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Original Article

Effect of goal-directed fluid therapy on the prognosis of elderly patients with hypertension receiving plasmakinetic energy transurethral resection of prostate

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Abstract: *Objective:* We aimed to investigate the influence of perioperative goal-directed fluid therapy (GDFT) on the prognosis of elderly patients with benign prostatic hyperplasia and hypertension. *Methods:* Sixty elderly patients (60-80 years old) with primary hypertension who received plasmakinetic energy transurethral resection of prostate (PKRP) surgery were divided randomly into two arms, comprising a conventional intraoperative fluid management arm (arm C, n=30) and a GDFT arm (arm G, n=30). Patients in arm G were infused with 200 ml hydroxyethyl starch over 15 minutes under the FloTrac/Vigileo monitoring system, with stroke volume variation between 8% and 13% and $DO_2I \geq 500$ ml/min.m^2; those in arm C were infused with crystalloids or colloids according to MAP, HR and CVP. Hemodynamics, tissue perfusion laboratory indicators and administration of vasoactive agent in patients were recorded after the operation. *Results:* Compared with arm C, the average intraoperative intravenous infusion quantity in arm G was significantly reduced (1830±348 ml *vs.* 2075±466 ml, P<0.05), whereas average colloid fluid volume was significantly increased (1020±210 ml *vs.* 569±138 ml, P<0.05). In addition, there were more patients exhibiting intraoperatively and postoperatively stable hemodynamics and fewer patients with low blood pressure in arm G. Postoperative complications were less frequent, and the time of postoperative hospital stay was shorter in arm G. No significant differences were observed in mortality between the two arms. *Conclusion:* Our research showed that GDFT stabilized perioperative hemodynamics and reduced the occurrence of postoperative complications in elderly patients who underwent PKRP.

Keywords: Goal-directed fluid therapy, stroke volume variation, aged, plasmakinetic energy transurethral resection of prostate, hypertension

Introduction

The incidence of benign prostatic hyperplasia (BPH) has been rising in China in the context of an aging population. Long-term hypertension and an elderly age are all risk factors of predicting the progression of BPH, high surgical risk, tissue hypoperfusion and organ dysfunction [1]. For these patients, perioperative fluid therapy deserves extra caution and a reasonable scheme of fluid therapy can benefit prognosis. Goal-directed fluid therapy (GDFT) is intended for maintaining circulation volume and improving tissue oxygenation and microcirculation through an individualized fluid therapy according to patients' systemic conditions and volume status. The present study explored the effect of GDFT on the prognosis of elderly patients with hypertension receiving plasmakinetic energy transurethral resection of prostate (PKRP).

Materials and methods

Baseline data

Sixty elderly patients with grade I-III primary hypertension plus BPH (aged 60-80 years old), who were treated at our hospital from January

2014 to December 2015, were included. According to the criteria of American Society of Anesthesiologists (ASA), all patients were assessed as grade II-III before surgery with normal liver and kidney function, body mass index <30 kg/m^2 and perioperative hematocrit >0.30. All included patients were combined with primary hypertension and surgically indicated for BPH [1, 2]. Antihypertensive treatment was given conventionally before surgery to control blood pressure at 140-170/75-90 mmHg on a continuous basis until the morning of the day of surgery. Secondary hypertension, prostate cancer, severe cardiopulmonary diseases, liver & kidney dysfunction, arrhythmia, demand for long-term maintenance with vasoactive agent due to intraoperative hemodynamic instability and other intolerance events were excluded. The patients were randomly divided into two arms using a random table generator, comprising a conventional intraoperative fluid management arm (arm C, n=30) and a GDFT arm (arm G, n=30). This study adopted the single-center randomized controlled trial and the protocol was approved by the Ethics Committee of the First Affiliated Hospital of Fujian Medical University. Informed consent was obtained from all patients.

Anesthetic procedures

Two groups received the same anesthetic procedures of general anesthesia via laryngeal mask airway. None of the patients were treated by preoperative medication. Under local anesthesia biopsy and arterial cannulation of the left radial artery as well as the right internal jugular vein were performed. Intraoperative monitoring of the following indicators was performed using Datex-Ohmeda S/5 Light Monitor: heart rate (HR), electrocardiogram (ECG), invasive blood pressure (IBP), mean arterial pressure (MAP), central venous pressure (CVP), oxygen saturation (SpO_2) and partial pressure of carbon dioxide in exhaled gas ($P_{ET}CO_2$). Hemodynamic indicators were monitored using FloTrac/Vigileo monitoring system (Edwards Lifesciences, USA): cardiac output/cardiac index (CO/CI), stroke volume/stroke volume index (SV/SVI), systemic vascular resistance/systemic vascular resistance index (SVR/SVRI) and stroke volume variation (SVV).

