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Extracellular Fluid Deficit Following Operation and Its Correction with Ringer's Lactate

A Reassessment

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The changes in extracellular fluid volume (ECV) in two groups of surgical patients, one receiving Ringer's lactate solution intraoperatively and the other receiving only dextrose and water, were assessed. A deficit in the ECV, as measured by radioactive sulfate, of 1.9 ± 0.8 l ($p < 0.003$) compared to the preoperative volume was found in the dextrose group. This was accompanied by a decrease in the mean creatinine clearance (−13% $p < 0.01$), the mean urinary sodium excretion (−57% $p < 0.05$), and the mean rate of clearance of the sulfate tracer (−18% $p < 0.01$). The use of intraoperative Ringer's lactate (1660 cc ± 96 cc) resulted in no change in the ECV, an increase in the mean creatinine clearance (+10% $p < 0.05$), and no change in sodium excretion or tracer clearance. As a result of these findings, it appears that postoperative sodium retention is a physiologic response to a decreased ECV, which can be prevented by the administration of Ringer's lactate.

THE CONTROVERSY OVER the intraoperative management of fluids containing sodium is based on differing perceptions of the effect of operation on the body's mechanism for sodium homeostasis. Early studies of sodium balance revealed that postoperative patients conserved sodium secondary to a decrease in urinary sodium excretion after surgery.[1] The sodium and water retention was attributed to elevated levels of aldosterone and antidiuretic hormone (ADH) that resulted from the stimulus of surgical trauma.[2–4] These hormone elevations, if nonspecific, would suggest that operation altered the normal homeostatic controls of sodium and water balance leading to its pathologic retention. This led to the recommendation of sodium restriction to prevent its excessive accumulation. An alternative explanation was that the kidney, reacting in a physiologically appropriate manner, conserved sodium because of an absolute or relative deficit in sodium.

One known physiologic reason for renal conservation of sodium is a decrease in extracellular fluid volume (ECV).[5,6] Shires et al. measured the apparent ECV in patients who received no salt or fluids during their operations, and found the measured ECV decreased after surgery.[7] This decrease did not correlate with the

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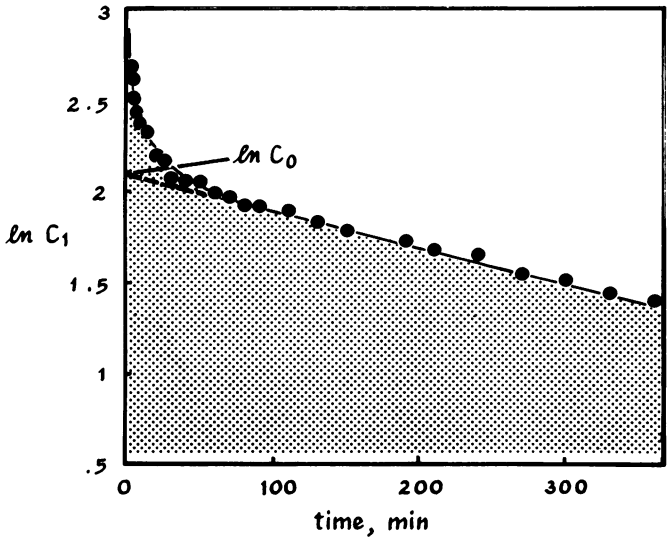

FIG. 1. Plot of the natural logarithm of the plasma tracer concentration (C_0) *versus* time. Circles are the experimental points, solid line is the nonlinear regression equation fitted by computer to the experimental points, dashed line is the linear regression equation fitted to the final monoexponential slope. Ln C_0 is the extrapolated plasma concentration at zero time assuming instantaneous distribution and equilibration of the tracer.

blood or plasma loss, but did correlate with the estimated degree of operative trauma. These findings have been criticized on the basis of the technique used to measure the ECV and contradictory reports have been published.[8,9]

The purpose of this study is to reexamine the previous measurements of changes in the apparent ECV in postoperative surgical patients and to assess the need for sodium containing fluids intraoperatively.

