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The Use of Thoracic Fluid Content As A Guide For 6% HES Infusion during Hypervolemic Hemodilution Among Placenta Accreta Patients Undergoing Cesarean Section. A Randomized Controlled Trial

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ABSTRACT
Background: Hypervolemic hemodilution used in major surgeries is an effective method for reducing blood transfusion requirements. However, it may cause fluid overload and even pulmonary edema. Patients with placenta accreta are the focus of this study, which examines if TFC may be used as a guide for 6 percent HES infusion to minimize fluid overload.

Patients and Methods: This randomized controlled study was done on 108 patients with placenta accreta scheduled for cesarean section. They were split into two equal groups: the control group received an IV infusion of 6 percent HES at 15 ml/kg for 30 minutes before surgery for hypervolemic hemodilution and the TFC group received the same regimen but stopped if TFC =40 k ohm−1. The occurrence of pulmonary edema detected by lung ultrasound was reported. Hypoxia, total volume infused, heart rate, and mean arterial pressure were documented.

Results: A significant proportion of the control group had pulmonary edema, compared to just 1.8 percent of the TFC group. In the TFC group, hypoxia was less common, and the total volume infused was lower. U/S score was positively correlated with delta TFC and other parameters, while was negatively correlated with total fluid infused.

Conclusion: TFC was able to reduce the incidence of pulmonary edema, hypoxia, ultrasound scores, and the total infused volume. In patients undergoing significant procedures such as placenta accreta surgery, our data show that TFC is an effective guide for hypervolemic hemodilution.

Keywords: Hypervolemic hemodilution, Thoracic fluid content, Lung ultrasound, Pulmonary edema, Placenta accreta.

INTRODUCTION

The timely application of evidence-based medical and surgical approaches designed to maintain hemoglobin (Hb), maximize hemostasis and minimize blood loss to improve patient outcomes was defined by the Society for the Advancement of Blood Management. Promoting the safe and reasonable use of blood products and thereby minimizing the risk of blood product exposure [(1,2)].

Interventions tailored to each patient's specific needs are critical to reducing the need for blood transfusions. These include patient positioning, use of antifibrinolytics, hermoregulation, regional anesthesia, blood pressure management, operative techniques, cell salvage that lacks availability in some facilities and needs appropriate training of personnel besides its contraindications [(3)], and hemodilution either acute normovolemic hemodilution (ANH) which is time-consuming, having consequences and reduces the demand for homologous blood just somewhat or hypervolemic hemodilution, which has been reported as being equally effective as ANH at lowering the demand for homologous blood and being considerably easier to implement. However, large volume infusion may cause fluid overload and even pulmonary edema [(4)].

One of the several parameters monitored by the ICON electrical cardiometry (EC) equipment is thoracic fluid content (TFC) (Osypka Medical). ICON, or "thoracic electrical bio-impedance," is a device that uses electrical current to assess changes in the thorax's overall resistance; this resistance is supposed to provide a quantitative indicator of the thorax's entire fluid content (intravascular and extravascular). TFC estimates the rise in intrathoracic fluids to help reduce the risk of pulmonary edema even though it measures both extra and intravascular thoracic fluid [(5)].

Though a large number of studies have been conducted on the capacity of TFC to detect pulmonary edema after lengthy surgery and during fluid management in heart failure, ARDS, as well as preeclampsia [(6-10)], In major obstetric surgery, however, no research has been done on the use of TFC as fluid therapy guidance during hypervolemic hemodilution among cases with placenta accreta The most prevalent reason of peripartum hysterectomy is a life-threatening obstetric hemorrhage [(11-14)]. It was our goal to see if using TFC as guidance for HES infusions of 6 percent hypervolemic hemodilution in patients with placenta accreta would help prevent fluid overload in those patients.

