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ORIGINAL ARTICLE

The effect of patient-controlled intravenous analgesia on postoperative hypokalemia in patients undergoing laparoscopic cholecystectomy

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Abstract
Purpose We investigated whether hypokalemia developed during the postoperative period and whether the use of intravenous patient-controlled analgesia (IV-PCA) could decrease the incidence of postoperative hypokalemia in patients who underwent laparoscopic cholecystectomy.
Methods Sixty patients undergoing laparoscopic cholecystectomy were randomly assigned to either IV-PCA ($n = 30$) or control ($n = 30$) groups. We measured serum potassium concentration at the outpatient department (T1), at 8:00 a.m. on the day of surgery (T2), at 6 h after the end of surgery (T3), and at 8:00 a.m. on the first (T4), second (T5), and third (T6) postoperative days. Serum potassium concentration, incidence of hypokalemia, mean blood pressure, heart rate, respiratory rate, and the patient-reported visual analogue scale score were compared within each group and between groups at each time point.
Results Serum potassium concentrations in all patients showed a significant decrease at T2–T4 compared to the preoperative concentration (T1). Serum potassium concentrations at T3 and T4 in the IV-PCA group were significantly higher than those in the control group. Also, the incidence of hypokalemia at T3 and T4 was significantly lower in the IV-PCA group. Mean blood pressure and heart rate were significantly lower in the IV-PCA group than in controls at T3 and T4.
Conclusions The results show that hypokalemia developed during the perioperative period and the use of IV-PCA in patients undergoing laparoscopic cholecystectomy effectively decreased the degree and incidence of postoperative hypokalemia on the day of the operation and postoperative day one.

Keywords Patient-controlled intravenous analgesia · Hypokalemia · Arrhythmia · Catecholamine · Laparoscopic cholecystectomy

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Introduction

Potassium is the principal intracellular ion, and its concentration and gradients greatly influence the electrical activity of excitable membranes. Hypokalemia is known to increase the incidence of perioperative arrhythmia [1–3]. It has been suggested that hypokalemia triggers ventricular tachyarrhythmia via cellular hyperpolarity, in that it increases resting potential, hastens depolarization, and increases automaticity and excitability [4, 5]. The adverse association between hypokalemia and arrhythmia in animal and human studies appears to be more significant in the presence of acute myocardial ischemia [3, 6–8]. Hypokalemia can be induced by various conditions, including respiratory or metabolic alkalosis, salt-wasting renal disease, diuretic therapy, and hormone effects [9, 10]. Previous studies have revealed that preoperative anxiety can lead to hypokalemia as a result of catecholamine release as a neuroendocrine stress response [11–13]. As such, it was contended that postoperative pain could induce the neuroendocrine stress reaction and subsequently result in hypokalemia. It was postulated that the severity of the neuroendocrine stress reaction due to postoperative pain

was correlated with plasma potassium concentration, and that the reaction could be effectively blocked by the use of intravenous patient-controlled analgesia (IV-PCA). The goal of this study was to investigate whether hypokalemia developed during the perioperative period and whether the use of IV-PCA in patients undergoing laparoscopic cholecystectomy could decrease the incidence of hypokalemia and hypokalemia-associated arrhythmia.

Patients, materials, and methods

This randomized controlled prospective study was approved by the Institutional Review Board (IRB) of our institution and all patients provided informed consent. Sixty patients (American Society of Anesthesiologists [ASA] class I or II) who were scheduled for laparoscopic cholecystectomy during the period from January 2011 to March 2011 were enrolled in the study. Patients were randomized into two groups—either the IV-PCA or the control group, using a computer program (http://www.randomizer.org). Patients with endocrine disorders, including primary or secondary hyperaldosteronism, renovascular hypertension, renin-secreting tumor, Cushing's syndrome, or salt-wasting renal diseases such as Bartter's syndrome or renal tubular acidosis, were excluded. Patients with recent or current steroid, insulin, β-blocker, diuretic, or antidepressant treatment were also excluded. Those with metabolic or respiratory alkalosis as determined by preoperative arterial blood gas analysis (ABGA) were also excluded. Those with antihypertensive drug treatment or systemic hypertension diagnosed as grade 2 or higher (systolic value $\geq$160 mmHg, or diastolic value $\geq$100 mmHg) [14] were excluded to allow for the comparison of blood pressure between the two groups. Subjects with initial hyper- or hypokalemia determined during the preoperative blood test at the outpatient department (time [T] 1) were included only after confirming normal potassium concentrations with a repeated blood test or they were excluded from the study. Therefore, the preoperative potassium concentrations in all the patients were within the normal range.