For induction of anesthesia, 0.06 mg/kg midazolam, 0.2 mg/kg etomidate, 3 μg/kg fentanyl and 0.2 mg/kg cisatracurium besilate were administered intravenously in succession. With intubation the respiration was controlled using Datex-Ohmeda 7100 Aespire Anesthesia Machine under fraction of inspired oxygen 50%, oxygen flow rate 1 L/min, inhalation/exhalation ratio (IE) 1:2, tidal volume 8-10 ml/kg, ventilation frequency 10-14 times/min, airway pressure <30 cmH_2O (1 cmH_2O=0.098 kPa) and $P_{ET}CO_2$ 32-38 mmHg (1 mmHg=0.133 kPa). For maintenance of anesthesia, 1%-2% sevoflurane was inhaled along with continuous infusion of 0.2 μg/Kg.min fentanyl and 3 mg/Kg.h propofol using a pump. According to patients' conditions, 1 μg/kg fentanyl and 0.04 mg/kg cisatracurium besilate were infused additionally on an intermittent basis. Bispectral index (BIS) was maintained at 40-60. When MAP declined by over 30% of the baseline, 1 mg of dobutamine was administered intravenously; when HR<50 beats, 0.5 mg atropine was given intravenously. The above anesthetic procedures were repeated if necessary.

Body temperature was maintained above 36°C using a thermal blanket and heating device.

Venous self-control analgesia pump was used for postoperative analgesia with 1 μg/ml sufentanyl (loading dose 4 μg, PCA 2 μg and lockout period 15 min).

Fluid therapy

The patients were fasted from food for 8 h and from water for 6 h before surgery. Peripheral vein access was established and 8-10 ml/kg Lactated Ringer's Injection was infused in 1 h as a replacement of the lost fluid due to fasting. For arm G, GDFT was performed based on SVV under Vigileo/FloTrac monitor. The goal of management was the infusion of 200 ml of 6% hydroxyethyl starch (Voluven, Fresenius Kabi, Germany) within 15 min each time so that 8%<SVV<13% and DO_2I≥500 ml/min.m^2. For arm C, fluid therapy was administered conventionally according to MAP, HR and CVP [3]. No therapy was given if MAP≥65 mmHg and CVP was 8-12 mmH_2O; if MAP≤65 mmHg and CVP≤8 mmH_2O, 500 ml of Lactated Ringer's Injection was infused. After administration, if MAP≤65 mmHg and CVP≤8 mmH_2O, 200 ml of 6% hydroxyethyl starch was infused. If the patient still failed to reach the above standard (8%<SVV<13% and DO_2I≥500 ml/min.m^2), 200

Table 1. Baseline data (n=30)

Group	Age (years)	Hypertension classification (1/2/3)	ASA status (II/III)	BMI (kg/m^2)	Hemoglobin level (g/L)	Operation time (h)
C	72.2±4.3	7/14/9	22/8	25.1±3.3	132.6±4.7	2.1±0.5
G	71.6±3.9	6/14/10	21/9	24.8±4.1	133.2±6.8	1.9±0.6

Data were shown as mean ± SD. Note: Arm C, conventional intraoperative fluid management arm; arm G, GDFT arm; ASA: American Society of Anesthesiologists.

Table 2. Hemodynamic indicators of the two groups at different time points (n=30)

Indicator	Group	T_0	T_1	T_2	T_3	T_4	T_5	T_6
MAP (mmHg)	C	105.5±7.2	104.5±7.6	108.2±7.5	100.3±7.4	98.3±7.3	99.9±6.3	95.1±5.3
	G	105.9±6.8	108.3±6.1	110.9±6.7	113.9±7.7^a	107.6±6.6^a	107.0±6.2^a	105.1±4.8^a
HR (bpm)	C	73.8±6.7	69.8±5.8	70.8±5.3	71.2±5.0	74.4±7.8	74.5±4.0	82.6±4.1
	G	74.5±9.5	70.8±11.1	71.3±8.4	69.5±8.3	70.0±8.0^a	72.2±8.9^a	71.9±8.5^a
CVP (cmH_2O)	C	7.5±1.7	8.4±1.8	11.0±2.2	13.1±1.6	9.4±1.3	7.9±1.2	7.0±1.1
	G	7.0±1.6	7.6±1.7	9.5±1.8	10.8±2.0	10.8±1.7^a	10.9±1.3^a	8.8±1.4^a

