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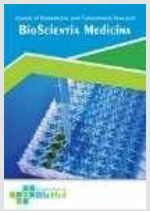

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Intraoperative Fluid Management Correlates with Intraoperative Complications in Cesarean Section: A Prospective Clinical Trial

Michael Humianto[1]*, Marilaeta Cindryani[1], Tjokorda Gde Agung Senapathi[1]

[1]Department of Anesthesiology and Intensive Therapy, Faculty of Medicine, Universitas Udayana/Prof. Dr. I.G.N.G. Ngoerah General Hospital, Denpasar, Indonesia

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***Corresponding author:**
Michael Humianto

E-mail address:
humianto.michael@gmail.com

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A B S T R A C T

Background: This study focused on perioperative fluid administration in pregnant women undergoing a caesarean section (CS) by comparing liberal and non-liberal fluid administration in a multicentre setting across various Hospitals in the Bali province and its surrounding areas. **Methods:** Sampling was conducted using a total sampling method. All patients meeting the inclusion criteria were included in this study. A total of 310 samples of pregnant patients undergoing CS surgery in various operating rooms across hospitals in the Bali province and surrounding areas were obtained during the period of January to December 2022. The fluid administration strategy was divided into two types: liberal and non-liberal. Data analysis was performed using the Chi-square test with the correlation test of the contingency coefficient. **Results:** The results showed that liberal fluid administration significantly increased complications in the operating room for pregnant patients undergoing cesarean section ($p<0.001$; $r=0.305$; OR 6.22) but not in the recovery room or postoperative hospital ward. **Conclusion:** Liberal fluid administration could significantly increase complications in the operating room for pregnant patients undergoing cesarean section but not in the postoperative period.

1. Introduction

The appropriate fluid administration in patients undergoing surgery remains controversial. Fluid administration should be considered a pharmacological treatment and aims to achieve an effective plasma volume while ensuring optimal total intraoperative fluid.[1] Generally, there are three strategies for perioperative fluid management: liberal, restrictive, and goal-directed.[2,3] Administering large amounts of fluids can increase the occurrence of cardiac and pulmonary complications, as well as tissue healing factors. On the other hand, fluid restriction can also cause adverse effects, such as kidney failure. Goal-directed therapy (GDT) is a strategy that considers individual needs to achieve better overall outcomes, aiming to maintain peripheral oxygen delivery while preventing fluid overload.[4] Pregnancy causes dynamic changes in the total body fluid, occurring immediately after conception, which drastically changes following delivery.[5] This causes a significant impact on fluid management. A slight fluid overload in pregnant women can cause fatal complications, such as pulmonary edema.[5,6] This study focused on the administration of perioperative fluid strategy in pregnant patients. This study aims to determine the best fluid administration strategy for pregnant patients. We compared liberal and non-liberal fluid administration in a multicenter setting

across various Hospitals in the Bali province and its surrounding areas.

2. Methods

This cross-sectional study used a descriptive-analytical approach, including a correlation analysis of the amount of crystalloid fluid administration and the occurrence of complications in the operating room, recovery room, and postoperative hospital ward. The inclusion criteria for this study included all patients scheduled for caesarean section (CS) surgery in the operating rooms of various hospitals in the Bali province and its surrounding areas. Exclusion criteria for this study included patients who had the CS procedure canceled, patients who passed away before the surgery, and patients with comorbidities involving pulmonary diseases. The study population comprised all patients scheduled for CS surgery during the research period. Sampling was conducted using a total sampling method; all patients meeting the inclusion criteria were included in this study. A total of 310 samples of pregnant patients who were undergoing CS in various operating rooms across hospitals in the Bali province and surrounding areas were obtained during the period of January to December 2022. The fluid administration technique was divided into two types: liberal and non-liberal. Liberal fluid administration includes fluid replacement for various components, such as intravascular expansion due to anesthesia, fasting fluid deficit, physiological body maintenance, third space redistribution, and bleeding.[8] On the other hand, restrictive fluid administration involves partial or no replacement of intravascular expansion due to anesthesia, no fluid replacement for third space loss, and partial fluid replacement for fasting fluid deficit. Maintenance of physiological fluid balance and handling bleeding are similar in both liberal and restrictive techniques.[9]

