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Usefulness of bicarbonate Ringer's solution as perfusate during transurethral resection of the prostate

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ABSTRACT

Transurethral resection of the prostate (TURP) is the most common standard surgical procedure used for benign prostatic hyperplasia. Transurethral resection in saline (TURis) is a bipolar electrosurgery system used to prevent TURP (or TUR) syndrome. The bicarbonate Ringer's solution is not generally used as perfusate for TURP. Hence, we compared the efficacy of the bicarbonate Ringer's solution with that of physiological saline as perfusate during TURP. This prospective, multicenter, cooperative study was conducted on 40 adult patients admitted to a medical college hospital. After obtaining informed consent from all the patients, they were divided into two groups (20 patients per group). For patients of one group, bicarbonate Ringer's solution, and for other group, physiological saline was used as perfusate. Compared to the physiological saline, the electrolyte composition of the bicarbonate Ringer's solution was closer to that of plasma. Hence, the group using bicarbonate Ringer's solution as perfusate was exhibited less variation in plasma electrolytes and blood gas data. The primary endpoints were adverse events of grade 1 or higher according to the JCOG postoperative complication criteria ver. 2.0, unintended diseases, or related signs in patients who underwent the protocol therapy. The secondary endpoints were changes in blood pH, bicarbonate ion level, anion gap (AG), base excess (BE), and chloride (C1), which occurred during and after the surgeries. Therefore, bicarbonate Ringer's solution has superior with that of physiological saline as perfusate during TURP which is directly administered into the blood vessels as an infusion solution.Bicarbonate Ringer's solution is directly administered into the blood vessels as an infusion solution.

1. Introduction

Transurethral resection of the prostate (TURP) is the most common standard surgical procedure used for benign prostatic hyperplasia. Non-conductive irrigation solution is mandatory during the use of a monopolar electric resectoscope to clear the operating field [1–3]. Glycine solution is universally used as an irrigation solution in traditional therapeutic endoscopic urological procedures. Non-conductive distension solution is an electrolyte-free hypotonic solution; its excessive absorption results in fluid overload and dilutional hyponatremia [1–3]. Consequently, it leads to transurethral resection (TUR) syndrome, which may potentially cause systemic complications, including neurologic disturbance, pulmonary edema, cardiovascular compromise, and death [1–3]. In this context, the surgeon should be informed promptly to stop the intervention immediately and start appropriate treatment without delay. The incidence of TUR syndrome is between 0.78% and 1.4% [1]. The multifactorial pathophysiology of TUR syndrome has recently been elucidated, yet it remains a risk.

Transurethral resection in saline (TURis) is a bipolar electrosurgery system used to prevent TUR syndrome; in this system, a reflux current is collected by the external cylinder of an endoscope using physiological saline as perfusate [4,5]. TURis functions effectively in a saline-irrigated environment, where saline is both safe and cost-effective as compared to a non-electrolyte solution for TUR of benign prostatic hy-

Abbreviations: TURPTransurethral resection of the prostateTURisTransurethral resection in salineTURTransurethral resectionAGanion gapBEbase excessC1chloridePACpulmonary artery catheterPVIpleth variability indexBUNblood urea nitrogenCrecreatinine.

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perplasia [4,5]. Moreover, TURis does not need a patient plate or obturator nerve block, even in cases with bladder cancer on the lateral wall [5]. Currently, TURis is routinely used throughout Japan [6–8]. However, it has been reported that the rate of patients with a decrease in the sodium level was significantly lower [9,10]. Moreover, the absorption of physiological saline cannot be avoided. Absorption of a large volume of physiological saline may lead to dilution acidosis.

Electrolyte balance and plasma volume replacement are essential perioperatively. Saline causes metabolic acidosis, and the level of bicarbonate decreases drastically after its infusion [11]. Ringer solutions are either lactated or acetated, mostly used as the initial crystalloid for resuscitation and perioperative maintenance. Although both ions are metabolized to bicarbonate, acetate is more quickly metabolized compared to lactate [12]. The new bicarbonate Ringer's solution improves the blood base excess (BE) values and the serum magnesium levels [13]. The alkalinizing effect of bicarbonate-Ringer's solution tended to be a better and more suitable perioperative solution for metabolic acidosis [13] and serum electrolyte disbalance [13,14].

On the other hand, the use of bicarbonate Ringer's solution, the electrolyte composition of which is comparable to that of blood, as perfusate may make it possible to avoid this risk. However, there is little to no information on the use of bicarbonate Ringer's solution as perfusate for TURP. Hence, we conducted a multicenter cooperative study to compare the efficacy of bicarbonate Ringer's solution with that of physiological saline as perfusate during TURP.

2. Methods

After receiving approval from the hospital's Research Ethical Committee, this prospective, multicenter, cooperative study was conducted on 40 adult patients who were admitted to a medical college hospital. After explaining the study, verbal consent was obtained from either the patients or their relatives. Forty patients were recruited for this study.

2.1. Case registration

As this was a randomized study, the choice of perfusate was randomly assigned in this study. As a rule, the principal investigator sent a specific case registration sheet by FAX to the data center for case registration. A registration number was provided to the patients who were considered to be eligible for enrolment at the registration/data center. Based on the results of randomization, a test perfusate was assigned.

