Acute Change in Extracellular Fluids Associated with Major Surgical Procedures *

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Introduction

Adequate management of the surgical patient today demands a thorough knowledge of the changes in fluid and electrolyte balance incident to the operation itself. More accurate assessment and correction of preoperative blood, fluid and electrolyte deficits and excesses are now possible. The changes induced by surgical procedures, however, are understood far less completely. These are the acute changes which directly determine the operative and postoperative management of fluids and electrolytes in surgical patients.

Acute changes in renal function in the operative and postoperative period have been observed for many years.[19, 23, 38] The decreased renal excretion of sodium in the postoperative period is a well recorded event.[25] It recently has been well established that extracellular fluid volume, or more precisely the "functional" extracellular fluid volume, is a major determinant of renal sodium excretion.[7, 32, 35]

The present study was designed to measure as precisely as possible the changes in extracellular fluid volume which occur incident to major operations. This was done employing a new method for the simultaneous measurement of plasma volume, red blood cell mass, and extracellular fluid volume.[30] The method was so designed that these volumes could be accurately measured on two occasions during the operative period. This consisted of the use of I^{131} (RISA) tagged serum albumin, chromate ^{51} tagged red blood cells, and sulphur ^{35} tagged sodium sulphate. In addition, losses of plasma, red blood cells and extracellular fluid were measured via the wound and through the kidneys. Serum and urine electrolyte concentrations were also measured.

The data indicate a marked loss of functional isotonic extracellular fluid during the first two hours of a major surgical procedure, which is independent of actual whole blood loss. The data also indicate that this loss of functional extracellular fluid is largely due to an internal redistribution of extracellular fluid.

Materials and Methods

Two groups of patients have been studied. The control group consisted of five patients having general anesthesia and minor surgical procedures involving minimal tissue trauma and minimal blood loss. These patients received no fluids or electrolytes during the surgical procedure and were used to demonstrate the accuracy and reproducibility of the method. The study group consisted of 13 adults undergoing elective major surgical procedures. As in the control group simultaneous measurements of plasma volume, red blood cell mass, and extracellular fluid volume were made at the beginning of operation and were then remeasured after two hours of

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TABLE 1. *Controls*

Pt.	Pre-op.			Post-op.			Change			% of Original ECF Lost	Total Blood Vol.		Loss		
	RBC	Plasma	ECF	RBC	Plasma	ECF	RBC	Plasma	ECF		Pre-op.	Post-op.	Isotope	Sp. Wt.	Hemoglo.
3	1,627	2,523	10,925	1,532	2,598	10,617	−95	+74	−308	2.8	4,150	3,950	95	177	180
11	2,252	2,496	8,300	2,223	2,324	8,041	−29	−172	−259	3	4,748	4,547	201	191	181
12	1,242	1,766	7,800	1,173	1,702	8,100	−63	−64	+300	0	3,008	2,875	127	102	123
22	2,292	2,200	16,219	2,253	2,147	16,051	−39	−53	−168	1.03	4,492	4,400	92	—	—
23	1,100	2,565	11,861	1,120	2,500	11,701	+20	− 65	−160	1.34	3,665	3,620	65	—	—

TABLE 2. *Experimental*

Pt.	Pre-op.			Post-op.			Change			% of Original ECF Lost	Total Blood Vol.		Loss		
	RBC	Plasma	ECF	RBC	Plasma	ECF	RCB	Plasma	ECF		Pre-op.	Post-op.	Isotope	Sp. Wt.	Hgb.
4	1,835	2,400	15,173	1,724	2,201	11,452	−111	−199	−3,721	25.0	4,235	3,925	310	290	275
5	1,748	2,777	18,776	1,435	2,378	16,383	−313	−399	−2,393	12.7	4,525	3,813	712	725	700
8	1,153	2,328	11,278	1,181	1,830	8,109	+ 28	−498	−3,196	28.0	3,481	3,011	498	473	509
9	1,253	2,036	11,315	1,082	1,845	10,530	−171	−191	− 785	6.9	3,289	2,927	362	340	304
10	830	1,882	18,408	624	1,430	10,055	−206	−452	−1,557	13.3	2,712	2,054	658	601	622
13	1,042	2,666	17,532	729	2,116	14,435	−313	−550	−3,097	17.66	3,708	2,845	863	822	811
14	1,005	2,041	9,787	881	1,699	9,318	−124	−342	− 754	7.0	3,046	2,580	466	—	—
15	2,569	3,196	16,800	2,119	2,678	13,816	−450	−518	−2,984	17.76	5,765	4,797	968	874	923
16	1,736	2,711	11,626	1,436	2,282	10,277	−300	−429	−1,354	14.0	4,447	3,718	729	658	684
17	1,786	2,760	13,387	1,786	2,545	12,567	0	−215	− 820	6.0	4,546	4,331	215	200	184
18	1,579	2,698	11,124	1,588	2,344	10,094	+ 9	−354	−1,030	9.3	4,277	3,932	354	—	—
19	1,001	1,822	7,853	997	1,743	7,897	− 9	− 79	+ 44	0	2,828	2,740	88	50	62