Patients were fasted from the midnight before surgery. All patients were scheduled to have surgery at 9:00 a.m., with no premedication. Lactated Ringer's solution was preoperatively administered from 8:00 a.m. on the day of surgery at a rate of 2.0 mL/kg/h, and was continued in the operating theater through the second postoperative day until oral intake was resumed. An anesthetist individually adjusted the infusion rate during surgery. Patients infused with colloid solution or transfused with blood products were excluded from this study. If other fluid was used at the ward by the surgeon after surgery, the patient was excluded from the study. Serum potassium concentration was measured at six time points; in the outpatient department (T1), at 8:00 a.m. on the day of surgery (T2), 6 h after the end of surgery (T3), and at 8:00 a.m. on the first (T4), second (T5), and third (T6) postoperative days. Serum potassium concentration was measured by venous sampling and not by ABGA, as heparin in the ABGA syringe may interfere with the result of serum potassium concentration. In addition to serum potassium concentration, ABGA (at T2–T5), non-invasive blood pressure, heart rate, respiratory rate (at all time points), and patient-reported visual analogue scale (VAS: a visual indicator of pain with a slide ruler with drawing of human faces and 100-mm scale at the back) pain scores (at T3–T6) were measured and compared at each time point. 12-Lead electrocardiographic examinations were performed to evaluate the incidence of arrhythmia at T1 and T3–T5. The same group of surgeons treated all the patients using identical surgical techniques. Anesthesia was induced with pentothal 5 mg/kg, rocuronium 0.6 mg/kg, and fentanyl 1 μg/kg and maintained with sevoflurane. No infiltration of skin or intraperitoneal cavity with local anesthetic was performed and peak intraabdominal pressure was monitored during the surgery. A maintenance dose of vecuronium was administered to make a train-of four count of 0–1 during the surgery. During the surgery, the end-tidal CO_2 was strictly controlled between 35 and 40 mmHg by the anesthetist.

A disposable IV-PCA device (Accufuser Plus®; Wooyoung Healthcare, Seoul, Korea) was connected to the intravenous line and infusion began when skin closure was completed. For blinding, the IV-PCA device was also connected for the control group, and saline was infused. The IV-PCA regimen consisted of 15 μg/mL fentanyl and the IV-PCA device was initially programmed to deliver at a 2.0 mL/h basal rate and a 1.0 mL bolus dose with a lockout duration of 15 min. IV-PCA was infused during the first 48 h after the end of surgery. If nausea, vomiting, or pruritus was severe and poorly controlled with antiemetic or antihistamine, the IV-PCA was removed and the subjects were excluded from the study. In the control group, postoperative pain was controlled with intravenous ketorolac 30 mg as the first-line drug and the dose was repeated for up to three times a day. In both groups, if pain control was not adequate, 0.5–1 mg/kg meperidine was administered and the dose and frequency of meperidine use was recorded.

Hypokalemia was defined as potassium $\leq$3.5 mEq/L, severe hypokalemia as potassium $\leq$3.0 mEq/L, and hyperkalemia as potassium $\geq$5.5 mEq/L. If severe hypokalemia or hyperkalemia developed, the patient underwent appropriate treatment and was excluded from the study. The differences in potassium concentration at T2–T6 from that at T1 were measured and compared between the two

