Association between hypokalemia and small bowel capsule endoscopy completion rates in patients in South China: A prospective single-center study

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INTRODUCTION

Small bowel capsule endoscopy (SBCE) was first introduced by Iddan et al. in 2000 as a safe and non-invasive method to record images of the digestive tract.[1-3] The advantages of SBCE include its simplicity and lack of discomfort. SBCE facilitates the detection of small intestinal abnormalities[4,5] and is regarded as one of the most important milestones in gastrointestinal diagnostics.
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One important limitation of the technique is that approximately 20–30% of SBCEs do not reach the cecum at the completion of the examination because of the limited battery life.[6] In these cases, uncertainty about the remaining small-bowel pathology remains, thus, limiting the value of SBCE. The cost of SBCE is high, and incomplete examinations are an unnecessary expense. Therefore, the possible risk factors for incomplete examinations should be identified.

The European Society for Gastrointestinal Endoscopy guidelines on SBCE recommends using polyethylene glycol (PEG)-based regimens as the first-line of small bowel preparation before SBCE.[7]

Hypokalemia after bowel preparation is not rare. Hospitalization has been considered a risk factor associated with hypokalemia before bowel preparation.[8] Hypokalemia may prolong the capsule small bowel transit time (SBTT) and influence the completion of the procedure.

To evaluate the effect of hypokalemia on SBCE, we conducted a prospective trial of patients who underwent SBCE in our hospital.

PATIENTS AND METHODS

Study design and patient population
This study was a prospective trial from January 2017 to December 2017. The age of the patients ranged from 18–75 years and included all patients undergoing SBCEs.

Eligible patients undergoing capsule endoscopy procedure with OMOM capsule (Jinshan Science and Technology Group, Chongqing, China) at The Sixth Affiliated Hospital of Guangzhou Medical University (Qingyuan People’s Hospital, Qingyuan, Guangdong Province, China) were consecutively enrolled. The exclusion criteria included patients with a history of gastric and/or small bowel surgery, small bowel or large bowel surgery involving the ileocecal valve, obstructive symptoms, ileostomies, diabetes mellitus with evidence of end-organ damage, use of prokinetic medications in the 5 days prior to the procedure, clinical hyper- or hypothyroidism, pregnancy, and the presence of any psychological, familial, or sociological condition that would potentially hamper compliance with the study protocol. Each patient provided written informed consent before beginning the study procedure. Normal potassium was defined as a serum potassium level of 3.5–5.5 mmol/L. Hypokalemia was defined as a serum potassium level <3.5 mmol/L and was categorized as mild (3.0–3.5 mmol/L), moderate (2.5–3.0 mmol/L), or severe (<2.5 mmol/L). The subjects were divided into the hypokalemia and normal potassium groups according to their baseline serum potassium levels. The baseline data were evaluated after bowel preparation was finished and before capsules were ingested. This study was approved by the Institutional Review Board of The Sixth Affiliated Hospital of Guangzhou Medical University and was registered in the Chinese Clinical Trial Registry (clinical trial registration number: ChiCTR-OPN-15007242).

Bowel preparation
For bowel preparation, patients received a PEG electrolyte solution starting the day before the procedure. Patients were instructed to eat a soft breakfast the day before the procedure and subsequently maintain a fluid-only diet starting at lunch time. Further, the patients were asked to consume 3 L of a PEG electrolyte solution (WanHe Pharmaceutical Co., Ltd., Shenzhen, Guangdong Province, China). Specifically, 1 L was consumed between 7:00 PM and 9:00 PM the night before the procedure, and the remaining 2 L was consumed between 4:00 AM and 6:00 AM the morning of the procedure. The patients were encouraged to drink clear liquids following the purgative to ensure adequate hydration and were instructed to take nothing by mouth after 6:00 AM on the day of the procedure.

Procedure
On the day of the procedure, a blood test was performed prior to capsule ingestion. All SBCE procedures commenced between 8:00 AM and 9:00 AM. During the procedure, the patients were asked to take a walk to shorten the gastric transit time (GTT). The location of the capsule endoscope was checked 2 h later using the workstation’s real-time monitoring system. If the capsule was found to be present in the stomach, an upper gastrointestinal endoscopy was performed. The serum potassium level results were obtained at 11:00 AM. Patients with moderate or severe hypokalemia were immediately provided with oral potassium supplementation. Those with mild hypokalemia were provided with oral potassium supplementation after the procedure. A blood test to determine the serum potassium level was performed again the day after the procedure in patients with hypokalemia.

