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A RETROSPECTIVE ANALYSIS OF CUMULATIVE FLUID BALANCE AND ITS EFFECT ON RECOVERY IN PATIENTS WITH WHIPPLES SURGERY.

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ABSTRACT

Introduction- Large amount of fluid is administered in whipples owing to its long duration of surgery and major resection of pancreas and gastrointestinal structures. Excessive fluid may lead to cellular swelling ,disruption of renal architecture and tension in the renal capsule leading to AKI. Thus the primary objective of the study was to study the effect of positive cumulative fluid balance on development of postoperative Acute kidney injury (AKI) and length of intensive care stay (ICU). Secondary objective was to find the effect of positive fluid balance on development of sepsis and surgical complications.

Methodology- A retrospective analysis was conducted in 106 patients undergoing whipples surgery.

Results- Cumulative fluid balance in first 24 hours was 6.5 ± 1.9 litres. Acute kidney injury occurred in 20.6% of patients. On bivariate analysis, older age, longer duration of surgery and the highest lactate were found to be statistically significantly associated with the development of acute kidney injury. The same factors were also found significant in the multivariate analysis for development of AKI.

Conclusion- Increased positive cumulative fluid balance at 24 hours did not increase the development of AKI or increased the length of intensive care stay in patients undergoing whipples surgery .

KEYWORDS :

INTRODUCTION

Whipples surgery incurs major fluid shifts owing to its long duration of surgery and major resection of pancreas and gastrointestinal structures. This may lead administration of large amounts of fluid to maintain haemodynamic stability. As such the amount of fluid administered in any major abdominal surgery ranges from 5 to 30 ml/kg/hour depending on the discretion of anaesthetic conducting the case. Many dynamic monitoring techniques such as PPV, SVV, transesophageal echocardiography have evolved over the static methods of assessment of fluid responsiveness such as heart rate, Central venous pressure, urine output and give a better assessment of whether the patient needs fluid or vasopressors.[1] Despite these new techniques , anaesthetist generally end up giving large volumes of fluid to maintain haemodynamic stability. Administration of excessive fluid may cause cellular swelling and may adversely affect the outcomes and may increase the overall length of stay in both intensive care unit and hospital. There is a controversy as to the fluid management leading to development of acute kidney injury as an excessive restriction may lead to prerenal failure and an excessive fluid administration may lead to tension in the renal capsule due to it non distensible nature.[2] Thus fluid administration is still not well defined for whipples surgery.

Whipples surgery has a morbidity of 17 to 44 % and there are very few studies are there for the effect of amount of perioperative fluid administered on the postoperative complications. None of the studies has seen if increased cumulative fluid balance on day 1 increased the development of AKI and increased the length of intensive care stay leading to poorer outcome of the patient. Thus the aim of this study was to see the effect of positive cumulative fluid balance on development of postoperative AKI and length of intensive care stay.

METHODOLOGY

After approval by the Institute of liver and biliary sciences institutional ethics board, a retrospective analysis was conducted. A total of hundred and six patients of ASA grade 1,2 and 3 were studies between age of 18 to 65 years who underwent whipples surgery between 2014 to 2016 were taken for the study. Patients with body mass index > 30, significant arrhythmias, cardiopulmonary dysfunction, pregnant patients, patients with incomplete records, significant pre-existing renal or liver diseases, pre-existing coagulopathic patients were excluded from the study.

All the charts and electronic files were reviewed by a single observer. Anaesthesia was administered by standard technique of general anesthesia with epidural insertion for all patients. Initially after consent of patient, epidural is inserted anywhere between 6th thoracic intervertebral state to 11 th thoracic intervertebral level. For general anesthesia propofol 1.5 to 2 mg/kg , fentanyl 1- 1.5 micrograms/ kg along with atracurium 0.5 ug /kg is administered. After tracheal intubation , arterial and central line were inserted. Normal saline or ringer lactate was used at our centre as maintenance fluid with the discretion of anaesthetist for the type and amount of fluid. For colloid hexa ethyl starch was used. In epidural 0.1 % bupivacaine infusion was given to all patient and continued in the postoperative period till 48 hours.

The intraoperative fluid balance is calculated by adding the total amount of crystalloid, the total amount of colloid and the amount of blood products (Packed red blood cells, fresh frozen plasma, cryoprecipitate, platelets) given minus the urine output and blood loss. For cumulative fluid balance at day 1 the intraoperative fluid balance was added to postoperative fluid balance on day 1 (crytalloid , colloid and blood products given on day one minus the urine output) given on day one after surgery.