Table 1 Demographic and perioperative patient data

Variables	IV-PCA ($n = 26$)	Control ($n = 28$)
Age (years)	54.5 ± 15.2	55.8 ± 16.8
Sex (M/F)	17/11	11/15
Weight (kg)	63.2 ± 10.8	66.1 ± 12.7
Height (cm)	160.0 ± 9.6	163.6 ± 8.2
Total volume of IV fluid (mL)	8126.9 ± 257.0	8085.7 ± 243.0
Urine output during surgery (mL)	262.7 ± 77.2	260.4 ± 69.9
EBL during surgery (mL)	210.4 ± 60.8	215.0 ± 23.6
Mean surgery time (min)	66.1 ± 9.1	68.3 ± 7.7
Mean anesthesia time (min)	80.7 ± 4.9	81.0 ± 4.5
Intraabdominal pressure (mmHg)	12.5 ± 1.2	13.1 ± 2.1
Hospital stay (days)	4.4 ± 0.6	4.2 ± 0.7

Values are expressed as the mean ± SD (range)

EBL estimated blood loss, *IV-PCA* intravenous patient-controlled analgesia

groups. The incidence of hypokalemia was compared between the two groups.

All data were analyzed using SPSS 14.0 (SPSS, Chicago, IL, USA) and all measured variables were expressed as means ± standard deviation. Demographics were compared using a two-sample *t*-test and a χ^2 test as appropriate. The absolute values of serum potassium, mean blood pressure, heart rate, and respiratory rate at T2–T6 were compared with those at T1 within each group using a repeated measure analysis of variance (ANOVA) with the Student–Newman–Keuls method as post-hoc analysis. A two-sample *t*-test or Mann–Whitney test was used to compare the absolute values of potassium concentration, mean blood pressure, heart rate, respiratory rate, VAS score, arterial pH, and $PaCO_2$ at each time point and the magnitude of change from the preoperative value (T2–T1, T3–T1, T4–T1, T5–T1, T6–T1) between the two groups. χ^2 analysis was used to analyze differences in the incidence of hypokalemia between the groups. A p value of <0.05 was considered statistically significant.

Results

Sixty individuals were initially enrolled in this study and 54 subjects (26 in the IV-PCA and 28 in the control group) finished the study protocol. Three subjects in the IV-PCA group were excluded from the study because they stopped using IV-PCA on the first postoperative day due to severe nausea, vomiting, or pruritus. Three subjects (one in the IV-PCA group and two in the control group) were also excluded because of severe hypo- or hyperkalemia developed at T3 or T4.

There was no significant difference in demographic factors between the two groups (Table 1). Perioperative data including input and output values were not different between the two groups (Table 1). The mean total fentanyl consumption of the IV-PCA group was 1505.64 ± 58.3 μg.

Plasma potassium concentration at T2–T4 was decreased significantly compared with the concentration measured at the outpatient department (T1) in both groups. Among the T2–T4 time points, the potassium concentration was significantly different between the two groups at T3and T4 (Table 2; Fig. 1a). Also, the absolute fall from the preoperative potassium concentration was significantly smaller in the IV-PCA group compared to that in the control group at T3and T4 (Table 2). The incidence of hypokalemia was also significantly lower in the IV-PCA group compared to that in the control group at T3 and T4 (Table 2).

There were no episodes of severe arrhythmia in any of the subjects, even though there were a few cases of atrial or ventricular premature beat (Table 3). The incidence of arrhythmia did not differ between the two groups (Table 3). Mean blood pressure and heart rate were elevated at T2 compared with T1 in both groups (Table 3). Mean blood pressure and heart rate were significantly elevated at T3 and T4 compared with T1 (Table 3) only in the control group. The respiratory rate was significantly elevated at T2–T4 compared to T1 in both groups.

VAS scores were not significantly different between the IV-PCA and control groups at T3–T6 (Table 3). Mean blood pressure and heart rate were significantly different between the two groups at T3 and T4 (Table 3; Fig. 1b). However, the respiratory rate was not significantly different between the two groups at any time point (Table 3). Arterial blood pH and CO_2 tension were within normal ranges in both groups at T2–T5 (Table 3).