The allocation of these techniques was based on the definition of fluid administration techniques, and adjustments were made for various confounding factors that could introduce bias into the study, including weight, height, body mass index, fasting before anesthesia, duration of surgery, as well as blood loss and urine volume during the surgery. The data obtained were analyzed using SPSS for Windows 25. Once the data were collected, data processing was performed, followed by a descriptive analysis of the population characteristics. In this study, we observed the effects of fluid administration on the occurrence of complications in the operating room, such as dyspnea, desaturation, hemodynamic changes, hypothermia, and various other complications that were found in the operating room. We also observed complications occurring in the recovery room up to 24 hours post-operation in the post-operative ward. We recorded all types of fluids given, the amount of fluids administered, and the use of blood components. Furthermore, a 2x2 table-based descriptive analysis was conducted using the chi-square test for three components of the study: the technique of fluid administration in relation to complications in the operating room, post-operative recovery room, and post-operative hospital ward.

3. Results

A total of 310 pregnant women undergoing CS in various Hospitals in the Bali province and its surrounding areas were obtained. The subjects' age has a median of 29 (IQR 10) in the liberal fluid administration group and 30 (IQR 7) in the non-liberal group. Based on the pregnant subjects' Body Mass Index (BMI), most subjects were in the normal category, accounting for 127 subjects with BMI ranging from 18.5 to 24.9. In terms of educational level, the highest number of subjects had completed high school or equivalent (n=186; 60%). Regarding the number of pregnancies, most subjects were experiencing their first pregnancy (n=105; 39%). Based on comorbidities, the highest number of subjects had no comorbidities (n=217; 70%). Based on the surgical indication, the most common indication for cesarean section was a maternal indication (n=135; 43.5%). According to the ASA classification, most subjects had ASA physical status II, accounting for 238 subjects (76.8%), followed by ASA physical status

III with 67 subjects (21.6%), and ASA physical status IV with 5 subjects (1.6%). Regarding the initial anesthesia procedure, the most common was regional spinal anesthesia, with 301 subjects (97.1%).

In this study, the anesthesiologists had the liberty of deciding the fluid administration technique. Based on our data, 179 subjects (57.7%) received liberal fluid administration, while 131 subjects (42.3%) received non-liberal fluid administration. These details are shown in Table 1.

Table 1. Characteristic of patients with liberal and non-liberal fluid administrations.

Variables	Liberal (n= 179)	Non-liberal (n=131)	p-value
Age (years), median (IQR)	29 (10)	30 (7)	0.02
BMI (kg/m²), median (IQR)	26.3 (6.5)	25 (6.7)	<0.001
Current pregnancy			
1	58 (32.4%)	47 (35.9%)	
2	49 (27.4%)	39 (29.8%)	
3	41 (22.9%)	26 (19.8%)	<0.001
4	20 (11.2%)	13 (9.9%)	
>4	11 (6.1%)	6 (4.6%)	
Type of surgery			<0.001
Emergency	63 (35.2%)	62 (47.3%)	
Elective	116 (64.8%)	69 (52.7%)	
ASA physical status			<0.001
1	5 (2.8%)	0 (0.0%)	
2	132 (73.7%)	101 (77.1%)	
3	39 (21.8%)	28 (21.4%)	
4	3 (1.7%)	2 (1.5%)	
Type of anaesthesia			<0.001
General	3 (1.7%)	3 (2.3%)	
Regional	176 (98.3%)	128 (97.7%)	
Intraoperative complications			<0.001
Dyspnea	12 (6.7%)	2 (1.5%)	
Desaturation	6 (3.3%)	1 (0.76%)	
Hypotension	8 (4.5%)	5 (3.8%)	
Hypothermia	37 (20.7%)	2 (1.5%)	
Other complications	2 (1.1%)	1 (0.76%)	
Postoperative complications (<1 h)			<0.001
Dyspnea	2 (1.1%)	1 (0.76%)	
Hypothermia	23 (12.8%)	7 (5.3%)	
Hypotension	6 (3.4%)	6 (4.6%)	
Other complications	4 (2.2%)	1 (0.76%)	
Postoperative complications (1-24 h)			<0.001
Dyspnea	0 (0%)	0 (0%)	
Hypothermia	0 (0%)	0 (0%)	
Hypotension	8 (4.5%)	3 (2.3%)	
Other complications	3 (1.7%))	4 (3.05%)	