Data collected was cumulative fluid balance on day one post surgery, demographics, preoperative albumin levels, AST, ALT, duration of surgery, Acute kidney injury (defined according to Kidney disease improving global outcome ie KDIGO criteria[3]), surgical complications (Delayed gastric emptying, re-exploration, Postoperative pancreatic fistula, surgical site infection), sepsis, length of Intensive care and hospital stay.

The primary objective of the study was to determine if a positive perioperative fluid administration led to increased development of acute kidney injury and increased the duration of intensive care stay. The secondary objective of the study was to study the effect of perioperative fluid on development of sepsis and surgical complications.

STATISTICAL ANALYSIS

Descriptive statistics were presented in the form of mean± standard deviation for continuous variables and in the form of frequencies and their percentages for categorical variables. Bivariate associations between categorical variables were assessed using Chi-square test or Fisher's exact test, whichever is applicable. To test the difference in mean values between two groups independent samples t-test were used. For determining factors associated with various binary outcomes such as lung complications status , AKI status, surgical complications status and sepsis logistic regression analyses were used. Linear regression models were used to identify factors associated with the length of ICU and hospital stays. Results of logistic regression analyses were reported in the form of odds ratios and their 95% Confidence Intervals (CIs). A p-value of less than 0.05 was considered as statistically significant. All the analyses were done using SPSS version 21.

RESULTS

One hundred and seven patients were included in the study. The mean age of the patients included in the study was 54.1 ± 11.5 years. The mean intraoperative fluid balance was 5218.1 ± 1762.0 ml of which mean colloid usage was 2500.6 ± 2087.9 ml. The mean cumulative fluid balance in first 24 hours was 6000 ± 900 ml. Other demographic, preoperative and intraoperative findings are presented in table 1.

Acute kidney injury occurred in 20.6% of patients. The mean length of ICU stay was 3.6 ± 2.7 days and of hospital stay was 14.0 ± 7.9 days. (Table1)

Table 1: Characteristics of patients

Factor	Descriptive statistic (n=107)
Age (years)	54.1 ± 11.5
Sex male/ female	76/30
Body mass index	22.9 ± 3.5
Diabetes mellitus	42 (40.4%)
Hypertension	47 (45.2%)
Duration of surgery (hours)	9.3 ± 2.1
ASA 1/2/3	20/56/31
Haemoglobin	11.5 ± 1.8
Urea	28.3 ± 16.5
Creatinine	0.8 ± 1.8
SGOT	74.5 ± 56.8
SGPT	82.9 ± 110.1
Sodium	136.8 ± 4.3
Albumin	3.0 ± 0.9
Intraoperative variables	
Blood loss (litres)	0.6 ± 0.3
Interoperative fluid balance (litres)	5.2 ± 1.8
Cumulative fluid balance at 24 hours (litres)	6.5 ± 1.9
Total colloid used (litres)	2.5 ± 2.1
Highest lactate	3.2 ± 1.5
Number of Blood products	0.8 ± 1.4
Mortality and morbidity	
AKI	22 (20.6%)
Sepsis	19 (17.9%)
Mortality	6 (5.6%)
Length of ICU (days)	3.6 ± 2.7
Length of Hospital (days)	14.0 ± 7.9

Data presented as mean± SD, AKI= acute kidney injury

On bivariate analysis, older age, longer duration of surgery and the highest lactate were found to be statistically significantly associated with the development of acute kidney injury (Table 2). The same factors were also found significant in the multivariate analysis (Table 2 and 6)