Methods

Patients undergoing either vagotomy and antrectomy or cholecystectomy were studied. None of the patients had either bowel preparations or dehydrating radiologic studies in the 3 days prior to operation.

The amount of sodium and water given intraoperatively was the treatment variable. Group I (N = 5) received lactated Ringer's solution at a rate of 300–500 cc/hr. Group 2 (N = 10) received a total of 350–1150 cc of D_5W without sodium intravenously.

The patients were admitted 24 hours before surgery to a clinical research unit, the bladder catheterized, and central venous access obtained. Two hundred microcuries of $Na_2\ ^{35}SO_4$ in 10 ml of normal saline was given through the venous catheter, which was flushed with 30 ml of D_5W following injection. Three-ml blood smples were taken from a central venous catheter according to the following schedule: five at 2 min intervals, five at 5 min, six at 10 min, three at 20 min, and seven at 30 min. After each collection, the catheter was refilled with heparinized saline solution. No other fluids were given during the measurement periods. The ECV was measured in the same manner immediately following the surgical procedure. Samples of blood for background counts and chemical measurements were collected prior to injection of the isotope. During the measurements of the ECV, urine was collected for measurement of the excretion rate of the tracer, sodium, and creatinine.

The blood samples taken for the measurement of tracer concentration were centrifuged to obtain the plasma; duplicate 0.5 cc aliquots of the plasma were placed in 15 cc of scintillation cocktail in counting tubes and the radioactivity measured following overnight dark adaptation. The correction for quenching was established by the two-channel ratio method. Standards for the determination of the amount of radioisotope used for each injection were prepared by diluting the same volume of stock tracer solution as injected into 500 cc of saline. Three 0.2-cc aliquots of this solution were counted and the tracer dose taken as the average of these dilutions. Duplicate 0.2-cc aliquots of urine were added to 15 cc of scintillation cocktail and counted in the same fashion as the plasma samples. The samples were counted in a Nuclear-Chicago Mark I® deep well scintillation counter. The plasma samples were corrected for plasma water content and the Donnan equilibrium by multiplying the concentration by 1.08 and 1.05, respectively. Serum and urinary sodium and creatinine were measured by standard laboratory methods.

The ECV was estimated by the use of a stochastic analysis similar to that used by Ladegaard-Pederson,[10] in that the key element was to obtain the integrals under the curves for the concentration (c) plotted against time (t). In order to obtain the integrals, equations are needed that fit the experimental points. Ladegaard-Pederson used a mathematical "peeling off" of exponentials to obtain the necessary integrals. Because this can be an inaccurate technique,[11] the current approach used a least-squares regression to numerical integration of the following set of differential equations that model a three-compartment exchanging system.

$$dC_1/dt = -k_0C_1 - k_1C_1 + k_{-1}C_2$$

$$dC_2/dt = -k_{-1}C_2 - k_2C_2 + k_1C_1 + k_{-2}C_3$$

$$dC_3/dt = -k_{-2}C_3 + k_2C_2$$

Here, C_1 refers to the concentration of the tracer in the plasma; C_2 denotes the concentration of tracer in a component of the ECV which exchanges tracer directly with the plasma by the forward and backward rate constants k_1 and k_{-1}, respectively. C_3 is the concentration of tracer in the remainder of the ECV which exchanges with C_2 with the forward and backward rate constants k_2 and k_{-2}; k_0 is the rate constant for urinary excretion.

All processes are assumed to be governed by first-order rate laws. An example of the fit of the equations to the experimental points can be seen in figure 1.

