissue accretion rather than water retention as the mechanism of weight gain in the long-term, large-volume, total parenteral nutrition of these infants.

INTRODUCTION

The use of large-volume central and peripheral total parenteral nutrition has gained increased acceptance and wide application in the fields of neonatology and pediatric surgery [9]. With this therapy weight gain superior to oral caloric supplementation has been demonstrated in low-birth-weight infants [5]. In addition, ample weight gain has been demonstrated along with satisfactory wound healing in the postoperative pediatric and adult patient unable to receive oral alimentation for a prolonged period of time. The nature of this weight gain, however, whether water retention or increase in body mass, is still debated. Brans *et al.* [1, 2] using the technique of corrected bromide space to calculate extravascular water suggest that water retention accounts for weight gain, while Pildes *et al.* [16] and Driscoll *et al.* [5] support increase in body mass. Prior to previous publication from this laboratory [17] no total body water (TBW) studies in infants had been carried out to explore this question.

While the tritiated water dilution technique has been used in adults to study water balance, its use is ethically precluded in infants due to the radiation hazard of the isotope. On the other hand, the deuterium oxide dilution method, while cumbersome, is safer and well suited for determination of total body water content. Accuracy comparable to mass spectrophotometry adds to the attractiveness of the technique.

The following study was undertaken to determine total body water content and its contribution to weight gain in infants receiving high-volume peripheral total parenteral nutrition.

MATERIALS AND METHODS

Five infants with initial weight ranging from 1600 to 2550 g hospitalized in Holden Neonatal Intensive Care Unit of the University of Michigan Mott Children's Hospital were studied for periods of 2 weeks to 4 months. The patient group included two premature males, one full-term male, and two full-term females. During the study period the patients were maintained on peripheral total parenteral nutrition combining solutions of 2% amino acids, 12% glucose, and 10% fat emulsion (Intralipid, Cutler) administered at a rate of 140–160 cc/kg/day and 100–110 cal/kg/day.

[1] To whom requests for reprints should be addressed: F 7516 Mott Children's Hospital, University of Michigan Medical Center, Ann Arbor, Mich. 48109.

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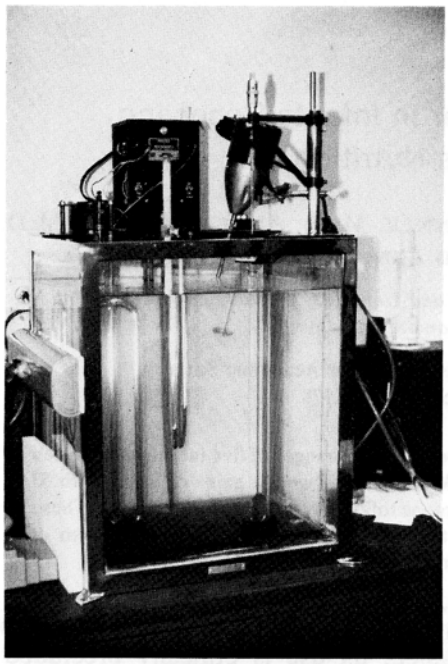

FIG. 1. Photograph of falling drop chamber used for determination of deuterium oxide concentration.

Total body water was determined at intervals varying from 1 to 4 weeks using the deuterium oxide dilution technique described by Schloerb *et al.* [18, 19]. The study was performed only after receiving informed consent of parents and was conducted in accordance with standards established by the Human Use Committee. This technique is based on derivation of a standard curve relating known concentration of deuterium oxide (vol%) to length of time (to 0.1 sec) required for isovolumic drops of double-vacuum-distilled standard solution to fall a constant distance through a column of *ortho*-fluorotoluene. The apparatus shown in Fig. 1 is designed to maintain the temperature of the water bath surrounding the falling drop chamber within 0.01 of a degree centigrade. This is critical to the accuracy of the procedure. Multiple determinations are made for each standard point to achieve precision within 2%.