Table 2: Association of various factors with AKI

	AKI present (22)	AKI absent (85)	p-value
Age (years)	59.6 ± 8.2	52.6 ± 11.9	0.011*
Sex male/female	18/3	58/27	0.11
Body Mass Index	21.9 ± 3.5	23.2 ± 3.5	0.11
Diabetes Mellitus	9 (41%)	33 (40%)	0.95
Hypertension	7 (32 %)	40 (49%)	0.16
Duration of surgery (hours)	10.3 ± 2.5	9.1 ± 2.0	0.024*
ASA1/2/3	4/14/4	16/42/27	0.41
Haemoglobin	11.2 ± 2.0	11.5 ± 1.8	0.48
Urea	30.9 ± 13.6	27.6 ± 17.2	0.41
Creatinine	0.6 ± 0.3	0.9 ± 2.0	0.53
SGOT	74.4 ± 40.2	74.5 ± 60.6	0.99
SGPT	71.8 ± 47.2	85.8 ± 121.3	0.60
Sodium	135.7 ± 4.5	137.1 ± 4.2	0.18
Albumin	2.86 ± 0.45	3.09 ± 0.93	0.27
Blood loss	629.5 ± 334.8	627.7 ± 341.6	0.98
Intraoperative FB	5182.7 ± 1787.5	5227.3 ± 1766.0	0.92
Cumulative FB	6549.7 ± 1717.3	6484.9 ± 1911.8	0.89
Total colloid	2593.9 ± 2050.0	2476.5 ± 2108.9	0.82
Highest lactate	3.8 ± 2.0	3.0 ± 1.3	0.026*
Blood products	1.1 ± 1.5	0.7 ± 1.4	0.23

Data presented as mean± SD, * P< .05, FB = fluid balance

For sepsis age, lesser preoperative sodium and total blood products used were significant in bivariate analysis.(Table 3) These factors were also found significant on the multivariate analysis. (Table 5)

Table 3: Association of various factors with sepsis and surgical complications

	Sepsis Present (19)	Sepsis Absent (87)	p-value
Age (years)	58.6 ± 7.8	53.0 ± 12.0	0.055
Sex male/ female	16/2	60/27	0.085
Body mass index	22.2 ± 2.8	23.1 ± 3.6	0.29
Diabetes mellitus	8 (44%)	34 (40%)	0.73
Hypertension	9 (53%)	38 (44%)	0.51
Duration of surgery (hours)	9.6 ± 1.7	9.3 ± 2.2	0.54
ASA 1/2/3	2/10/7	18/45/24	0.52
Haemoglobin	10.8 ± 2.0	11.6 ± 1.8	0.091
Urea	28.8 ± 16.2	28.2 ± 16.6	0.89
Creatinine	0.7 ± 0.2	0.9 ± 2.0	0.73
Bilirubin	5.1 ± 5.9	3.8 ± 5.5	0.35
SGOT	61.9 ± 34.3	77.2 ± 60.4	0.29
SGPT	51.8 ± 32.9	89.7 ± 119.6	0.18
Sodium	134.3 ± 4.8	137.4 ± 4.0	0.004*
Albumin	2.80 ± 0.50	3.09 ± 0.91	0.18
Blood loss (ml)	612.6 ± 331.3	631.4 ± 342.0	0.83
Interoperative fluid balance	5310.3 ± 1440.4	5197.9 ± 1831.4	0.80
Cumulative fluid balance	6678.3 ± 1396.5	6459.1 ± 1957.5	0.64
Total colloid (ml)	1781.8 ± 1577.3	2686.3 ± 2151.9	0.086
Highest lactate	3.7 ± 2.3	3.1 ± 1.2	0.16
Blood products	1.5 ± 2.0	0.7 ± 1.2	0.017*

ml= millititres, Values presented as mean ±SD, * P< .05

For surgical complications females, greater ASA grade, higher urea, greater SGOT, SGPT, greater intraoperative blood loss, intraoperative fluid balance, fluid balance in first 24 hours and total colloid were found significant in bivariate analysis. (Table 4) On multivariate analysis only total intraoperative colloid (OR 0.513, 95% CI 0.346 - 0.760) was found to be significant. (Table 5)

Table 4: Association of various factors with surgical complications

Factor	Surgical complications		
	Yes (68)	No (39)	p-value
Age (years)	52.9 ± 12.0	56.1 ± 10.6	0.17
Sex			0.005*
Male	55 (81%)	21 (55%)	
female	13 (19%)	17 (45%)	
Body mass index	23.0 ± 3.2	22.9 ± 3.9	0.89
Diabetes mellitus	25 (37%)	17 (46%)	0.39
Hypertension	32 (48%)	15 (39%)	0.37
Duration of surgery (hours)	9.3 ± 2.2	9.4 ± 2.1	0.92
ASA 1/2/3	17/37/14	3/19/17	0.013*
Haemoglobin	11.5 ± 1.9	11.4 ± 1.7	0.67
urea	30.9 ± 16.3	23.7 ± 16.0	0.030*
Creatinine	0.7 ± 0.2	1.1 ± 3.0	0.21
Bilirubin	3.4 ± 5.4	5.1 ± 5.9	0.12
SGOT	64.2 ± 28.6	92.9 ± 84.5	0.012*
SGPT	60.7 ± 50.8	122.6 ± 164.9	0.005*
Sodium	137.4 ± 4.2	135.8 ± 4.2	0.064
Albumin	2.95 ± 0.77	3.21 ± 0.97	0.13
Blood loss (ml)	679.5 ± 346.1	536.1 ± 308.0	0.036*
Interoperative fluid balance	5525.8 ± 1838.6	4667.5 ± 1484.7	0.015*
Cumulative fluid balance	6663.0 ± 1939.7	6203.7 ± 1709.8	0.23