In the postoperative measurements of the ECV, there were small concentrations of tracer in the plasma remaining from the preoperative measurements. Because these background counts could effect the measurement of the ECV, the following procedure was used to correct for this potential error. The assumption was made that the residual tracer in the plasma would be lost at the same rate as the tracer dose given during the postoperative measurement. Therefore, the final monoexponential slope of the natural logarithms of the tracer concentration *versus* time would reflect the rate of loss of the residual tracer over the period of measurement. The slope (k) of linear regression line fitted to these points was taken as the rate of loss of the residual tracer and the residual tracer concentration at time zero as B_0. The effect of the background was accounted for at each data point by the equation $C = C(t) - B_0e^{-kt}$, where C(t) is the measured plasma tracer concentration and C is the tracer concentration corrected for the residual tracer. Following this correction, the curve-fitting procedure was applied in the same fashion as the preoperative measurement.

Excellent fits were obtained to the experimental data, with most nonlinear regressions having correlation coefficients of 0.99 or better. This ensures accuracy in the integration and the resultant volumes, flows, and mean transit times. Because of the large number of unknowns in the equations, nearly identical ECV values could be obtained with a range of rate constants for the same set of experimental points. Consequently, the absolute values or even relative values of the rate constants are not important.

The regression analyses were performed with a FORTRAN-coded program running on a Hewlett-Packard 9000 model 502 computer. The numerical integrals were taken over 10,000 min. The total clearance, mean transit time, and the volume of distribution of the tracer were obtained from the equations described in the discussion section of the text.

A deterministic or compartmental analysis was performed on the data to obtain the ECV by a method used previously in this and other laboratories. The natural logarithms of the plasma $^{35}SO_4$ disintegrations per minute (DPM) values were plotted against time. A linear regression line was fitted to the final monoexponential slope by a computer and was extrapolated to zero time. The intersection of the line with the ordinate was taken to represent the radiosulfate concentration in the plasma had the tracer been instantaneously and uniformly distributed. This extrapolated point was the value (C_0) used in the calculations of the ECV by the formula

$$ECV = \frac{\text{Injected Dose}}{C_0}$$

An example of the linear regression line and the extrapolated point can be seen in Figure 1.

TABLE 1. *Group Comparisons (Mean ± SD)*

Patient Characteristics	Salt (N = 5)	No Salt (N = 10)
Age (yrs)	50 ± 17	32 ± 10*
Weight (kg)	67.9 ± 10.4	84.1 ± 18.3*
Fluid (ml)	1660 ± 96 (LR)	530 ± 92 (D5w)*
Whole blood (ml)	200 ± 274	100 ± 210
Estimated blood loss (ml)	440 ± 134	388 ± 157
Operative time (min)	253 ± 50	187 ± 113

* Significant difference between groups at 0.05 level.

Statistical analysis was performed on an Apple IIe® microcomputer using the Microstat® statistical package. Nonparametric analysis of the data was performed using the Wilcoxon rank-sum test, signed-rank tests, and the Spearman rank correlation (r_s) where appropriate. Statistical significance was assumed when p was less than 0.05.

The protocol was approved by the Human Subjects Committee and informed consent was obtained from all patients.

Results

The characteristics of each patient group are presented in Table 1. The patients in the group that received no saline (group II) were significantly younger, heavier, and had a higher creatinine clearance than those who received lactated Ringers solution (group I). There were no significant differences between operative time, blood loss, and amount of blood administered. There was no significant difference between the measured ECV, mean transit times, or total clearances of the tracer before surgery (Table 2). The two groups of patients received the same amount of sodium in the 24 hours before surgery.

TABLE 2. *Calculated Tracer Values (Mean ± SD)*

	Salt	No Salt
ECV preoperative (l)	12.5 ± 2.3	12.5 ± 2.4
ECV postoperative (l)	12.3 ± 2.7	10.6 ± 1.9*
TC preoperative (ml/min)	32.0 ± 7.0	33.9 ± 11.3
TC postoperative (ml/min)	35.0 ± 7.4	27.9 ± 5.5*
$\bar{t}$ preoperative (min)	408 ± 124	380 ± 84.1
$\bar{t}$ postoperative (min)	363 ± 95*	388 ± 89.0

* Significant difference *versus* preoperative at 0.05 level.