Serum samples (1.5 cc) are obtained, centrifuged, and frozen 2.5 hr after intravenous administration of a precisely weighed dose of deuterium oxide (99.7%, Merck).

Prior to administration the D_2O is sterilized by passage through a series of hospital pharmacy micropore filters. Great care is taken to assure reliable venous access so that none of the isotope is extravasated into surrounding tissues. Following double-vacuum distillation, falling times of these serum distillates are determined and D_2O concentration (X) is calculated by interpolation from the standard curve according to the following formula,

$$X = \frac{\frac{1}{E_x} - \frac{1}{t_s}}{\frac{1}{t_{s'}} - \frac{1}{t_s}} (s' - s) + s,$$

where X = D_2O concentration of patient serum volume %; E_x = falling time of study serum distillate in seconds; t_s = falling time of lower standard distillate in seconds; $t_{s'}$ = falling time of higher standard distillate in seconds; s = deuterium oxide concentration of lower standard in volume percentage; s' = deuterium oxide concentration of higher standard in volume percentage. Total body water can then be calculated given the known weight of injected D_2O, serum concentration of D_2O, and established (Schloerb *et al.* [18, 19]) D_2O excretion rate of 0.4% of injected volume over the 2.5-hr equilibration period,

$$v = \frac{c_1 v_1 - c_u v_u}{c_2}.$$

- v Total body water in liters (volume of water into which injected deuterium oxide diffuses at equilibrium)
- c_1 Concentration of injected deuterium oxide (0.997)
- v_1 Volume of deuterium oxide injected corrected at 37°C (grams of deuterium oxide solution injected divided by its density at 37°C = 1.10098 g/ml [3])

$c_u v_u$ Total amount of excreted deuterium oxide from time of injection to time of sampling, 2.5 hr (this represents insensible water loss plus urine loss and has been suggested by Schloerb *et al.* to equal 0.4% of injected deuterium oxide ($c_1 v_1$))

c_2 Study serum concentration of deuterium oxide at equilibrium (X from previous formula divided by 100)

RESULTS

Average weight gains of 14–53 g/day were documented in the study patients. Patient 1 (Table 1), an infant with gastroschisis and short bowel syndrome, demonstrated gradual decrease in TBW% with concurrent weight gain. Figure 2 summarizes the hospital course in great detail including weight (kg), intravenous plus oral intake, and crown–heel length. Changes in patient's TBW% are plotted along with literature control values (Friis-Hansen *et al.* [11], Friis-Hansen [10, 12, 13], Flexner *et al.* [9], Edelman *et al.* [7], and Osler [15]). Similarly patient 2 with duodenal atresia, patient 3 with gastroschisis, patient 4 with perforated

TABLE 1

TOTAL BODY WATER CHANGES DURING PERIPHERAL HYPERALIMENTATION

Age (weeks)	Weight (kg)	Total body water (liters)	Total body water (% body wt)
Patient 1			
3	1.88	1.450	77.1
4	2.24	1.537	68.6
7	2.60	1.699	65.4
11	2.62	1.591	60.7
14	2.70	1.739	64.4
17	2.80	1.694	60.5
Patient 2			
1	2.59	1.842	71.0
2	2.78	1.603	57.6
Patient 3			
1	2.40	1.994	83.0
2	2.92	1.782	61.0
Patient 4			
1	1.60	1.641	100.0
4	2.52	1.892	75.0
16	3.00	1.597	53.0
17	3.16	1.264	40.0
Patient 5			
3	2.59	2.460	95.0
4	3.06	2.800	91.4
5	2.86	2.230	79.0