Data were shown as mean ± SD. Note: Arm C, conventional intraoperative fluid management arm; arm G, GDFT arm; MAP, mean arterial pressure; CVP, central venous pressure; HR, heart rate; T_0, 30 min before surgery; T_1, at the beginning of surgery; T_2, 1 h after surgery; T_3, at the end of surgery; T_4, 6 h after surgery; T_5, 12 h after surgery; T_6, 24 h after surgery. ^{a}*P*<0.05 compared with arm C.

ml of 6% hydroxyethyl starch was infused continuously until the criteria were met. If MAP≤65 mmHg and CVP≥14 mmH_2O, 1 mg dobutamine was infused intravenously.

The necessity for blood transfusion was assessed depending on hemoglobin level (Hb) and hematocrit (Hct). Blood transfusion was recommended if blood loss was above 1/3 of the blood volume or Hct was below 20%.

Monitoring indicators

Baseline indicators: Baseline information of patients, including gender, age, body weight, hypertension grade, ASA status, BMI and hemoglobin level, was collected before surgery.

Hemodynamic indicators: Invasive systolic and diastolic pressure, MAP, HR, CVP, SVV, $ScvO_2$, lactate (Lac) and oxygen delivery index (DO_2I) were measured 30 min before surgery (T_0), at the beginning of surgery (T_1), 1 h after surgery (T_2), at the end of surgery (T_3), 6 h after surgery (T_4), 12 h after surgery (T_5) and 24 h after surgery (T_6), respectively. Perioperative hypotension incidents were recorded according to the criteria below: systolic pressure <90 mmHg, diastolic pressure <50 mmHg, or a decline of blood pressure by over 30% as compared with the baseline. In case of hypotension, the rate of fluid administration was accelerated and dobutamine was administered intravenously if necessary. The infused amounts of crystals, colloids and blood, blood loss and urine amount were measured in the two groups.

Postoperative complications: For all patients, intraoperative and postoperative management was undertaken by one physician, who was blinded to the scheme of fluid therapy used. The complications of nausea & vomiting, hypotension, arrhythmia, deliration and postoperative hemorrhage as well as hospital stay were recorded.

Statistical process

Statistical analyses were performed using SPSS 18.0 software. Measurements obeying normal distribution were expressed as mean ± standard deviation. One-way ANOVA and SNK was adopted for intragroup comparisons and independent two-sample t-test for intergroup comparisons. Counts were compared by χ^2 test or Fisher's exact test and P<0.05 was considered significant difference.

Results

Baseline data

The two groups showed no significant difference in age, hypertension classification, ASA

Table 3. Fluid infusion amount and intraoperative administration of vasoactive agent in the two groups (n=30)

Group	Total infusion amount (ml)	Infusion amount of 6% hydroxyethyl starch (ml)	Blood loss (ml)	Blood transfusion amount (u)	Number of patients with hypotension and treated by dobutamine (%)
C	2075±466	586±138	373±146	0	12 (40.0)
G	1830±348[a]	1020±210[a]	382±158	0	2 (6.7)[a]

Data were shown as mean ± SD. Note: Arm C, conventional intraoperative fluid management arm; arm G, GDFT arm. [a]*P*<0.05.

Table 4. $ScvO_2$ and Lac of the two groups at different time points (n=30)

Indicator	Group	T_0	T_1	T_2	T_3	T_4	T_5	T_6
$ScvO_2$ (%)	C	70.4±6.1	72.8±5.6	73.4±5.4	73.5±4.2	71.6±4.8	70.8±4.8	70.8±4.2
	G	68.5±4.8	73.7±3.3	76.7±3.0[a]	78.5±2.9[a]	75.8±2.5[a]	75.1±2.3[a]	74.3±3.0
Lac (mmol/L)	C	1.3±0.5	1.2±0.5	0.9±0.5	1.4±0.7	1.4±0.6	1.4±0.5	1.4±0.5
	G	1.1±0.4	1.0±0.3	1.0±0.4	1.0±0.2[a]	1.0±0.2[a]	1.0±0.3[a]	1.1±0.3

Data were shown as mean ± SD. Note: Arm C, conventional intraoperative fluid management arm; arm G, GDFT arm; MAP, mean arterial pressure; CVP, central venous pressure; HR, heart rate; T_0, 30 min before surgery; T_1, at the beginning of surgery; T_2, 1 h after surgery; T_3, at the end of surgery; T_4, 6 h after surgery; T_5, 12 h after surgery; T_6, 24 h after surgery. [a]*P*<0.05 compared with arm C.

status, BMI, hemoglobin level and operation time (P>0.05) (**Table 1**).