Discussion

The major new observations presented in this study are that, in patients undergoing laparoscopic cholecystectomy, there was a significant incidence of hypokalemia during the immediate preoperative and postoperative period (the day

Table 2 Comparison of serum potassium concentration, change in serum potassium concentration, and incidence of hypokalemia at each time point

Variables	Group	T1	T2	T3	T4	T5	T6
Absolute value (mEq/L)	IV-PCA	4.1 ± 0.3	3.8 ± 0.4†	3.9 ± 0.3†,*	3.8 ± 0.4†,*	4.0 ± 0.4	4.0 ± 0.4
	Control	4.2 ± 0.4	3.8 ± 0.3†	3.5 ± 0.2†	3.6 ± 0.3†	4.0 ± 0.3	4.1 ± 0.4
Change from preoperative value (T1)	IV-PCA	–	−0.33 ± 0.23	−0.13 ± 0.24*	−0.26 ± 0.34*	−0.03 ± 0.17	−0.09 ± 0.28
	Control	–	−0.39 ± 0.23	−0.72 ± 0.28	−0.58 ± 0.35	−0.14 ± 0.36	−0.05 ± 0.33
Incidence of hypokalemia (*n*)	IV-PCA	0	6 (23.1%)	4* (15.4%)	3* (11.5%)	2 (7.7%)	1 (3.8%)
	Control	0	5 (17.9%)	11 (39.3%)	10 (35.7%)	2 (7.1%)	2 (7.1%)

Values are expressed as the mean ± SD

Time points were as follows: outpatient department (T1), 8:00 a.m. on the day of surgery (T2), 6 h after the end of surgery (T3), 8:00 a.m. on the first (T4), second (T5), and third (T6) postoperative days

* p value <0.05 versus control group, $^{\dagger}p$ value <0.05 versus T1 value

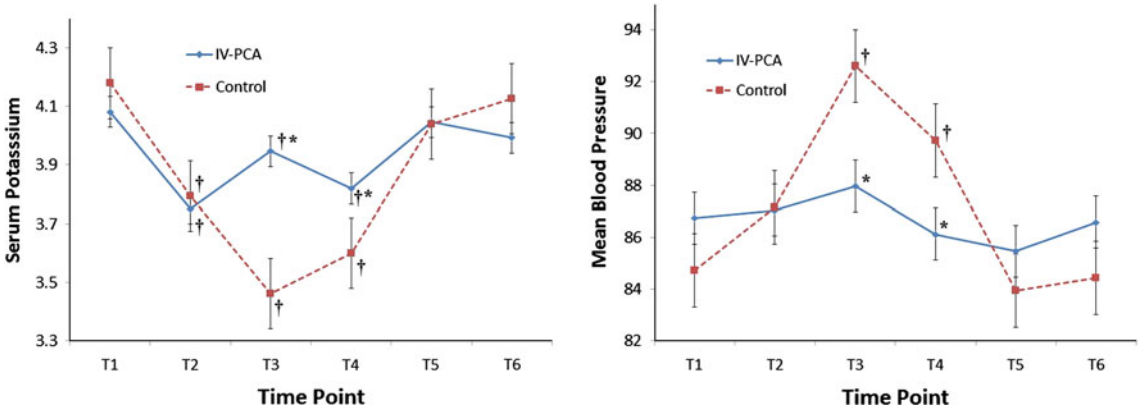

Fig. 1 Comparison of serum potassium concentration (**a**) and mean blood pressure (**b**) between groups at each time point. Data are presented as the mean ± standard deviation; $^{\dagger}p$ value <0.05 versus T1 value, *p value <0.05 versus control group. Time points were as follows: outpatient department (*T1*), 8:00 a.m. on the day of surgery (*T2*), 6 h after the end of surgery (*T3*), 8:00 a.m. on the first (*T4*), second (*T5*), and third (*T6*) postoperative days. *IV-PCA* intravenous patient-controlled analgesia

of the operation and postoperative day one) and that the use of IV-PCA reduced the degree of postoperative serum potassium concentration decrease and the incidence of hypokalemia.