TABLE 3. *Measured Urinary Values (Mean ± SD)*

	Salt	No Salt
$^{35}SO_4$ preoperative (% of injected counts excreted by 360 min)	44.4 ± 14.9	49.4 ± 11.9
$^{35}SO_4$ postoperative (% injected counts excreted by 360 min)	46.0 ± 13.1	39.9 ± 7.4*
Na^+ preoperative (meq/hr)	6.0 ± 3.6	4.9 ± 3.0
Na^+ postoperative (meq/hr)	6.9 ± 3.3	2.1 ± 1.4*
Creatinine clearance preoperative (ml/min)	79 ± 29	107 ± 22†
Creatinine clearance postoperative (ml/min)	87 ± 30*	93 ± 27*

* Significant difference at p = 0.05 *versus* preoperative.
† Significant difference at p = 0.05 between groups.

After surgery there was a marked decrease in the measured ECV of group II of 1.9 l ($p < 0.003$) (Table 2). There was essentially no change in group I. In group II, the decreased volume was associated with a decrease in the clearance of the tracer (18% $p < 0.01$), with no change in the mean transit time. In group I, there was an insignificant increase in the rate of clearance of the tracer (9% $p = 0.07$) and a significant decrease in the mean transit time (11% $p < 0.05$).

The creatinine clearance was depressed in the immediate postoperative period in group II (13% $p < 0.01$) (Table 3), while it rose in group I (10% $p < 0.05$). There was a significant decrease in the rate of urinary sodium excretion in group II (57% $p < 0.05$), while the patients in group I maintained the preoperative rate of sodium excretion. The change in the creatinine clearance correlated with the change in sodium excretion ($r_s = 0.626$; $p < 0.02$). The percentage of the injected counts excreted by 360 min fell in group II (19% $p < 0.05$), while there was no significant change in group I.

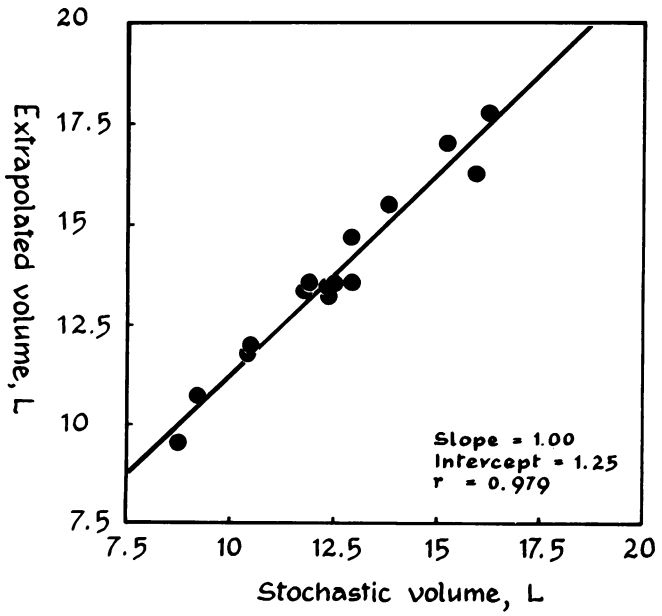

FIG. 2. Correlation of preoperative ECV as calculated from the extrapolation model *versus* the stochastic method of data analysis. Numerical values shown are for the calculated regression line.

A comparison of the preoperative calculated ECV by both mathematical methods is shown in Figure 2. There was a good correlation ($r = 0.979$; $p < 0.001$) between the two values. In further support of the ability of the stochastic model to reliably measure the tracer parameters, the calculated mean transit time correlated with the percentage of the tracer dose excreted in the urine by 360 min ($r_s = -0.621$; $p < 0.001$). Furthermore, there were significant correlations between the calculated change in the ECV and the measured change in the rate of urinary sodium excretion ($r_s = 0.643$; $p < 0.02$), the change in the ECV and change in the percentage of the injected tracer excreted in the urine by 360 min ($r_s = 0.585$; $p < 0.05$), and the change in ECV and the change in creatinine clearance ($r_s = 0.688$; $p < 0.01$).