the surgical procedure. During this time no fluids or electrolytes were administered to the patients.

Using a method previously described,[30] isotopes were administered simultaneously intravenously in one arm and blood samples were drawn from the opposite arm with the use of an indwelling polyethylene catheter.

The counting method was devised using a combination of energy differentiating monitors which would allow differentiation of S^{35}, I^{131}, and Cr^{51} in a single blood sample.[30] Reinjection technic was employed and the volume distribution curve of all isotopes was determined to be the same for both test periods, as no patient demonstrated any significant change in pulse or blood pressure during the period of observation.[30, 37] Samples were taken at 10, 20 and 30 minutes after each injection as well as samples at 20-minute intervals between injections. All samples were run in duplicate.

Sponges and laparotomy packs were collected fractionally during the 20-minute isotope equilibration time, during the surgical procedure, and during the equilibration time of the second injection. Urine samples were simultaneously fractionally collected. In addition to the isotope measurements serum sodium and potassium as well as urine sodium and potassium were measured on all patients. Saline was not used in the operative field during the two hour study period. Suction blood was collected and assayed for isotope content by differential energy emission as previously described.[30]

Laparotomy packs, sponges, and suction blood were also analyzed for hemoglobin content by washing packs and sponges with distilled water and determining hemoglobin content, as well as estimating blood loss by pack and sponge weights combined with suction blood loss.

A. Control Group

1. Results of the determinations in the control group are summarized in Table 1. It can be seen that the total blood loss in these patients is consistently 200 cc. or less. This agrees with the laparotomy pack and sponge weight estimate of blood loss, as well as by hemoglobin determination on pack and sponge wash water and on the suction blood itself. This was further confirmed by differential isotope counting of the sponges and pack wash fluid as well as suction fluid.

2. In this group of patients the extracellular fluid loss averaged only 1.4 per cent more than the expected decrease in this space from the actual measured and calculated plasma loss. This difference was within the reproducibility of the method of simultaneous space measurements. From this control group of patients it can be seen that the variation in the plasma volume, red blood cell mass, and extracellular fluid volume is less than 3.0 per cent. This has also been determined in normal subjects.[31] Patients 3, 11 and 12 of this group represent spaces done immediately before and after the induction of anesthesia. This was done in order to eliminate the possibility that any variation in space measurements during major operative surgery could be ascribed to the anesthetic agent used.

3. It should be further pointed out that the values for the spaces agree closely with measurements obtained by others utilizing this as well as other substances for measurement of the various spaces.[3-5, 9, 10, 16, 17, 34, 37]

B. Experimental Group

1. The results of the determinations in this group are summarized in Table 2. The measured total blood loss in this group of patients varied from a minimum of 215 cc. during the course of the cholecystectomy to a maximum of 968 cc. during the performance of a subtotal gastric resection. Again this agrees with blood loss predicted from laparotomy pack and sponge weights as well as by hemoglobin determination on pack and sponge wash water and on suction blood. This estimated blood loss was