Previous studies reported that hypokalemia before the induction of propranolol [15, 16]. It has also been demonstrated that elevated epinephrine arising from preoperative anxiety stimulated the β-2 adrenoceptor and the Na/K-ATPase that transports potassium into liver or skeletal muscle cell bodies and reduces extracellular and plasma potassium concentrations [11–13, 16–19]. Previous studies reported that preinduction serum potassium concentrations were significantly lower than those measured in the outpatient department, a finding which was attributed to increased catecholamine due to preoperative anxiety, as determined by measurements of serum epinephrine levels [11, 12]. Similar results showing a difference between T1 and T2 were found in the present study. Furthermore, there was a statistically significant decrease in potassium concentration in the postoperative period (T3, T4). From these results it was postulated that stress hormones, including catecholamine released in response to postoperative pain, decreased serum potassium concentrations, similar to the way in which preoperative anxiety caused hypokalemia. We did not premedicate the patients, in order to rule out the effect of premedication on serum potassium concentration. The effect of premedication may influence the postoperative serum potassium concentration, and these two effects may be mixed during the postoperative period.

There was a significant increase in mean blood pressure and heart rate at T3 and T4 compared with T1 only in the control group. From this result, we could assume that the effect of IV-PCA blocked the elevation of blood pressure and heart rate at T3 and T4. It was assumed that the elevated blood pressure and heart rate were the result of stress hormone release. The reduction in the incidence of hypokalemia at T4 was subsequently postulated to be due to a reduction of stress hormone release. Adams et al. [20] investigated the interaction between postoperative pain score and endocrine stress response and found no

Table 3 Comparison of clinical features at each time point

Variables	Group	T1	T2	T3	T4	T5	T6
Incidence of arrhythmia[a]	IV-PCA	1	–	2	1	2	–
	Control	2	–	3	3	2	–
VAS score	IV-PCA	–	–	3.3 ± 1.3	2.5 ± 0.9	1.0 ± 0.7	1.1 ± 0.5
	Control	–	–	3.5 ± 1.2	2.8 ± 1.1	1.1 ± 0.8	1.0 ± 0.7
Mean blood pressure (mmHg)	IV-PCA	86.7 ± 4.4	87.0 ± 3.8	88.0 ± 3.3*	86.1 ± 3.6*	85.5 ± 4.1	86.6 ± 7.0
	Control	84.7 ± 6.7	87.1 ± 5.3†	92.6 ± 5.5†	89.7 ± 6.1†	83.9 ± 3.9	84.4 ± 5.1
Heart rate (beats/min)	IV-PCA	59.4 ± 7.4	63.8 ± 5.8†	62.6 ± 4.9*	61.3 ± 3.6*	61.5 ± 3.3	59.1 ± 7.1
	Control	61.8 ± 6.7	65.0 ± 5.5†	66.3 ± 5.5†	64.8 ± 6.8†	62.4 ± 2.2	59.4 ± 8.1
Respiratory rate (/min)	IV-PCA	16.8 ± 1.9	17.7 ± 1.6†	18.6 ± 1.3†	17.7 ± 1.3†	16.7 ± 1.5	16.2 ± 1.5
	Control	16.1 ± 1.3	17.1 ± 1.3†	17.8 ± 2.3†	17.6 ± 1.2†	16.4 ± 1.3	15.6 ± 1.6
Arterial blood pH	IV-PCA	–	7.44 ± 0.05	7.43 ± 0.04	7.45 ± 0.04	7.45 ± 0.03	–
	Control	–	7.44 ± 0.04	7.42 ± 0.05	7.44 ± 0.06	7.44 ± 0.03	–
Arterial blood $PaCO_2$ (mmHg)	IV-PCA	–	38.5 ± 2.4	38.6 ± 2.4	37.2 ± 2.4	38.2 ± 2.8	–
	Control	–	38.6 ± 1.9	38.7 ± 2.5	37.8 ± 3.0	38.3 ± 2.9	–

The values are expressed as means ± SD

Time points were as follows: outpatient department (T1), 8:00 a.m. on the day of surgery (T2), 6 h after the end of surgery (T3), 8:00 a.m. on the first (T4), second (T5), and third (T6) postoperative days

VAS visual analogue scale

[a] Arrhythmia (atrial or ventricular premature beats)

* p value <0.05 versus control group

† p value <0.05 versus T1 value

correlation between them. In their study, there was a difference of stress hormone release according to different anesthetic techniques even though VAS was similarly reduced irrespective of anesthetic techniques [20]. Thus, from this result, we can conclude that the primary determinant of serum potassium is the stress hormone level rather than the pain score reported by the patients [20]. For example, a 15-fold increase in epinephrine in normal volunteers was shown to lead to a 0.4–0.9 mEq/L decrease in potassium in a previous study [19]. We can also postulate that the stress hormone level was different between the two groups in the present study, although the VAS scores reported by the patients were not different between the groups.