Discussion

The theory of measurement of the volumes and flows of interrelated compartments is well-established.[12,13] Because of its complexity, a brief description of the theories and models involved is necessary to allow an understanding of the problems and assumptions associated with these measurements.

The anatomic extracellular space is the fluid in the body that is outside the cells, not including the transcellular fluid (*e.g.*, CSF). Practically, this can be thought of as the fluid space that would contain sodium if the intracellular fluid and transcellular fluids were omitted. To measure this space, a tracer is needed that follows the paths of sodium throughout the body except for its entrance into cells. Any deviation of the tracer from these paths will reflect negatively on the accuracy of measurement of the ECV as it relates to sodium. As sodium is the ion that the body uses to control the ECV, a tracer that follows the sodium ion might also be expected to provide insight into the regulation of the extracellular fluid.

Injection into the blood stream of a tracer of extracellular sodium could lead to the individual tracer particles taking a variety of paths prior to elimination from the body. These paths could include remaining in the intravascular space, crossing the capillary membrane to the interstitial space, or being filtered, then reabsorbed, from the glomerular filtrate. Each of these paths will have a time constant associated with it that represents the time from injection of the tracer to its excretion. Obviously, a tracer particle could take multiple paths prior to leaving the system, but an average time of

excretion of the tracer particles could be found. The flow of particles is the rate of movement of particles injected into the blood out of the system. Although this is usually the rate of urinary excretion, any loss from the system would be included. Tracer movement into slowly equilibrating pools in the body could either be treated as such or as irreversible losses from the system, depending on the length of time the system is studied.

An equation, not immediately obvious, can be derived from this model wherein the apparent volume of distribution is equal to flow × mean transit time. This is the Stewart Hamilton equation, which is well-known for the calculation of cardiac output by thermal dilution and is used to measure the volume of extravascular lung water. The derivation of this equation can be found elsewhere.[13]

To measure the extracellular volume (ECV) of distribution, equations are needed allowing the expression of output and mean transit time ($\bar{t}$) in terms of the measured tracer concentration in the plasma over the time of the experiment. These equations have been derived by Ladegaard-Pederson[10] and a more formal proof is provided by Anderson.[14] Because the movement of the tracer out of the system is of interest, flow is equated to total clearance (TC).

$$TC = Dose/\int_0^\infty C(t)dt$$

$$ECV = D\frac{\int_0^\infty tc(t)\,dt}{\left[\int_0^\infty c(t)dt\right]^2}$$

$$\bar{t} = \frac{ECV}{TC}$$

In these equations, $\int_0^\infty c(t)dt$ is the area under the curve of the plasma concentration *versus* time and $\int_0^\infty tc(t)dt$ is the area under the curve of the product of time and plasma concentration *versus* time. The relative size of these areas can be seen in Figure 3, which extends the time range of figure 1. It can be seen from the shapes of the curves that the accurate determination of the final monoexponential slope is crucial.

There are several inherent assumptions in this method: (1) that the tracer follows the paths of distribution of the tracee; (2) that the tracer leaves the system proportional to its concentration in the blood; (3) that the total clearance and volume remain the same during the measurement; (4) that the distribution of transit times (the pathways of the tracer) be unchanged during the measurement; (5) that all the tracer be eventually excreted; (6) that equilibrium is established nearly instantaneously within the compartments, but not necessarily