As to hemodynamics, comparison showed that the hemodynamic stability was higher in arm G postoperatively than in arm C, with less frequent hypotension incidents (P<0.05). Arm G showed an obvious reduction in intravenous infusion amount (1830±348 ml *vs.* 2075±466 ml, P<0.001), but higher amount of colloid infusion (1020±210 ml *vs.* 569±138 ml, P<0.05) (**Tables 2**, **3**). As compared with arm C, arm G was capable of maintaining a higher $ScvO_2$ and faster decline of Lac (P<0.05, see **Table 4**) and the incidence of mild complications (e.g., postoperative nausea & vomiting, hypotension) was lower (P<0.05). However, the two groups did not differ significantly in mortality and postoperative prostatic bleeding (**Table 5**). Moreover, arm G had shorter hospital stay (7.2±1.3 days *vs.* 8.5±1.6 days, P<0.05).

Discussion

Fluid therapy is important for maintaining perioperative hemodynamic stability and sufficient tissue perfusion. But for elderly patients with hypertension and other underlying disease or organ dysfunctions, fluid therapy may cause the risk of insufficient or excessive circulation volume due to poor tolerance to anesthesia and surgery, which further induces hemodynamic disorders and tissue hypoperfusion. GDFT is found to have a great impact on the prognosis of patients receiving surgery by maintaining normal structure and functions of cells, tissues and organs, and thereby reducing mortality and hospital stay [4-6]. GDFT can prevent insufficient or excessive circulation volume in the perioperative period through an individualized fluid replacement, thus ensuring the circulation volume, microcirculation perfusion and oxygen supply of the tissues. As a result, both the incidence of complications and mortality are reduced.

We performed perioperative GDFT under Vigileo/FloTrac monitor which measures SVV dynamically. SVV is an important hemodynamic indicator in mechanical ventilation that reflects the degree of variation of stroke volume and predicts the fluid responsiveness of the circulation system. This indicator is extensively used for fluid volume management and cardiac function assessment [7]. Study shows that for the assessment of fluid responsiveness, SVV measured from systolic arterial waveform analysis closely correlates to transpulmonary thermodilution method. This means SVV is capable of predicting fluid responsiveness [8]. Zeng K *et al.* applied SVV to the prediction of fluid responsiveness among elderly patients with hypertension receiving abdominal surgery and GDFT. The result indicated higher sensitivity and specificity of SVV as compared with static indicators. Therefore, SVV is an ideal indicator for preventing insufficient or excessive circulation

Table 5. Postoperative complications (n=30)

Complications	Arm C (n=30)		Arm G (n=30)		*P* value
	Case	Incidence (%)	Case	Incidence (%)	
Nausea and vomiting	8	26.67	1	3.33[a]	0.026
Hypotension	9	30.00	2	6.67[a]	0.020
Deliration	5	16.67	2	6.67	0.424
Fever and coughing	8	26.67	3	10.00	0.095
Pulmonary infection	5	16.67	1	3.33	0.195
Arrhythmia	1	3.33	1	3.33	1.000
Oliguria	4	13.33	2	6.67	0.671
Heart failure	0	0.00	0	0.00	1.000
Pulmonary edema	0	0.00	0	0.00	1.000
Urinary tract infection	1	3.33	1	3.33	1.000
Postoperative hemorrhage	4	13.33	2	6.67	0.671
Death	0	0.00	0	0.00	1.000

Note: Arm C, conventional intraoperative fluid management arm; arm G, GDFT arm. [a]$P<0.05$.

volume in fluid therapy based on an individualized scheme and for reducing complications [9].