However, the clinical significance of our study was limited because IV-PCA could not completely block the development of hypokalemia and there was no significant arrhythmia. We could attribute this result to the IV-PCA regimen. The dose of IV-PCA might not have been enough to block the whole process of endocrine stress response. The small bolus dose and long lock-out time may have not fully blocked the neuroendocrine response in our patients. There were no cases of severe arrhythmia in the present study, even though there was a high incidence of hypokalemia (up to 39.3%, 11 subjects at T3 in the control group). The clinical effect of hypokalemia prevention was limited, as clinically significant arrhythmia did not occur. However, this may be because the present study included only normal healthy subjects without cardiovascular disease, and subjects with severe hypokalemia were excluded during the course of the study. Therefore, even though there were no cases of severe arrhythmia in the present study, subjects with cardiovascular disease will likely be influenced more than healthy subjects by the use of IV-PCA in terms of clinically significant arrhythmia. Furthermore, in our study, electrocardiographic examinations were not performed continuously throughout all of the postoperative period. The use of 24-Hour Holter examination may have detected arrhythmia more sensitively.

There are studies reporting that patients with ischemic heart disease or baseline electrocardiographic abnormalities including left ventricular hypertrophy are particularly vulnerable to hypokalemia, ventricular arrhythmia, and sudden death [2, 21]. Hulting [2] reported that a near fivefold increase in the incidence of early ventricular fibrillation within 12 h after coronary care unit admission was observed in patients with serum potassium below 3.9 mmol/L. Siscovick et al. [21] reported that the addition of a potassium-sparing drug to low-dose thiazide therapy was associated with a reduced risk of cardiac arrest in patients with hypertension. Shah et al. [22] showed that hypokalemia was one of the individual factors that was useful in predicting the outcome of perioperative myocardial infarction or cardiac death in patients with cardiac

diseases undergoing non-cardiac operations. However, there have been studies that denied the association of hypokalemia with arrhythmia or poor outcome. Hirsch et al. [23] reported that frequent and complex ventricular arrhythmias were common in those with a history of long-term digoxin therapy or congestive heart failure, but hypokalemia did not increase the incidence or severity of ventricular ectopy. Vitez et al. [24] reported that the occurrence of intraoperative arrhythmia was not related to chronic hypokalemia but to preexisting preoperative arrhythmia. They reported that the only risk factor for malignant arrhythmias intraoperatively was the presence of cardiovascular disease with concurrent digoxin therapy. The most recent multicenter study reported that perioperative arrhythmia and the need for cardiopulmonary resuscitation increased as the preoperative serum potassium level decreased below 3.5 mmol/L [6].

In the present study, laparoscopic cholecystectomy was selected as the surgery type as this surgery is thought to be painful with intermediate intensity; it is not so painful as to absolutely need IV-PCA, nor is it so pain-free as to not need IV-PCA. Based on the patients enrolled in this study, laparoscopic cholecystectomy was not so painful as to need the IV-PCA, because only two patients in the control group (7.1%) required the use of meperidine. Furthermore, the VAS scores were not significantly different between our two groups. Therefore, even though the use of IV-PCA reduced the incidence of hypokalemia in the postoperative period, the control of subjective pain was not the key to making the difference. We postulated that the stable control of the underlying neuroendocrine response by IV-PCA reduced the incidence of hypokalemia. In other words, compared with intermittent bolus doses of nonsteroidal anti-inflammatory drugs (NSAIDs) with or without opioid, a continuous infusion of opioid might have controlled the neuroendocrine response more stably. The incidence of hypokalemia might have been reduced as a consequence of the stable control of the stress hormone level. Postoperative pain as assessed by patient-reported VAS scores may be only a secondary indicator of stress, and even sufficient analgesia with subjective well-being cannot prove a stress-free state [20, 25].