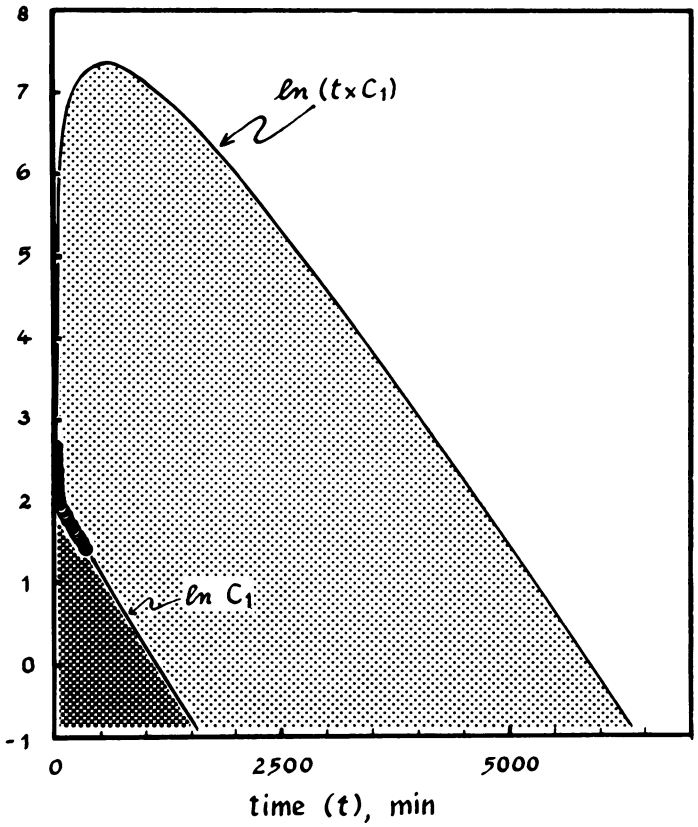

FIG. 3. Plot of the natural logarithm of the tracer plasma concentration *versus* time. Circles are experimental points, heavy stippled area is $\int_0^\infty$ ln c(t)dt, and light and heavy stippled areas are $\int_0^\infty$ ln tc(t)dt.

between the compartments; and (7) that the equilibration of the tracer between compartments is governed by first order rate laws. The model does not require that the excretion equal the rate of glomerular filtration, since the tracer which is reabsorbed from the tubules returns to the blood prior to excretion. In fact, to fulfill assumption 1, reabsorption is desirable if the tracer is to model the extracellular movement of sodium ion.

With this model, the apparent volume of distribution, the rate of output, and the mean transit times of the tracer can be estimated from the tracer dose given and the integrations of the functions that describe the change in the plasma concentrations over time. This model has been characterized as a stochastic or "black-box" model in that the number and relationships of the compartments involved do not need to be completely described.

Another type of model describing the volume of distribution is compartmental or deterministic analysis, which is based on the description of the change in the concentration over time by using a series of exponential decay curves. Each decay curve simulates the movement of the tracer within a compartment. The solution for the volume of distribution is usually found by extrapo-

lation of the final monoexponential portion of the plasma concentration decay when the log of the concentration is plotted against time. By extrapolating this slope back to zero time, a concentration (C_0) is derived that allows calculation of the volume of distribution, V = Dose/C_0.

The critical assumptions with this model are the instantaneous and uniform distribution of the tracer across all compartments. Because most tracers are excreted, the tracer is not uniformly distributed as the rates of change of concentration in each compartment differ. The excretion of the tracer leads to an overestimation of the volume of distribution, with the extent of overestimation proportional to the rate of excretion.[10,12] The relatively slow rate of excretion of the sulfate ions compared to their exchange between compartments means that it is unlikely that there will be a large error in the measurement of the volume of distribution using this method. The regression line plotted in figure 1 has an intercept of 1.25 L, suggesting a 10% overestimation by the extrapolation technique when applied to sulfate. The overestimation of the volume of distribution is more important when tracers such as EDTA and inulin are used, as these tracers are excreted rapidly.[10] The extrapolation technique will give an accurate estimation when applied to a closed system, *i.e.,* one with no urinary excretion.[12] Application of the extrapolation technique to the present data led to a similar significant decrease in the extracellular fluid in the patients who did not receive salt, as was found by the stochastic method of data analysis.