Total colloid (ml)	3235.9 ± 2194.0	1218.6 ± 1009.0	<0.001*
Highest lactate	3.3 ± 1.3	3.0 ± 1.8	0.26
Blood products	0.9 ± 1.6	0.7 ± 1.1	0.60

Values presented as mean ±SD, * P< .05

One univariate regression, length of ICU stay and length of hospital stay were found to be significantly prolonged by higher ASA grading, higher bilirubin, lower preoperative sodium level, higher intraoperative lactate, lesser intraoperative colloid use while higher fluid balance in first 24 hours of surgery increased the total duration of ICU stay and higher intraoperative fluid balance led to increased length of hospital stay. (Table 5)

Table 4: Bivariate association of various factors with the length of ICU stay and the length of hospital stay

Factor	Length of ICU stay		Length of hospital stay	
	Beta	95% CI	Beta	95% CI
Age	0.0335	[-0.01,0.08]	0.0527	[-0.08,0.18]
Male	0	[0.00,0.00]	0	[0.00,0.00]
Female	-0.0322	[-1.20,1.14]	3.211	[-0.12,6.54]
BMI	-0.0476	[-0.20,0.10]	-0.377	[-0.81,0.06]
Diabetes Mellitus present	-0.614	[-1.68,0.45]	0.934	[-2.10,3.97]
DM absent	0	[0.00,0.00]	0	[0.00,0.00]
Hypertension present	-0.214	[-1.26,0.84]	-1.198	[-4.29,1.89]
Hypertension absent	0	[0.00,0.00]	0	[0.00,0.00]
Duration of surgery	0.157	[-0.09,0.40]	0.427	[-0.28,1.13]
ASA 1	0	[0.00,0.00]	0	[0.00,0.00]
ASA 2	1.414*	[0.05,2.78]	5.209**	[1.32,9.10]
ASA 3	1.844*	[0.35,3.34]	6.926**	[2.65,11.20]
Haemoglobin	0.0366	[-0.25,0.32]	0.983*	[0.18,1.79]
urea	-0.0306	[-0.06,0.00]	-0.134**	[-0.22,-0.05]
Creatinine	-0.144	[-0.43,0.15]	0.334	[-0.51,1.18]
Bilirubin	0.131**	[0.04,0.22]	0.360**	[0.10,0.62]
sgot	0.00375	[-0.01,0.01]	0.00478	[-0.02,0.03]
sgpt	0.00073	[-0.00,0.01]	0.00402	[-0.01,0.02]
sodium	-0.160**	[-0.28,-0.04]	-0.542**	[-0.88,-0.20]
albumin	-0.0854	[-0.70,0.53]	0.520	[-1.26,2.30]
Blood loss	-0.624	[-2.16,0.91]	-3.916	[-8.34,0.51]
Interoperative Fluid Balance	-0.0814	[-0.38,0.21]	-0.990*	[-1.83,-0.15]
Cumulative Fluid Bbaalnce	0.0641	[-0.22,0.34]	-0.61	[-1.42,0.20]
Fluid balance 24hr	0.654*	[0.05,1.25]	1.307	[-0.46,3.07]
Total colloid	-0.447**	[-0.68,-0.21]	-1.862**	[-2.50,-1.23]
Highest lactate	0.359*	[0.00,0.72]	-0.7	[-1.72,0.32]
Blood products	0.0413	[-0.32,0.41]	-0.166	[-1.23,0.90]

Table 5: Results of multivariate analysis showing independent factors associated with various postoperative complications, and the length of ICU and hospital stays

Complication	Odds Ratio/Beta	95% CI
AKI[2]	**Odds Ratio**	
Age	1.070*	[1.013,1.131]
Duration of surgery	1.361*	[1.035,1.788]
Highest lactate	1.484*	[1.025,2.147]
Sepsis[3]	**Odds Ratio**	
Sodium	0.832**	[0.729,0.950]
Total blood products given	1.462*	[1.051,2.033]
Length of ICU stay[5]	**Beta**	
Total colloid used	-0.370**	[-0.63,-0.11]
Highest lactate	0.580**	[0.24,0.92]
Length of hospital stay[6]	**Beta**	
ASA grade 3	4.214*	[0.08,8.35]
Total colloid used	-1.443**	[-2.32,-0.57]