TABLE 3

Patient	Age, Sex	Race	Wt. (kg.)	Procedure	Anesthetic	Trauma Degree
4	30 F	C	102	Cholecystectomy	N_2O-cyclopropane	8
5	66 M	W	76	Colectomy	Pentothal, ether, cyclopropane	5
8	37 F	C	60	Cholecystectomy	Pentothal, Anectine, C_3H_6, ether	8
9	65 F	W	60	Cholecystectomy	Pentothal, cyclopropane, ether	3
10	64 F	W	62	Laminectomy	Pentothal, Anectine, N_2O, Trilene	4
13	74 F	W	75	Excision of mesenteric cyst & cholecystectomy	Pentothal, Anectine, N_2O, Fluothane	4
14	48 F	LA	70	Cholecystectomy	2% Pentothal, C_3H_6, ether	3
15	31 M	W	76	Subtotal gastrectomy	Pentothal, Anectine, cyclopropane, ether, N_2O	5
16	39 M	W	70	Subtotal gastrectomy	Pentothal, C_3H_6, ether	5
17	49 F	W	70	Cholecystectomy	Ether, cyclopropane, pentothal	3
18	42 F	W	75	Cholecystectomy	Pentothal, cyclopropane, ether-O_2, Anectine	4
19	30	C	60	Cholecystectomy	Pentothal, C_3H_6, ether	2

also confirmed by differential counting of the wash fluids as previously described.

2. In this group of patients the loss of extracellular fluid volume varied from the low of 0 to a high of 28 per cent of the original total body extracellular fluid. It can be seen from Table 2 that there is no linear correlation between the actual blood loss and the amount of the functional extracellular fluid loss. Further it could be seen that the sponge loss of $S^{35}O_4$ tagged extracellular fluid approximated only that which would be expected to appear as plasma loss alone.

3. The urinary loss of isotopes was measured during the isotope equilibration time. The volume distribution determinations were calculated according to the formula: amount injected-minus the amount excreted divided by the concentration in the space being measured.[37]

4. In addition the wound and urinary loss of isotopes during the entire surgical procedure was measured; however, the actual loss of any isotope by either route does not interfere with volume measurements since the reinjection technic was employed.

5. It can be seen from Table 3 that there was a marked difference in the estimated degree of trauma during the various procedures reported. We have attempted to grade the degree of trauma in similar procedures with particular regard to the observed amount of necessary retraction, difficulty in exposure and depth of anesthesia. It would appear from the functional loss of extracellular fluid observations that the only factor which could be seen to correlate

with the degree of loss of functional extracellular fluid was the amount of trauma involved. This generally followed a pattern of increasing functional loss of extracellular fluid with increasing trauma.

6. The determinations of serum electrolytes are summarized in Table 4. It can be seen that despite the demonstrated change in extracellular fluid volume that serum sodium and potassium concentrations stay within the normal range. It is concluded from these studies that loss of extracellular fluid was essentially a loss of isotonic fluid.

Discussion

The decreased renal excretion of sodium is a well documented feature of the postoperative state.[19, 23, 25, 38] Functional extracellular fluid volume has been recently shown to be a major determinant of renal sodium excretion in the normal individual.[7, 32, 35] The decrease in this portion of the body fluid might well represent a major physiological stimulus to postoperative sodium retention, as has been previously postulated.

Previous measurements of the total extracellular fluid volume have usually shown postoperative enlargement of the extracellular fluid volume by the methods used.[1, 6, 21, 33] However, these determinations were made after the changes in extracellular fluid volume might have occurred, and in addition were limited in the accuracy of acute volume changes by the methodology which was available at that time.

As pointed out previously,[37] the total extracellular space is somewhat larger than the functional extracellular space. It has been demonstrated that acute measurements of the extracellular space by $S^{35}O_4$ represent the functional, or physiologically active, extracellular space.

The present data demonstrate a marked reduction in the $S^{35}O_4$ space in response to the acute trauma of operation. This could be explained by either: 1) External loss from the body by such routes as whole

TABLE 4. *Control*

Patient	Preop. Na	Preop. K	Postop. Na	Postop. K
3	140	4.5	139	4.8
12	144	5.0	142	5.1
22	139	4.6	141	4.6
Experimental				
4	144	4.6	140	4.5
5	135	4.8	139	5.0
8	136	4.4	136	4.5
9	138	5.1	139	5.0
10	142	4.2	142	4.2
11	142	4.8	139	4.9
12	139	5.0	140	4.7
14	145	4.7	143	4.9
16	136	4.6	138	4.9
17	139	5.1	136	5.1
19	140	4.9	140	4.8

blood loss, plasma oozing, or by drainage of ultrafiltrate in some fashion such as drainage from the operative site; or 2) Internal redistribution or sequestration into an area where $S^{35}O_4$ no longer equilibrates with the extracellular pool.