Based on the complications that occurred in the operating room, a total of 76 subjects (24.5%) had complications, while 234 subjects (75.5%) did not have any complications. Out of the 76 subjects who had complications, 14 (18.4%) had shortness of breath, characterized by discomfort during breathing, which felt worse than usual. Additionally, 5 subjects (6.5%) had shortness of breath leading to desaturation, and 2 subjects (2.6%) had shortness of breath leading to desaturation, necessitating the conversion of regional anesthesia to general anesthesia. Furthermore, 13 subjects (17.1%) had hypotension, 39 subjects (51.3%) had hypothermia, and 3 subjects (3.9%) had other complications. These details are shown in Table 1. In Table 2, the data revealed that the number of subjects who received liberal fluid administration and had

complications in the operating room was 65 subjects (36.3%), while those who did not have complications were 114 subjects (63.7%). Among the subjects who received non-liberal fluid administration, 11 subjects (8.4%) had complications in the operating room, and 120 subjects (91.6%) did not. Based on these data, we conducted a comparative data analysis. The statistical tests used were the chi-square test and the correlation analysis using the contingency correlation coefficient between the fluid administration technique and the complications that occurred in the operating room. The results indicated a significant relationship between the fluid administration technique and complications in the operating room, with a p-value of <0.001. Additionally, our data was supported by the contingency correlation coefficient value. The fluid administration technique showed a positive correlation with the occurrence of complications in the operating room (r=0.305). Based on statistical analysis, a contingency correlation coefficient exceeding 0.3 signifies clinical significance. Therefore, the fluid administration technique's impact on complications in the operating room is not only statistically significant but also clinically meaningful. The calculated odds ratio (OR) value was 6.22, indicating that subjects who received liberal fluid administration have a 6.22 times higher risk of experiencing complications in the operating room compared to subjects who received non-liberal fluid administration.

In addition to finding a correlation between fluid administration technique and complications in the operating room, we also analyzed the correlation between fluid administration technique and complications in the recovery and post-operative hospital wards. Based on the complications in the recovery room, a total of 40 subjects (16.1%) had complications, and 260 subjects (83.9%) did not. Among subjects with complications in the recovery room, a total of 3 subjects (6%) had shortness of breath, 30 (60%) had hypothermia, 12 (24%) had hypotension, and 5 (10%) had other complications. Based on the fluid administration technique, in subjects who received the liberal administration technique, 35 subjects (19.6%) had complications, and 144 (80.4%) did not, while in the non-liberal fluid administration technique, 15 subjects (11.5%) had complications, and 116 (88.5%) did not. Based on these data, we conducted a comparative analysis using the chi-square test. The results showed that the fluid administration technique did not have a significant relationship with the occurrence of complications in the recovery room, with a p-value of 0.055. Based on the complications in the post-operative hospital ward, a total of 18 subjects (5.8%) had complications, and 292 subjects (94.2%) did not. Based on the fluid administration technique, in subjects who received the liberal administration technique, 11 subjects (6.1%) had complications, and 168 (93.9%) did not; while for subjects who received the non-liberal fluid administration technique, a total of 7 subjects (11.5%) had complications, and 124 subjects did not. Our results showed that the fluid administration technique did not have a significant relationship with complications in the post-operative hospital ward, with a p-value of 0.766. Data are shown in detail in Tables 3 and 4.