PATIENTS AND METHODS

We conducted this RCT in the obstetric theatre, after approval of the Cairo University Anesthesia Department research and institutional ethical committee. Before any patients were enrolled in the trial, they had to give their permission. 108 patients with placenta accreta, increta, or percreta scheduled for cesarean section with or without hysterectomy were involved in the trial and allocated in a random way using

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computer randomization numbers into 2 groups, Hypervolemic hemodilution at 15 ml/kg for 30 minutes with a 6 percent HES IV infusion load was administered to the TFC Group (15) that started preoperatively as the patient reaches the operation room. In addition, the patient's thoracic fluid content and LUS score were closely monitored, with the infusion being terminated if TFC =40 k ohm1 (6) or once the infused volume had been completed and the LUS evaluation had been performed, whichever came first, IV infusion of 6 percent HES at 15 ml/kg for 30 minutes was started preoperatively as soon as the patient entered the operating room, and LUS examination was performed after the infusion was completed in the control group referred as (C) group.

Certain groups of people, including those who are under the age of 18, have an elevated risk of cardiovascular illness or cardiac arrhythmias, renal insufficiency, sepsis, and death can occur if a person's BMI is above 40 kg/m^2, PPV higher than13, baseline LUS score of 10 or greater indicating hypovolemia, TFC > or = 26 k ohm1 and individuals with neck or chest lesions that prevent the electrodes from being applied to the heart were not included in the research.

An ECG, pulse oximetry, and non-invasive blood pressure monitor were all applied before anesthesia was administered; a full monitor (ECG, pulse oximetry, and non-invasive blood pressure monitor) was attached.

The following four electrodes of electrical cardiometry equipment (ICON; Cardiotonic, Osypka; Berlin, Germany) were placed on the patient: (1) Underneath of left ear; (2) Above the left clavicle's midpoint; (3) On the horizontal axis of the xiphoid process, the left mid-axillary line; (4) two inches below the third electrode. To establish a baseline, the TFC was measured every five minutes for the duration of the experiment, which included a 6% HES infusion. The greatest and lowest values were averaged to create the baseline value. Mindray equipment (DC-N6, with a phased array transducer, model P4-2, 3-6 megahertz) was used by a skilled operator to perform a 12-region lung ultrasound examination utilizing anatomical landmarks of the anterior and posterior axillary lines as a guide.

There are three distinct regions in each hemithorax: anterior, lateral, and posterosuperior, and inferior areas are separated in each area. Each area of interest was assigned an LUS score based on the worst ultrasound pattern that could be detected in that area: no abnormality = 0, well-separated B-lines = 1, coalescent B-lines = 2, and consolidation = 3.

The baseline value was an LUS score ranging from 0 to 36, and every 5 minutes thereafter, until the end of the study's 6 percent HES infusion, the number was calculated [16]. An IV infusion of 6 percent HES at 15 ml/kg for 30 minutes was started after the baseline values were taken 10 minutes before anesthetic induction.

Propofol (2 mg/Kg) was used to induce general anesthesia after 2-3 minutes of preoxygenation with 100% oxygen, Succinylcholine 1.5 mg/kg was used to help implant the endotracheal tube. Isoflurane (1-1.5 percent) and atracurium (10 mg/30min) were used to maintain anesthesia.

Catheters were placed in the arteries and the central venous system of the right internal jugular artery. The following mechanical ventilation settings were used: respiratory rate adjusted to keep end-tidal CO_2 to be 35-40 mmHg, PEEP 5 cm H2O and Tidal volume 6 mL/Kg. Central venous pressure, heart rate, as well as MAP, were monitored every five minutes beginning with the preoperative baseline reading and continuing through the infusion. After the infusion, an ABG was taken before and after, and the P/F ratio was derived from this data.

Primary outcome: LUS score > 15.7 was our major outcome measure for both groups, and it was used to determine the incidence of pulmonary edema [6].

Secondary outcomes:

Delta-TFC is the difference between preoperative baseline measurement and a post-infusion measurement of 6 percent HES, which was used to quantify the change in TFC.

Total 6% HES infusion volume in both groups. The relation between TFC delta-TFC and Total 6% HES infusion volume.

The relation between TFC delta-TFC and the MAP and CVP.

Ethical consent:

The research ethics committee of Cairo University's Faculty of Medicine gave its clearance, which was given the ID number N- 25 / 2020. Every patient signed informed written consent for the acceptance of participation in the study. This work has been carried out following The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

In a previous study on 80 patients, the incidence of pulmonary congestion in patients receiving bolus fluids for goal-directed therapy was 37.5% and 15% for the control group and group using LUS for early detection of pulmonary congestion. So, by using G power software 3.1.1 We determined that a sample size of at least 108 patients was necessary to achieve 80% power and 0.05 alpha error (54 patients per group) (17).