There is also potential for the development of preinduction (T2) and postoperative (T3, T4) hypokalemia resulting from acute hyperventilation due to preoperative anxiety or postoperative pain [26–28]. Muir et al. [28] quantified the effects of respiratory rates on arterial pH, $PaCO_2$, HCO_3, and potassium in normal anesthetized dogs. Each 10-mmHg decrease in $PaCO_2$ was associated with a potassium decrease of 0.4 mEq/L. In the present study, there were no significant differences in arterial pH and $PaCO_2$ from T2 to T5, even though respiratory rates were significantly increased during T2–T4. Furthermore, the pH, $PaCO_2$ level, and respiratory rate were not significantly different between the two groups at any time point. Therefore, it was concluded that although mild hyperventilation may have been present, respiratory alkalosis that was severe enough to be the primary cause of serum hypokalemia at T2–T4 was not observed. Therefore, it was assumed that the hypokalemia at T2–T4 was the result of stress hormone release and not the result of hyperventilation as a result of anxiety or postoperative pain.

The present study has several limitations. First, Comparisons of the levels of plasma stress hormones [29] including catecholamine, adrenocorticotropic hormone (ACTH), cortisol, and aldosterone, were not performed. Further study, including the measurement of these hormone levels, is required to clarify the underlying mechanism of hypokalemia. Second, as previously mentioned, three 12-lead electrocardiographic examinations were not sufficient to demonstrate reduction in arrhythmia; a 24-hour Holter examination may have been more sensitive for this. Third, the choice of laparoscopic cholecystectomy as the surgery might not have been suitable, because it is painful for only a very brief period and thus could not show the effect of blocking of the neuroendocrine response for a long enough period.

In summary, our findings showed a significant incidence of hypokalemia during the immediate preoperative and postoperative periods. The use of patient-controlled intravenous analgesia in patients undergoing laparoscopic cholecystectomy significantly reduced, but did not completely prevent, the degree of potassium concentration decrease and the development of hypokalemia in the postoperative period.

References

1. Surawicz B. The interrelationship of electrolyte abnormalities and arrhythmias. In: Mandel WJ, editor. Cardiac arrhythmias: their mechanisms, diagnosis, and management. Philadelphia: JB Lippincott; 1985. p. 89–110.
2. Hulting J. In-hospital ventricular fibrillation and its relation to serum potassium. Acta Med Scand Suppl. 1981;647:109–16.
3. Grumbach L, Howard JW, Merrill VI. Factors related to the initiation of ventricular fibrillation in the isolated heart: effect of calcium and potassium. Circ Res. 1954;2:452–9.
4. Fisch C, Knoebel SB, Feigenbaum H, Greenspan K. Potassium and the monophasic action potential, electrocardiogram, conduction and arrhythmia. Prog Cardiovasc Dis. 1966;8:387–418.
5. Gettes L, Surawicz B. Effects of low and high concentration of potassium on the simultaneously recorded Purkinje and ventricular action potentials of the perfused pig moderator band. Circ Res. 1968;23:717–29.
6. Wahr JA, Parks R, Boisvert D, Comunale M, Fabian J, Ramsay J, Mangano DT. Preoperative serum potassium levels and perioperative outcomes in cardiac surgery patients. JAMA. 1999;281:2203–10.