Table 2. Data analysis of fluid administration strategies and complications in the operating room.

		Complications in the operating room		**Correlation coefficient (r)**	**Odds ratio (OR)**	**p-value***
		Yes n (%)	**No n (%)**			
Fluid management	Liberal	65 (85,5%)	114 (63,7%)	0,305	6,22 (CI 95% 3,13-12,38)	<0,001
	Non-liberal	11 (14,5%)	120 (91,6%)			
Total		76 (24,5%)	234 (75,5%)			

*p-value obtained using Chi-square statistical analysis.

Table 3. Data analysis of fluid administration strategies and early complications (1-hour) postoperative.

		Complications in the recovery room		p-value*
		Yes n (%)	No n (%)	
Fluid management	Liberal	35 (19,6%)	144 (80,4%)	0,055
	Non-liberal	15 (11,5%)	116 (88,5%)	
Total		50 (16,1%)	260 (83,9%)	

*p-value obtained using Chi-square statistical analysis.

Table 4. Data analysis of fluid administration strategies and late complications (>1 hour-24 hours) postoperative.

		Complications in the hospital ward		p-value*
		Yes n (%)	No n (%)	
Fluid management	Liberal	11 (6,1%)	168 (93,9%)	0,766
	Non-liberal	7 (5,3%)	124 (94,7%)	
Total		18 (5,8%)	292 (94,2%)	

*p-value obtained using Chi-square statistical analysis.

4. Discussion

Perioperative fluid management has been extensively studied, yet the appropriate and accurate fluid volume remains a subject of ongoing debate. In recent years, this debate has led to the creation of two fluid management techniques: liberal and restrictive.[1,2] Liberal fluid administration strategy includes fluid replacement for various components: intravascular expansion due to anesthesia, fasting fluid deficit, physiological body maintenance, third space redistribution, and bleeding.[8] On the other hand, restrictive fluid administration involves partial or no replacement of intravascular expansion due to anesthesia, no fluid replacement for third space loss, and partial fluid replacement for fasting fluid deficit. Maintenance of physiological fluid balance and handling bleeding are similar in both liberal and restrictive techniques.[9]

Various factors influence fluid administration techniques, such as fluid evaporation from the skin, respiratory tract, and the surgical field, as well as the effects of anesthesia drugs leading to hypotension. These factors can lead anesthesiologists and intensive care specialists to either overestimate or underestimate fluid administration, and according to Rocca et al., the only scientifically proven approach is that excessive fluid administration (overload) without clear guidelines is a flawed strategy.[4] Our study showed that most anesthesiologists and intensive care specialists involved in this research still use the liberal fluid technique. Specifically, 179 patients (57.7%) received liberal fluid administration, while 131 patients (42.3%) received non-liberal fluid administration. This is in line with the experimental study by Lamke et al. showed that most doctors tend to overestimate rather than underestimate fluid requirements.[7]

Inappropriate fluid administration strategy can lead to complications in patients undergoing surgery. Our study showed a total of 76 subjects (24.5%) had complications, while 234 subjects (75.5%) did not. In Table 2, the data revealed that the number of subjects who received liberal fluid administration and had complications in the operating room was 65 subjects (85.5%). Out of the 76 subjects who had complications, 14 subjects (18.4%) had shortness of breath, characterized by discomfort during breathing, which felt worse than usual. Out of the 14 subjects with shortness of breath complications, 12 subjects had the liberal technique (85.7%), and 2 subjects had the non-liberal technique (14.3%). Additionally, 7 subjects had shortness of breath leading to desaturation. Among these 7 subjects, 6 had the liberal technique (85.7%), and 1 had the non-liberal technique (0.76%). Furthermore, 2 subjects experienced shortness of breath, leading to desaturation, and required the conversion of regional anesthesia to general anesthesia. Among these 2