The selection of the tracer is of great importance in the measurement of any fluid space. The extracellular fluid space, as defined, is that volume containing the sodium that is outside the cells; therefore, it is desirable that the tracer follow the paths of the sodium ions except for its entry into cells. In this respect, sulfate, being a divalent anion, may be the optimal tracer as its intracellular concentration would be ten-fold less than a monovalent anion (such as bromide), as determined by the Nernst equation assuming similar membrane permeabilities. The sulfate ion is reabsorbed from the glomerular filtrate in the proximal renal tubule by a process that is related to sodium reabsorption.[15,16] Therefore, the sulfate ion may provide a good marker for the renal processing of the sodium ion as well as the extracellular fluid space. This appears to be the case in this study, as the calculated change in the tracer clearance was correlated with the change in the measured rate of urinary sodium excretion ($r_s = 0.707$; $p < 0.01$).

The attempts to mimic the behavior of one molecular species with another are going to be fraught with the hazards of different routes of excretion, metabolism, and distribution. No one tracer is going to be a perfect representative of a chemically different tracee's volumes, flows, and transits.

The body responds to a decrease in extracellular fluid volume by retaining sodium ion. As the osmolality of the extracellular fluid is tightly controlled, the quantity of sodium ion in the extracellular fluid governs the volume of the extracellular fluid.[5] Small decreases in the blood volume (part of the extracellular fluid) that do not affect blood pressure or heart rate are accompanied by an increase in the renal reabsorption of water.[17] In a similar response, sodium depletion causes a decrease in urinary excretion of sodium and a decrease in the creatinine clearance.[6]

The decrease in the postoperative ECV found in the patients who did not receive salt intraoperatively was accompanied by decreases in the creatinine clearance rate, in the rate of tracer clearance, and the rate of urinary sodium excretion. These changes imply that the kidney was responding appropriately to a decrease in the ECV. The significant correlations of the change in the extracellular fluid volume with the changes in creatinine clearance, the changes in the rate of urinary sodium excretion, and the rate of urinary loss of the tracer further support this theory.

In two studies similar to the present study, where two groups of patients were studied, one group receiving salt solutions and the other dextrose solutions, similar urinary excretion changes following operation were found.[18,19] In the patients not receiving salt, these findings included decreases in urinary output, urinary sodium excretion, and (in the study where it was measured)[18] a decrease in creatinine clearance. These changes were ameliorated by the administration of salt solutions during the operations.

A complex system governs the response to a decreased ECV. Changes in the renin-angiotensin system along with elevated levels of ADH and aldosterone are part of this mechanism. The final pathway of the renal response to a decreased ECV is the decreased excretion of sodium and water.

One of the major control variables of urinary sodium excretion is aldosterone. Marked increases in postoperative plasma aldosterone concentrations, lasting for the duration of the study (22 hours), were found by Enquist et al.[20] in patients not receiving salt intraoperatively. A group of saline treated patients had a smaller rise in aldosterone levels that returned to normal within 6 hours after surgery. There was no effect of saline on the elevated cortisol levels found in both patient groups. In a similar study, Shizgal[21] found that increases in aldosterone production in patients receiving no salt perioperatively could be inhibited by the administration of salt-containing fluids. On the basis of these studies and the present study, it seems reasonable to conclude that

the elevated levels of aldosterone (and possibly ADH) found by other investigators in postoperative patients may largely represent an appropriate response to a decreased extracellular volume.

It might be argued that the differences between the groups after operation were related to the significant intergroup differences that existed before surgery in the age, weight, and creatinine clearance. The groups were too small to allow statistical separation of these variables by partial regression analysis. If the intergroup differences are of concern, it should be pointed out that a decreased extracellular volume was present in the patients who did not receive salt and this was accompanied by the physiologic changes in sodium homeostasis. Because sodium ion is used by the body to maintain the ECV, the logical treatment for the decrease in extracellular fluid volume would be the administration of sodium-containing fluids. It would be expected that sodium would repair the fluid deficit in these younger, heavier patients with a higher initial creatinine clearance to the same extent as it did in the other group.