On multivariate analysis, the length of ICU stay is found to decrease by 0.370 (95% CI 0.11 - 0.63) days per every one litre increase in the total colloid used. (Table 6) Similarly, for every one unit increase in highest lactate the length of ICU stay is found to increases by 0.580 (95% CI 0.24 - 0.92) days. Likewise, patients with ASA grade 3 have on an average 4.2 additional days of hospital stay (95% CI 0.08 - 8.35) than those with ASA grade 1, and with every unit litre increase in total colloid used the length of hospital stay is found to decrease by 1.4 days (95% CI 0.57 - 2.32).

DISCUSSION

The major findings of the study were, the total colloid used decreased the surgical complications, length of intensive care and hospital stay however, the perioperative fluid balance did not effect the development of complications and length of ICU stay. The length of ICU stay is found to decrease by 0.370 (95% CI 0.11 - 0.63) days per every one litre increase in the total colloid used. Another finding that patients with lower preoperative sodium had increased the development of sepsis and increased the length of intensive care stay.

Weingberg et al noted a total complication rate of 57% which included both surgical and medical complications.[4] They found a mean fluid of 2.1 litres on postoperative day 1 was associated with development of more complications though they commented on complications in total rather than individual complications.

Similarly Wright et al concluded increased morbidity in patients who received increased fluid in the postoperative fluid balance .[5] They divided the patients in four quartiles as per the increasing amount of fluid they received on day 1, 2, 3 in the postoperative period. An association was found between those who received more fluid in 48 and 72 hours postoperatively. Also increased intraoperative fluid was associated with more cardiopulmonary events at 0, 24 and 48 hours postoperatively. However in our study we did not find any association of complications to fluid, but we took into account only fluid administered till 24 hours and not till 72 hours postoperatively. Also their study mentions decreased morbidity with increasing use of colloid which was similar to finding of our study.

In our study we found a decrease in the total length of intensive care unit and hospital stay by increased use of colloid, however, in a study conducted by Kabon et al, administering colloid over crystalloid did not decrease cardiac, pulmonary, infectious , gastrointestinal, renal or coagulation abnormality or 30 day mortality.[6] Similarly another study did not find any difference in mortality or major complications with use of HES and >9% normal saline or only .9 % normal saline.[7]

Another significant finding in our study is presence of preoperative hyponatremia in patients developing postoperative sepsis. It was also associated with a longer ICU and hospital stay. Leung et al also demonstrated the presence of preoperative hyponatremia and increased development of pneumonia, major coronary events, wound site infection and to increase in length of hospital day by one day.[8] Another study found both hyponatremia and hypernatremia increased the admission to intensive care unit after surgical procedure, increased the chances of mechanical ventilation, requirement of intraoperative ionotropic support and mortality, however after adjusting for confounding variables, only hypernatremia was reported to increase the incidence of mortality.[9] Hyponatremia maybe a consequence of pneumonia and sepsis but has not been studied as a measure of predisposition of the same.[10] Acute stress after surgery such as pain, nausea, anaesthetic agents, and drugs may cause release of IL 6 and subsequent non osmotic release of vasopressin leading to hyponatremia. Thus hyponatremia is common after surgery specially in patients with anastomotic leak.[11] The association of hyponatremia in preoperative period to postoperative development sepsis, may point to an indirect indicator of at risk patients and these patients may need extra precaution for development of these complications.

The major limitation of our study is its retrospective design. Due to this few confounding factors leading to development of AKI may have been missed. AKI, certain surgical complication such as pancreatic leak may themselves lead to increased fluid retention and thus may increase fluid demand in some patients. Thus an increased fluid administration may actually be due to the disease itself rather than be a cause for the development of AKI, which cannot be ruled out in a retrospective analysis. Additionally the fluid administration regime was not standardized and depended on the discretion of anaesthetist conducting the case.

CONCLUSION

Perioperative fluid management did not effect the development of acute kidney injury or length of intensive care or hospital stay. However administration of colloid decreased the development of sepsis and the length of intensive care stay. More prospective multicentric trials are needed to conclude these findings and to use them in clinical practice.

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