subjects, 1 had the liberal technique (50%), and the other had the non-liberal technique (50%). Based on this data, it was found that a total of 16 out of 310 subjects, or 5.1%, experienced pulmonary complications with liberal fluid administration. The results of our analysis using the chi-square test and correlation analysis with the contingency correlation coefficient show that the fluid administration technique is significantly associated with complications in the operating room, with a p-value of <0.001. Furthermore, our data is supported by the contingency correlation coefficient value. The fluid administration technique has a positive correlation with the occurrence of complications in the operating room (r=0.305). Based on statistical analysis, a contingency correlation coefficient exceeding 0.3 indicates clinical significance. These results aligned with the findings of Malbrain et al., indicating that intravascular volume expansion carries risks. Cardiac work and pressure increase when fluid is administered and exceeds the level of vasodilation caused by anesthesia drugs. This vasodilation from the anesthesia drugs may also contribute to the tendency for excessive fluid administration. Furthermore, fluid overload reduces osmotic pressure, coupled with elevated cardiac pressure, ultimately leading to pulmonary edema.[9,10] Malbrain et al. also demonstrated that fluid overload and positive cumulative fluid balance are associated with increased morbidity and worse outcomes due to the occurrence of a normal systemic inflammatory response, which leads to increased capillary permeability and organ dysfunction. This response is a normal reaction of the body during illness or surgical stress. Therefore, fluid overload and interstitial edema can create a vicious cycle.[9,10] So, the impact of fluid administration technique on complications in the operating room is not only statistically meaningful but also clinically meaningful.

In this study, the effect of liberal fluid administration on complications, such as pulmonary edema leading to desaturation and conversion, may seem relatively small, with only 1 patient (1.3%) using the liberal technique. However, it is important to note that the total sample size in this study was only 310 patients. If this were scaled up extensively, the number of patients who could be affected would be significantly larger and substantial due to fluid management errors. These results aligned with the statement by Natarajan et al., which highlights that even slight fluid excess in pregnant women can lead to fatal complications such as pulmonary edema.[7] This is because pregnancy can cause physiological changes that significantly impact fluid dynamics and subsequently affect fluid management. Plasma volume increases about 15% during the first trimester, then rapidly increases in the second trimester to 50-55%, and then remains constant until the end of the pregnancy. These changes lead to increased blood volume of approximately 45%. Another important factor influencing fluid dynamics in pregnant women is oncotic pressure, which decreases the level of albumin in pregnant women, thus increasing the likelihood of interstitial edema. Our research results are also consistent with Malbrain et al., who found a significant correlation between liberal fluid administration on the day of surgery and worse outcomes, as well as an increase in total cost and length of hospital stay for all patients undergoing ileus or colorectal surgery.[9,10] Fluid overload can cause “resuscitation morbidity,” which is a combination of complications resulting from fluid overloads, such as impaired tissue healing, delayed return of gastrointestinal function, pulmonary edema, compartment syndrome in the extremities, orbital compartment syndrome, intraabdominal hypertension up to abdominal compartment syndrome, and in the worst case, multi-organ failure.[8]

On the other hand, a study by Myles et al. showed different results, which showed that a restrictive fluid administration strategy is associated with an increased incidence of acute kidney failure (p<0.001) and surgical-site infection (p 0.02). The study concluded that fluid administration strategy should avoid excessive positive fluid balance while also carefully avoiding under-resuscitation.[12] Nonetheless,

a study by da Silva et al. in 2020 showed that restrictive fluid administration strategy was not associated with acute kidney failure in severe preeclampsia patients undergoing CS, which was statistically significant ($p<0.05$) with parameters of serum cystatin C and neutrophil gelatinase-associated lipocalin (NGAL).[11] A randomized controlled trial by Schol et al. in 2021 on obstetric patients demonstrated that a restrictive fluid administration strategy in patients with post-partum hemorrhage did not increase the need for blood transfusion, did not affect coagulation factors, and did not lead to other complications, thus making it a potential alternative to replace the liberal fluid administration strategy.[14] Another study by Elsonbaty et al. showed that the restrictive fluid administration strategy was also associated with a lower incidence of post-dural puncture headache compared to the liberal fluid administration strategy in patients undergoing cesarean section without affecting the patient's hemodynamic profile. The data from these studies were statistically significant, with a p-value of 0.018.[13]