7. Yano K, Matsumoto Y, Hirata M, Hirata T, Hano O, Mitsuoka T, Hashiba K. Influence of sympathetic nerve activity on ventricular arrhythmogenicity in the dog with chronic hypokalemia. Angiology. 1991;42:878–88.
8. Obeid AI, Verrier RL, Lown B. Influence of glucose, insulin and potassium on vulnerability to ventricular fibrillation in the canine heart. Circ Res. 1978;43:601–8.
9. Tetzlaff JE, O'Hara JF Jr, Walsh MT. Potassium and anaesthesia. Can J Anaesth. 1993;40:227–46.
10. Wong KC. Hypokalemia and dysrhythmias. J Cardiothorac Anesth. 1989;3:529–31.
11. Hahm TS, Cho HS, Lee KH, Chung IS, Kim JA, Kim MH. Clonidine premedication prevents preoperative hypokalemia. J Clin Anesth. 2002;14:6–9.
12. Cho HS, Lee SM, Lee JJ, Jung IS, Kim YH, Choi DH, Shin BS. Prevention of hypokalemia before induction of anesthesia by clonidine or midazolam. Korean J Anesthesiol. 1998;34:920–4.
13. McCleane GJ, Watters CH. Pre-operative anxiety and serum potassium. Anaesthesia. 1990;45:583–5.
14. Graham I, Atar D, Borch-Johnsen K, Boysen G, Burell G, Cifkova R, Dallongeville J, De Backer G, Ebrahim S, Gjelsvik B, Herrmann-Lingen C, Hoes A, Humphries S, Knapton M, Perk J, Priori SG, Pyorala K, Reiner Z, Ruilope L, Sans-Menendez S, Scholte op Reimer W, Weissberg P, Wood D, Yarnell J, Zamorano JL, Walma E, Fitzgerald T, Cooney MT, Dudina A, European Society of Cardiology (ESC) Committee for Practice Guidelines (CPG). European guidelines on cardiovascular disease prevention in clinical practice: executive summary. Eur Heart J. 2007;28:2375–414.
15. Karasch ED, Bowdle TA. Hypokalemia before induction of anesthesia and prevention by β_2-adrenoceptor antagonism. Anesth Analg. 1991;72:216–20.
16. Massara F, Tripodina A, Rotunno M. Propranolol block of epinephrine-induced hypokalaemia in man. Eur J Pharmacol. 1970;10:404–7.
17. Tran CT, Schmidt TA, Christensen JB, Kjeldsen K. Atrial Na, K-ATPase increase and potassium dysregulation accentuate the risk of postoperative atrial fibrillation. Cardiology. 2009;114:1–7.
18. Dabar D, Smith M, Morike K, Roden DM. Epinephrine-induced changes in serum potassium and cardiac repolarization and effects of pretreatment with propranolol and diltiazem. Am J Cardiol. 1996;77:1351–5.
19. Brown MJ, Brown DC, Murphy MB. Hypokalemia from β2-receptor stimulation by circulating epinephrine. N Engl J Med. 1983;309:1414–9.
20. Adams HA, Saatweber P, Schmitz CS, Hecker H. Postoperative pain management in orthopaedic patients: no differences in pain score, but improved stress control by epidural anaesthesia. Eur J Anaesthesiol. 2002;19:658–65.
21. Siscovick DS, Raghunathan TE, Psaty BM, Koepsell TD, Wicklund KG, Lin X, Cobb L, Rautaharju PM, Copass MK, Wagner EH. Diuretic therapy for hypotension and the risk of primary cardiac arrest. N Engl J Med. 1994;330:1852–7.
22. Shah KB, Keinman BS, Rao RL, Jacobs HK, Mestan K, Schaafsma M. Angina and other risk factors in patients with cardiac diseases undergoing noncardiac operations. Anesth Analg. 1990;70:240–7.
23. Hirsch IA, Tomlinson DL, Slogoff S, Keats AS. The overstated risk of preoperative hypokalemia. Anesth Analg. 1988;67:131–6.
24. Vitez TS, Sopper LE, Wong KC, Soper P. Chronic hypokalemia and intraoperative dysrhythmias. Anesthesiology. 1985;63:130–3.
25. McGovern B. Hypokalemia and cardiac arrhythmias. Anesthesiology. 1985;63:127–9.
26. Watt JW, Silva P. Respiratory alkalosis and associated electrolytes in long-term ventilator dependent persons with tetraplegia. Spinal Cord. 2001;39:557–63.
27. Krapf R. Acid-base and potassium homeostasis. Nephrol Dial Transplant. 1995;10:1537–9.
28. Muir WW 3rd, Wagner AE, Buchanan C. Effects of acute hyperventilation on serum potassium in the dog. Vet Surg. 1990;19:83–7.
29. Desborough JP. The stress response to trauma and surgery. Br J Anaesth. 2000;85:109–17.