The two groups, arm C and arm G, did not show significant difference in baseline data. Arm G had smaller total infusion amount than arm C but higher colloid infusion amount, both reaching a significance level. As shown by the trend of MAP, HR and CVP, patients in arm G maintained a more stable hemodynamics after surgery with less frequent hypotension incidents, because GDFT can effectively and quickly address the problem of hemodynamic instability to prevent insufficient or excessive circulation amount. The type and total amount of infusion have an impact on prognosis [10, 11]. The traditional open fluid therapy may bring in large amounts of crystalloid, thus increasing the risk of edema, poor healing, postoperative hypotension and pulmonary infection. Although limited fluid therapy has been gaining popularity and acceptance, the risks of hypotension, tissue hypoperfusion and disequilibrium between oxygen supply and consumption still exist [12]. We found that the timing of fluid infusion was also important. Moreover, to maintain normal SVV and HR, colloidal solution was preferable, as agreed with Feldheiser A 's report [13].

The reason for the better outcome in arm G lied in faster recognition and intervention of hemodynamic disorders. Although the hemodynamic indicators did not change significantly at the end of surgery, the oxygen debt did change. For those with stable hemodynamics, prediction of tissue hypoperfusion based on IBP, HR, consciousness level and urine amount had low sensitivity and failure to indicate oxygen supply to peripheral tissues. In contrast, oxygen debt is better in predicting and maintaining tissue perfusion [14]. In this study, the indicators of Lac and central venous oxygen saturation were used. Lac is an intermediate of anaerobic metabolism and reflects systemic oxygenation and severity of diseases. Systemic hypoxia usually occurs during tissue hypoperfusion caused by low blood volume, leading to a rise in Lac. Rivers E *et al.* performed a clinical randomized controlled trial consisting of 263 patients and found that early GDFT greatly reduced the Lac [15]. Similarly, in our study, Lac began to decline rapidly 6 h after surgery in arm G. It should be kept in mind that liver insufficiency is associated with a reduction in lactate clearance rate and as a result, Lac can no longer reflect tissue hypoperfusion. Considering this possibility, patients with liver dysfunction were excluded and the result indicated that GDFT guided by SVV obviously reduced arterial Lac in postoperative period. As pointed out by other researchers, sufficient oxygen supply of the cells is crucial for preventing cell damage, so Lac monitoring of the artery is very important for the prognosis of patients [16]. Central venous catheters for the monitoring of $ScvO_2$ are responsive to the equilibrium between systemic oxygen supply and demand and predict tissue hypoxia timely [17]. Pearse *et al.* indicated the good predictive value of postoperative $ScvO_2$ in GDFT, proposing that the cut-off value was 64.4% [18] for predicting the prognosis of critically ill patients. In our study, $ScvO_2$ was higher in arm G at four time points, T_2, T_3, T_4 and T_5, which were all reaching a significance level. This indicated that arm G achieved better equilibrium between oxygen supply and demand and better microcirculation through an individualized fluid therapy to stabilize hemodynamics. However, no evidences were supportive of any association between $ScvO_2$ and postoperative complications.

GDFT aims to enhance oxygen supply and equilibrium between oxygen supply and consumption, reduce postoperative complications and mortality. In spite of the disparities in judgment criteria and research design, nearly all subsets benefited from GDFT with less frequent complications, especially in the high-risk group [4-6]. But some contend that intraoperative GDFT provided limited benefits [19]. In the present study, only mild postoperative complications, such as nausea & vomiting and hypotension, were observed, but no significant differences were found in mortality and severe complications such as prostatic hemorrhage. The reason was probably due to short duration of GDFT and the outcome of therapy spanning the whole perioperative period requires further investigation. Since the experiment was a small-sample-size single-center trial, the reliability of the findings may be affected. The absence of no significant differences in pulmonary infection and arrhythmia between the two groups may be due to small sample size. More large-sample-size multi-center studies are needed to confirm the findings. The hospital stay of patients in arm G was shortened by 15.8% as compared with arm C, but because of the lack of specific criteria for discharge, no further discussion was conducted over the indicator of hospital stay. According to existing literature, GDFT can reduce the economic burden for patients [20].

As shown by the present study, GDFT can meet the individualized demand of elderly patients with hypertension who receive surgical treatment. GDFT not only stabilizes hemodynamics, but also reduces postoperative complications and hospital stay. The findings provide valuable clues regarding the application of PKRP to elderly patients with hypertension.

To conclude, GDFT can effectively stabilize perioperative hemodynamics in elderly patients receiving surgery for BPH through improving tissue perfusion, reducing postoperative hypotension and hospital stay.

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Disclosure of conflict of interest

None.

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