Summary

The fate of the missing extracellular fluid is not yet well-established. There was no statistically significant difference between the groups with respect to blood loss and no correlation between the amount of blood loss and the change in the extracellular volume. Therefore, loss of blood volume does not appear to be the primary loss. Our previous study demonstrated that the loss of extracellular fluid was greater than could be accounted for by plasma loss alone. Therefore, the loss may have been loss of water by evaporation from the exposed peritoneal surfaces (unlikely, as the serum sodium did not increase in these patients); "third space" losses such as into the peritoneal cavity, the tissues around the wound, and retractors; or possibly translocation to the intracellular space.

Although it is known that the skeletal muscle cell transmembrane potential decreases during shock, with a concomitant translocation of extracellular fluid into the cell, the membrane potential has not been measured in postoperative patients. However, in animal studies, a decrease in the membrane potential, with concomitant translocation of fluid into the intracellular space, was found in muscle cells beneath a retractor (Shires, unpublished observations). Therefore, this may be one source of extracellular fluid loss.

Despite the generally recognized need for intraoperative saline administration, there are several studies where a decreased extracellular fluid volume following operations was not found.[8,9,21-23] This may be secondary to methodologic differences between these studies and the present study. In some studies,[8,9,22,23] all patients were administered salt-containing solutions that would replace the extracellular fluid deficit. An attempt was made, in one study, to correct for this by subtracting the amount of administered fluid from the measured extracellular space.[8] This assumes that the administered fluid did not influence the measurement of the volume of distribution of the tracer. As mentioned previously, when compartmental analysis is performed by extrapolating the final logarithmic slope, as was done in two studies,[8,9] changes in the rate of excretion relative to the rates of distribution between compartments are important in determining the measured tracer volume of distribution.[10,12] Administering fluids (particularly in the large quantities that were given in one study)[8] most likely results in an increase in tracer excretion relative to the distribution rates and an overestimate of the tracer volume of distribution. A demonstration of this problem can be found by analysis of data presented in this paper.[8] The authors present a graphic representation of one patient's pre- and postoperative tracer plasma concentrations *versus* time. The extrapolation model revealed no change in the postoperative volume compared to the preoperative volume. The same data, analyzed by the stochastic method used in this paper revealed a seven per cent decrease in the postoperative volume, despite the patient receiving crystalloid fluids during the operation and the postoperative period. Thus, it appears that the failure to find a decrease in the extracellular fluid space following operation in these papers may have been the failure of the extrapolation method to detect a decrease. It is also important that fluids not be given during the time of measurement of the extracellular space, as this will preclude the requirement for a steady state.

In a study similar to this one, with patients divided into salt and no salt groups, Shizgal[21] found a small (900 ml) but *statistically* insignificant decrease in the ECV in the patients who did not receive salt intraoperatively. As mentioned previously, there was an increase in the rate of aldosterone production in the salt-restricted patients which was inhibited in the patients who did receive salt, implying a *physiologically* significant decrease in ECV. The extracellular tracer used was ^{22}Na. As this tracer penetrates the intracellular compartment, it is possible that an increase in the intracellular uptake led to a falsely high measured volume of distribution of the tracer while a true decrease in the ECV existed.

Conclusion

This study demonstrated a decrease in the ECV in patients not receiving salt intraoperatively, accompanied by urinary retention of sodium. Salt-containing solutions administered to another group of patients ameliorated both effects. It appears that the postoperative sodium

retention in patients who do not receive sodium intraoperatively is largely reflective of a physiologically appropriate response to a decreased ECV, rather than a nonspecific pathologic reflex to the stimulus of surgery.

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