2.2. Assignment method

A test perfusate was assigned through a randomized 2-group assignment using the minimization method.

2.3. Observation and examination of items

Vital signs, such as systolic blood pressure, diastolic blood pressure, and pulse rate, were analyzed for all the patients. Next, 3 mL syringes with a filter cap with total balanced heparin for blood gas and electrolyte analysis were used for arterial venting of patients in the critical care unit at the University Hospital. Arterial samples were obtained from an arterial cannula and mixed venous samples from a pulmonary artery catheter (PAC). The samples were analyzed for gas analysis, including pH, HCO^{3-}, BE, anion gap (AG), and analysis of electrolytes, such as Na^+, K^+, and Cl^-, as soon as possible after sample collection.

Pulse oximeter parameters, such as SpO_2, SpHb, and pleth variability index (PVI), were analyzed using a noninvasive traditional fingertip pulse oximeter instrument. Blood counts, such as hemoglobin, leukocyte count, and platelet count, were estimated using a standard protocol. Blood biochemistry, such as blood urea nitrogen (BUN) and creatinine (Cre), was analyzed using an autoanalyzer. Prostate volume was analyzed using transrectal ultrasonography (Table 1).

2.4. Statistical analysis

Relationships between the clinical characteristics and adverse events were examined using the $\chi 2$ test. Changes in vital signs and laboratory data were examined using the *t*-test. The results were considered significant at $P < 0.05$. All analyses were performed using JMP 15.0.1 (SAS®).

3. Results

3.1. Observation and examination schedule

Compared to physiological saline, the electrolyte composition of bicarbonate Ringer's solution (Table 2) was closer to that of plasma. Since the alkaline agent contains bicarbonate ions that do not require to be metabolized, dilution acidosis is unlikely to occur even if it is absorbed in large amounts during the procedure. Thus, compared to a group using physiological saline as the perfusate, the group using bicarbonate Ringer's solution was expected to exhibit less variation in plasma electrolytes and blood gas data.

3.2. Primary endpoints

Safety and efficacy of bicarbonate Ringer's solution perfusion (presence or absence of dilution acidosis) The primary endpoints included the incidence of adverse events of grade 1 or higher according to the JCOG postoperative complication criteria ver. 2.0 (Clavien-Dindo Classification), unintended diseases, or related signs (including abnormal laboratory test values) in patients who underwent the protocol therapy.

3.3. Secondary endpoints

The secondary endpoints included changes in blood pH, bicarbonate ion level, AG, BE, and chloride (C1), that occurred during and after the surgeries.

Table 1
Observation and inspection schedule.

	At the start of surgery	45 min	60 min	75 min	90 min	At the end of surgery
Vital sign	○	○	○	○	○	○
Gas analysis	○	○	○	○	○	○
Pulse oximeter	○	○	○	○	○	○
Blood count	○		○		○	○
Blood laboratory test	○		○		○	○
Total irrigation volume	○	○	○	○	○	○
Adverse events	← ○ →					

Table 2
Composition of Ringer's solution.

Component	1000 ml
Sodium chloride	5.84 g
Potassium chloride	0.30 g
Calcium chloride hydrate	0.22 g
Magnesium chloride	0.20 g
sodium hydrogen carbonate	2.35 g
Sodium citrate hydrate	0.20 g

4. Discussion

Benign prostatic hyperplasia is commonly treated using pharmacotherapy, such as with alpha-blockers; however, surgical therapy may be adopted in case of inadequate therapeutic outcome [15]. In Japan, TURP is the standard and most common surgical procedure employed for benign prostatic hyperplasia [16]. It is mainly indicated for up to moderate benign prostatic hyperplasia, and its effect is highly persistent. Complications of this procedure include hyponatremia due to hemorrhage and the perfusate (TUR syndrome) [17].

Compared to physiological saline, the electrolyte composition of the bicarbonate Ringer's solution more closely resembles that of plasma. As an alkaline agent containing bicarbonate ions, which do not require to be metabolized, absorption of a large volume of bicarbonate Ringer's solution would not lead to dilution acidosis. This would result in minimal perfusate absorption-related changes in plasma electrolytes, facilitating safer TURP.

Bicarbonate Ringer's solution is directly administered into the blood vessels as an infusion solution. In clinical practice, it is routinely used. Therefore, there may be no risk in its use *in vivo*. However, no study has reported the use of this solution as an intravesical perfusate. Furthermore, investigated the influence of electrocautery current and found no impact of this current on the composition of the perfusate, such as the vaporization of bicarbonate.

Ethical approval/informed consent

This study protocol was approved by the Institutional Review Board of the Kyoto Prefectural University of Medicine. The Ethics Board approval number is ERB-C-93-4. This study has been registered and published in this database as a clinical study as specified in the Clinical Research Law. The approval number is jRCTs051180234. All patients included in this study provided informed consent for use of their data in the research.

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Author contribution

Fumiya Hongo: Conceptualization, Methodology, Software; Tsukasa Narukawa, Atsuko Fujihara: Data curation, Fumimasa Amaya: Visualization, Investigation; Teiji Sawa: Supervision; Osamu Ukimura: Writing- Reviewing and Editing.

Declaration of competing interest

The authors declare that they have no competing interests.

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