Data collection
Patient data including demographics, age, sex, body mass index (BMI), and plasma potassium values were recorded. The primary endpoints of the study were the SBCE completion rates and SBTTs. The secondary endpoints were the diagnostic yields and adverse events. All SBCE videos were reviewed by 2 experienced gastroenterologists.
We considered that the cleansing was adequate if at least 50% of the small bowel mucosa was in perfect condition for visualization, without any liquid, bubbles or debris. The completion rate was defined as the frequency of SBCEs that reached the cecum within the battery life, and SBTT was defined as the elapsed time from the first duodenal image to the first cecal image. An incomplete examination was defined by a small-bowel image when the battery power had expired before the camera entered the cecum. A positive SBCE was defined as any abnormal finding in the small bowel. Capsule retention was defined as the presence of the capsule in the gastrointestinal tract for at least 2 weeks after ingestion.

**Statistical analysis**

Our sample size \( (n = 71) \) was chosen before the study and was according to an evaluation of previously reported SBCE completion rates \( (86.8\%) \). The calculations were based on the following assumptions: \( \alpha = 0.05 \), \( 1 - \beta = 0.80 \), and the existence of an expected between-groups difference of 20% or greater, which is considered a minimal clinically meaningful difference.

Percentages were used to describe categorical variables, and the mean ± standard deviation or medians (ranges) were used to describe continuous variables. For categorical variables, associations between the two groups were evaluated with a Chi-square test (applying Fisher's correction when necessary); for continuous variables, a 2-sample \( t \) test or the Mann-Whitney U test was used. For patients without a complete small-bowel view, the SBTT was censored at the last recorded time. All statistical analyses were performed using IBM SPSS 18.0 software. All tests were performed with the \( \alpha \)-level set to 0.05 (2-tailed).

**RESULTS**

Figure 1 shows the patients’ flowchart. In total, 124 patients underwent SBCEs between January and December 2017. Of these patients, nine were excluded according to the exclusion criteria and three refused to participate in the study. Therefore, 112 patients were enrolled, and our target sample size was reached.

According to their baseline serum potassium levels, 27 patients were assigned to the hypokalemia group. The patients’ baseline levels were not significantly different between the two groups. The ages of the hypokalemia and normal potassium groups were 48.1 ± 16.8 and 41.8 ± 14.5 years, respectively. The mean BMIs of the hypokalemia and normal potassium groups were 21.9 ± 3.4 and 21.6 ± 3.6, respectively. Men represented 63.0% \( (n = 17) \) of the participants in the hypokalemia group and 62.4% \( (n = 53) \) of those in the normal potassium group. The number of patients with adequate small bowel cleansing in the hypokalemia and normal potassium groups were 22 \( (81.4\%) \) and 67 \( (78.8\%) \), which was not statistically significant \( (P > 0.05) \). The serum potassium level was 3.14 ± 0.24 mmol/L in the hypokalemia group. There were 22 patients with mild hypokalemia, 5 patients with moderate hypokalemia, and no patients with severe hypokalemia. All patients with hypokalemia had normal serum potassium levels the day after the procedure following oral potassium supplementation.

The most frequent indication for SBCE in the hypokalemia group was obscure gastrointestinal bleeding (OGIB) \( (n = 9) \), followed by assessment of abnormal findings from previous results (e.g., laboratory tests, scans, and other procedures) \( (n = 5) \). Other indications included abdominal pain \( (n = 4) \), inflammatory bowel disease \( (n = 3) \), and others \( (n = 6) \). In the normal potassium group, the most frequent indication for SBCE was abdominal pain \( (n = 26) \), followed by OGIB \( (n = 24) \). Other indications included inflammatory bowel disease \( (n = 11) \), assessment of abnormal findings from previous results \( (n = 6) \), and others \( (n = 18) \) [Table 1].

The SBCE completion rate was lower in the hypokalemia group than that in the normal potassium group \( (55.6\% \ [15/27] \ vs. 76.5\% \ [65/85], P = 0.036) \).

In the hypokalemia group, the SBTT was censored for 12 patients, whereas it was censored for 20 patients in the normal potassium group in cases where the SBCE battery lost power before the camera entered the cecum. The GTT was 55.5 ± 47.1 min in the hypokalemia group and 46.7 ± 44.5 min in the normal potassium group \( (P > 0.05) \).
The SBTT was 412.8 ± 123.3 min in the hypokalemia group and 367.3 ± 172.5 min in the normal potassium group (P > 0.05) [Table 2].

Five patients in the hypokalemia group and ten in the normal potassium group had gastroscopy-assisted SBCEs. The SBCE findings are presented in Table 3.

The diagnostic yields of the hypokalemia and normal potassium groups were 74.1% and 78.8%, respectively (P = 1.00). Among the hypokalemia group, we diagnosed ulcers (n = 6), followed by active bleeding (n = 4). Other diagnoses included tumors (n = 3), erosions (n = 2), angioectasia (n = 2), lymphangiectasia (n = 1), follicular hyperplasia of the terminal ileum (n = 1), and red spots (n = 2). In the normal potassium group, the most frequent diagnosis was ulcers (n = 19), followed by active bleeding (n = 12). Other diagnoses included erosions (n = 11), lymphangiectasia (n = 9), tumors (n = 8), angioectasia (n = 3), follicular hyperplasia of the terminal ileum (n = 3), red spots (n = 1), and parasites (n = 1).