In addition to complications in the operating room, our analysis showed that the fluid administration technique did not have a significant association with complications in the early postoperative period, with a p-value of 0.055, and the fluid administration technique did not have a significant association with complications in the late postoperative period, with a p-value of 0.766. Nevertheless, there were still 2 subjects (1.1%) who had shortness of breath in the early postoperative period following liberal fluid administration. For complications in the late postoperative period, no significant complaints were observed in either the liberal or non-liberal fluid administration. This result aligns with the findings of a meta-analysis study by Messina et al., which showed no significant difference in postoperative complications between restrictive and liberal fluid administration strategies [risk difference (95% CI) = 0.009 (− 0.02; 0.04); p-value = 0.62; I2 (95% CI) = 38.6% (0–66.9%)].[17]

The occurrence of hypotension can pose a challenge in the operating room and may affect the anesthesiologist's decision to administer additional fluids. This study found that a total of 13 subjects (17.1%) had hypotension. Of these 13 subjects, eight (61.6%) were managed with the liberal fluid technique. This indicates that fluid administration using the liberal technique does not prevent patients from experiencing hypotension. This is consistent with a study by Voldby et al., which indicated that during surgery, the liberal group experienced more hypotensive episodes, and post-surgery, more patients in the liberal group had hypotensive episodes and required vasopressors.[18]

During surgery, a patient's body temperature can significantly decrease due to a combination of factors, such as anesthesia medications, exposure to room air, and the administration of non-warmed fluids either intravenously or in the surgical field. Our study showed 39 subjects (51.3%) had hypothermia, with 37 subjects (94.8%) receiving the liberal fluid administration technique. This finding is consistent with the study by Parsa et al., which showed that the administration of non-warmed fluids could worsen hypothermia.[16] During surgery, patients may receive large amounts of intravenous fluids and irrigation. This situation can be exacerbated by the liberal fluid administration technique, where intravenous fluids are often not pre-warmed. This can be considered a drawback of the liberal fluid administration strategy. Based on these observations, we can identify another adverse effect of liberal fluid administration, namely significant heat loss in the patient's body. Hypothermia occurring during surgery can have negative impacts, including cardiac disturbances, bleeding, tissue healing, and length of hospital stay, as reported by Campbell et al.[14,15]

Postoperative nausea and vomiting (PONV) are common complications in surgery under anesthesia, particularly in obstetric patients undergoing regional anesthesia, and they can be no exception in pregnant women.[19] According to this statement, we did not include PONV as a complication in our study analysis.

Based on the aforementioned factors, it can be concluded that both excessive and insufficient fluid administration are associated with poor outcomes. Therefore, there is currently a strategy called "goal-directed fluid therapy" (GDT), which follows the principle of "administering the appropriate amount of fluid at the right time." This fluid administration strategy is based on hemodynamic parameters (such as stroke volume) with the goal of maximizing oxygen delivery and avoiding oxygen deficiency. Additionally, there is a generalized concept known as the R.O.S.E. model, which consists of the resuscitation, optimization, stabilization, and evacuation (deresuscitation) phases aimed at preventing fluid overload.

5. Conclusion

Liberal fluid administration could significantly increase complications in the operating room for pregnant patients undergoing cesarean section but not in the postoperative period. Therefore, it is advisable to adhere to the principle of administering the appropriate amount of fluid at the right time.

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