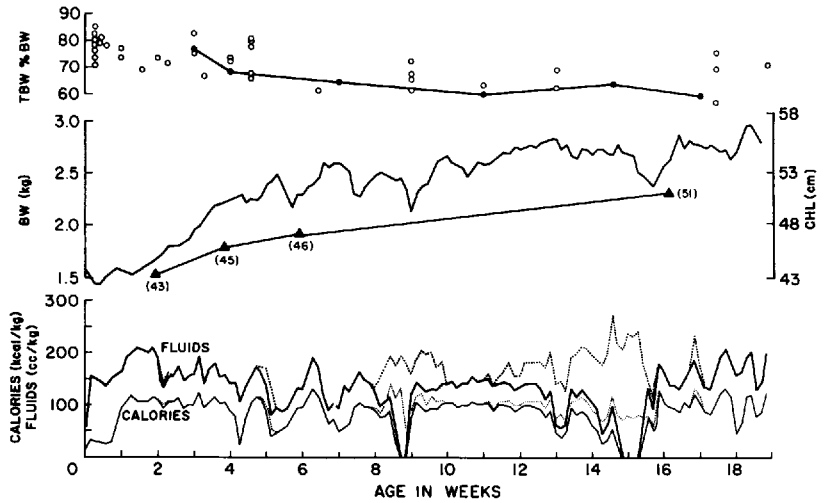

FIG. 2. Graph demonstrating total body water (% body wt) changes in patient 1 during 17 weeks of parenteral nutrition. The graph also depicts body weight changes and length changes in the infant. BW, body weight; TBW, total body water; ○, normal TBW measurement from the literature; ●, TBW measurement in study patient; ▲, crown–heel length (CHL); ——, intravenous intake; . . ., oral supplementation.

necrotizing enterocolitis and biliary cirrhosis, and patient 5 with omphalocele demonstrate decrease in TBW% (71–57%, 83–60%, 100–40%, 95–79%) with concomitant increase in weight. It should be noted that the course of patient 4 was complicated by congestive heart failure and respiratory distress.

DISCUSSION

Deuterium oxide is ideally suited for the study of total body water changes in infants. It lacks the exended half-life of the radioactive tritiated water and is distributed homogeneously throughout the body within a short period of time following intravenous or subcutaneous administration. In addition, it is totally nontoxic in the range of serum concentrations achieved. The acceptability of the accuracy of the falling drop method has been underscored by Friis-Hansen [13] who notes only 2% variation in multiple simultaneous sampling studies. The dynamics and rates of excretion have been carefully determined by Schloerb *et al.* [18, 19]. Moreover, Schloerb *et al.* [18] have shown agreement of within 1% in analysis of standard solutions with both the falling drop and mass spectrophotometric techniques. Of course, this depends on meticulous technique in weighing of standard and injected sample, reliable venous access, accurate patient weight, avoidance of contamination during storage and double-vacuum distillation, constant size of drops used in falling drop chamber, and careful control of chamber temperature. The 1–2% error in overestimation of TBW, due to exchange of deuterium with labile hydrogen of carbohydrate and protein, is offset by a probably incomplete equilibration of the small amounts of water in the gastrointestinal tract and bone.

While the total body water value of 100% in patient 4 is obviously not possible strictly speaking, given the prematurity of the infant, existence of cardiac failure, and established error of TBW determination, this value may be more readily accepted. The value of 40% at 17 weeks in the same patient is spurious, most likely because of inaccuracy of the recorded weight.

Many techniques including desiccation studies, radioactive isotope dilution, and spectrophotometric and falling drop methods of nonradioactive isotope detection have been used to define normal total body water composition of the fetus (94%) and newborn term infant (78%). However, while N_2 balance studies such as that of Driscoll *et al.* infer real weight gain in infants on total parenteral nutrition, to our knowledge the D_2O dilution technique has never been applied to serial determinations of TBW in order to more precisely define the contribution of water retention to weight gain. Our data showing weight increase along with serial decrease in TBW% support tissue accretion as the source of weight gain during high-volume peripheral hyperalimentation. Additional patients are presently being studied to confirm these findings in a much larger series of infants.

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