To analyze the data acquired, Statistical Package of Social Services version 15 was used to execute it on a computer (SPSS). To convey the findings, tables and graphs were employed. The quantitative data were presented in the form of the mean, median, standard deviation, and confidence intervals. The information was presented using qualitative statistics such as frequency and percentage. The student's t-test (T) is used to assess the data while dealing with quantitative independent variables. Pearson Chi-Square and Chi-Square for Linear Trend (X^2) were used to assess qualitatively independent data. The significance of a P value of 0.05 or less was determined. Measurement regularly more than two normally distributed variables were compared using the ANOVA test.

RESULTS

135 patients were involved in the trial but only 108 completed the investigation either due to not meeting the inclusion criteria or technical disorders in the devices. The demographic data shown in **Table 1** showed an insignificant difference between both groups.

Table (1): Demographic characteristics

Variable	Control	TFC	P-value
Age (year)	31.6±3.2	32.6±3.5	0.07
Weight (Kg)	48.9±7.9	81.1±7.6	0.06
baseline U/S	5.1± 1.7	5± 1.5	0.2
CVP (cm H_2O)	8.7± 1.8	8.9± 1.7	0.09
HR (beat/minute)	89.6± 6.9	90.3± 5.8	0.06
MAP (mmHg)	93.1± 16.6	92.6± 14.1	0.1

Data are represented as TFC is for thoracic fluid content, CVP is for central venous pressure, HR is for heart rate and MAP is for mean arterial pressure. P value < 0.05 is considered significant.

Utilization of TFC as a guide significantly decreased the incidence of pulmonary edema, hypoxia, ultrasound scores, and the total infused volume **(Table 2, Figure 1).**

Table (2): Comparison between groups for pulmonary edema, hypoxia, and infused volume

Variables	Control	TFC	P-value
Incidence of pulmonary edema	17[31%]	1[1.8%]	<0.001
Hypoxia	5 [9%]	0	<0.001
Total infused volume (ml)	1318 ±111.1	1203.8 ±104.9	<0.001

Data are represented as [percent] TFC is for thoracic fluid content, CVP is for central venous pressure, HR is for heart rate and MAP is for mean arterial pressure. P value < 0.05 is considered significant and < 0.001 is highly significant.

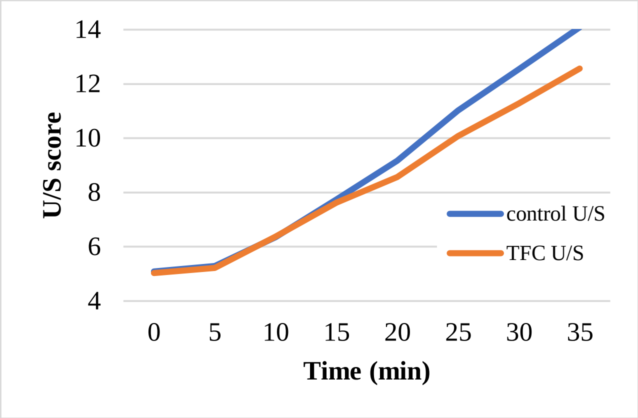

Figure (1): Ultrasound score trends between the control group and TFC group.

Delta TFC was 12.8 (7.3). The correlation between the delta TFC and other parameters showed a significant positive correlation with the U/S score and a significant negative correlation with the total infused volume **(Table 3).**

Table (3): Correlation between delta TFC and other parameters.

	Delta TFC	P-value
U/S score	0.3571	0.009
CVP	0.0888	0.5
Total infused volume	-0.3335	0.014
MAP	0.087	0.37

P-value < 0.05 is significant.

DISCUSSION

To avoid fluid overload in patients with placenta accreta, this randomized controlled research examined the effectiveness of TFC as a guide for a 6 percent HES infusion of hypervolemic hemodilution. There has never been a study done on the use of TFC as a guide for fluid therapy during hypervolemic hemodilution in major surgeries, despite its potential to identify pulmonary edema in many conditions. This research hypothesized that TFC will decrease the incidence of pulmonary edema during hypervolemic hemodilution. The results proved this hypothesis as the incidence of pulmonary edema, hypoxia, ultrasound scores, and the total infused volume were decreased significantly in the TFC group. Also, a significant positive correlation with the U/S score and a significant negative correlation with the total infused volume were shown with delta TFC.