The data presented would indicate that the possibilities enumerated in the first hypothesis alone are untenable; consequently it is believed that the apparent descrease in functional ECF must be due to internal redistribution. This would appear to be in 1) the tissue adjacent to the surgical wound; 2) translocated into an area where salt tends to be sequestered such as in the splanchnic bed; or 3) intracellular. Studies are currently in progress to elucidate the nature of this translocation.

In the present study the reduction of functional extracellular fluid which has been shown to occur during the operative procedure is independent of whole blood loss. The only factor observed which would tend to influence the degree of functional extracellular loss was the magnitude of the local trauma. It can be seen, for example, that Patient 9, who was an elderly, but thin, 60-kilogram woman undergoing cholecystectomy, required no wound retractors (Table 2, 3). As a result she sustained 362 cc. whole blood loss and functionally decreased her extracellular fluid volume 7.0 per cent of its original value. Patient 8, (Table 2, 3) on the other hand was a 60-kilogram, young, but obese woman who underwent cholecystectomy with similar (498 cc.) whole blood loss. This patient required continuous wound retraction, was in light surgical anesthesia on several occasions, and consequently presented difficult operative exposure throughout the procedure. In this individual the reduction of extracellular fluid volume is seen to be 28 per cent of the original value.

The perception of a diminished functional extracellular fluid volume and the pathways of the mediation to the kidney are still unknown in both the normal subject and in the surgical patient.[7, 32, 35] Previously demonstrated increased adrenal cortical activity in response to major operative trauma [8, 13, 14, 18, 24, 27] often has been implicated as the cause of postoperative sodium retention.[6, 11, 15, 19, 22–24] However, several recent studies, including measurements in animals and man who have been previously adrenalectomized, show that the renal response to change in volume remains relatively unchanged.[7, 29] Similarly, the response to standarized trauma in adrenalectomized animals receiving constant doses of adrenal cortical replacement differ in no way from non-adrenalectomized animals undergoing similar trauma.[12] One patient with unequivocal Addison's disease has been studied in regard to response to operation and again demonstrated the usual postoperative decrease in natriuresis.[26] Further, this decrease in natriuresis could be overcome by preoperative salt loading.

It has been shown that there is an increase in aldosterone secretion in response to major operative surgery.[20] Again following adrenalectomy, where there is no increase in aldosterone output in response to operation, the postoperative changes which occur are similar. While aldosterone may well play an intermediate role in the normal response to major operative trauma, it has been shown that all adrenal cortical hormones which are increased in response to major operative surgery can be eliminated and the renal response to trauma remains the same. It has also been shown quite recently that a contraction in extracellular fluid volume is in itself a strong stimulus for aldosterone secretion [36] and that this may be the major initiating factor for the observed increase in urinary aldosterone in major operative surgery.

Present evidence indicates that there is an increase in the antidiuretic hormone secretion (ADH) which may result from a number of factors including pain, emotion, etc.[35] Strauss has demonstrated that a decreased functional extracellular fluid volume is an effective stimulus for the increased secretion and output of the antidiuretic hormone.

In summary, one feels justified in postulating that many of the observed alterations in hormonal output, renal responses and compensatory efforts to correct extracellular fluid volume in the postoperative period can be ascribed to a progressive marked diminution in functional extracellular fluid incurred by the operative trauma itself.

Summary and Conclusions

1. Patients undergoing minor operative surgery were used as controls and patients undergoing major operations were studied as experimental subjects in measurements of acute changes in body fluid equilibria during the operative procedure.

2. The technic employed was a new method for the simultaneous measurement of plasma volume, red blood cell mass, and extracellular fluid volume so designed that these volumes could be measured on two occasions during the operative period. This consisted of the use of I^{131} (RISA) tagged serum albumin, Chromate ^{51} tagged red blood cells, and S^{35} sodium sulphate,

with re-injection of all isotopes after two hours.

3. The data indicated marked reduction in functional extracellular fluid occurring during a major operative procedure.

4. The loss of isotonic functional extracellular fluid could not be located as on external loss, and is therefore presumed to be largely an internal redistribution.

5. The magnitude of the internal redistribution of extracellular fluid was not related to whole blood loss, but seemed to be directly related to the degree of surgical trauma from the standpoint of degree and duration of retraction and ease of operative exposure.

6. These data support the hypothesis that a major stimulus to postoperative limitations of sodium excretion is an acute contraction of functional extracellular fluid incurred by the surgical procedure itself.

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