Clinical examination and chest X-ray are commonly used to confirm a diagnosis of pulmonary edema. However, because of interobserver variability and the low sensitivity of these methods, estimating the volume of extravascular lung water (EVLW) is significantly more difficult[18]. The gold standard is gravimetry in vitro and transpulmonary thermo-dye dilution in vivo [19,20], EVLW can also be estimated by CT [21] or MRI [22], however, they do not lend themselves to quick and easy reassessment. Methods based on isotopes [23] are used solely in electrical impedance tomography and research [24]. Lung ultrasound is a robust method for assessment of EVLW [25]. Ultrasound is a subjective, operator-dependent approach, despite its accuracy and non-invasiveness [26].

While TFC measures both intravascular and extravascular fluid compartments, LUS measures extravascular lung water. We found a high association between TFC and LUS despite the obvious physiological differences between the two measures; as a result, as a simple and non-invasive alternative to LUS, TFC can be used in lung examinations. To calculate TFC, the bioimpedance, or baseline resistance, to the flow of a very small electrical current across all of the tissues in the chest must be measured, It includes the skeletal muscles, the heart, the lungs, the chest wall, the subcutaneous fat, bone and fluid (extra and intracellular). Variations in baseline bioimpedance are mostly brought on by changes in thoracic fluid levels since there is a wide range of variation in chest fluids compared to the other components. Preliminary bioimpedance in animal and plastic models was shown to be linked to lung fluid content [8,25].

A reliable approach for assessing extravascular lung water is lung ultrasonography. In parturients with severe pulmonary edema [PE], **Zieleskiewicz *et al.***[27] demonstrated that lung ultrasonography had outstanding capabilities for detecting pulmonary edema. Although ultrasonography is seen to be a useful technique for lung evaluation, its usage is constrained by the requirement for a skilled operator. Although lung ultrasonography has been shown to have excellent inter-observer variability, it is still regarded as an operator-dependent, subjective approach. Lung ultrasonography cannot be performed if the patient has subcutaneous emphysema or surgical bandages. Using TFC for the measurement of lung congestion in PE may overcome all of these limitations [27-29].

Our findings were consistent with those of **Hammad *et al.*** [7]**,** who found that patients with pulmonary edema had greater thoracic fluid content and lung ultrasonography scores than other patients. There was a strong link between the amount of fluid in the thorax and the quality of the lung ultrasound results (r=0.82). AUROC values for pulmonary edema diagnosis were 0.941 for thoracic fluid content and 0.939 for lung ultrasonography score (0.849-0.986), 40 k ohm-1, and 0.961 (0.887-0.994), 15.7 respectively. Both the lung ultrasonography score and the thoracic fluid content in preeclamptic pregnant women demonstrated outstanding capabilities for detecting pulmonary edema.

Additionally, **Paviotti *et al.*** [8] demonstrated that TFC levels were higher in babies who had respiratory difficulty at delivery. (61.6 (16.1) KOhm versus 76.8 (24.9) KOhm), and they concluded that Late preterm and term newborns with respiratory difficulty after birth and 24 hours later were shown to have TFC by electric bioimpedance. According to **Fathy *et al.*** [10], the amount of thoracic fluid in critically ill surgical patients might predict weaning outcomes with considerable amount of accuracy. The subgroup of patients with an ejection fraction less than 40% showed that TFC > 50 k1 had a remarkable ability to predict weaning failure.

Limitations of this trial:

It was a single-center trial, we need to perform the study on various groups of patients other than pregnant patients to prove the efficiency of TFC to prevent pulmonary edema. The cut-off value of TFC was based on a study on preeclamptic patients so it needs to be studied on different cut-off values.

CONCLUSION

TFC was able to reduce the incidence of pulmonary edema, hypoxia, ultrasound scores, and the total infused volume. The correlation between the delta TFC and other parameters showed a significant positive correlation with the U/S score and a significant negative correlation with the total infused volume. These results prove the efficacy of patients undergoing major surgery, such as placenta accreta surgery, benefit from using TFC as a guide for a 6 percent HES infusion of hypervolemic hemodilution.

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