No SBCE device was retained in the gastrointestinal tract during the study. No cases of hyperkalemia occurred during the study.

**DISCUSSION**

SBCE is widely used to examine the small intestine in patients with a wide spectrum of disorders. Currently, common indications for SBCE include OGIB, Crohn’s disease, small-bowel tumors, polyps, celiac disease, and other inflammatory disorders.\(^5\)\(^-\)\(^6\) The life span of the battery that delivers power to the capsule is approximately 8–12 h. Given the limited battery life, approximately 20–30% of capsules fail to reach the cecum within the recording time.\(^20\)\(^-\)\(^21\) The value of SBCE is limited in patients who receive an incomplete examination because SBCE may miss lesions in the distal segments of the small bowel and thus require further examinations that increase costs. In several studies, investigators have attempted to determine the risk factors for incomplete SBCE examinations. Previous studies identified certain factors that might be associated with an incomplete SBCE examination, including inpatient status, older age, poor bowel preparation, hypothyroidism, bowel preparation type, previous small-bowel surgery, use of medication that alters bowel motility, prolonged GTT, and diabetes mellitus.\(^20\)\(^-\)\(^22\) In our study, we excluded those patients with a history of small-bowel surgery, diabetes mellitus with evidence of end-organ damage, use of prokinetic medications 5 days prior to the procedure, and hypothyroidism. There are few studies on the association between hypokalemia and SBCE completion rates.

Prior meta-analyses have demonstrated that the small bowel visualization quality and subsequent diagnostic yield can be improved by administering purgatives before the SBCE examination.\(^23\) Hypokalemia after bowel preparation is not rare. Several studies have shown that bowel preparations, such as sodium phosphate and PEG, may result in hypokalemia.\(^24\)\(^-\)\(^25\) For instance, in a study of patients with normal potassium levels before bowel cleansing, hypokalemia was present in 23.6% of the patients after bowel cleansing with low-volume PEG and ascorbic acid.\(^8\)

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**Table 1: Basic demographics and indications for capsule endoscopy**

| Characteristic            | Hypokalemia group (n=27), n (%) | Normal potassium group (n=85), n (%) | P   |
|---------------------------|---------------------------------|-------------------------------------|------|
| Age (years)               | 48.1±16.8                       | 41.8±14.5                           | 0.062|
| BMI                       | 21.9±3.4                        | 21.6±3.6                            | 0.698|
| Male, n (%)               | 17 (63.0)                       | 53 (62.4)                           | 0.955|
| Indication, n (%)         |                                 |                                     |      |
| OGGIB                     | 9 (33.3)                        | 24 (28.2)                           | 0.299|
| AAF                       | 5 (18.5)                        | 6 (7.1)                             |      |
| Abdominal pain            | 4 (14.8)                        | 26 (30.6)                           |      |
| IBD                       | 3 (11.1)                        | 11 (12.9)                           |      |
| Other*                    | 6 (22.2)                        | 18 (21.8)                           |      |

*Abnormal bowel movements, abdominal distension, polyp surveillance, chronic diarrhea, emaciation, reflux, malabsorption, iron-deficiency anemia, Peutz-Jeghers syndrome, and history of obstructive symptoms without stricture. BMI: Body-mass index; OGGIB: Obscure gastrointestinal bleeding; AAF: Assessment of abnormal findings; IBD: Inflammatory bowel disease

**Table 2: Primary outcomes of capsule endoscopy by group**

| Outcome                | Hypokalemia group (n=27) | Normal potassium group (n=85) | P    |
|------------------------|--------------------------|-------------------------------|------|
| CE completion, n (%)   | 15 (55.6)                | 65 (76.5)                    | 0.036|
| Total GTT (min)        | 55.5±47.1                | 46.7±44.5                    | 0.382|
| Total SBTT (min)       | 412.8±123.3              | 367.3±172.5                  | 0.207|

GTT: Gastric transit time; SBTT: Small-bowel transit time; CE: Capsule endoscopy

**Table 3: The capsule endoscopy findings in the hypokalemia and normal potassium groups**

| Findings                | Hypokalemia group (n=27), n (%) | Normal potassium group (n=85), n (%) | P   |
|-------------------------|---------------------------------|-------------------------------------|------|
| Positive findings       | 20 (74.1)                       | 67 (78.8)                           | 1.00 |
| Ulcer                   | 6 (22.2)                        | 19 (22.4)                           |      |
| Active bleeding         | 4 (14.8)                        | 12 (14.1)                           |      |
| Tumor                   | 3 (11.1)                        | 8 (9.4)                             |      |
| Erosion                 | 2 (7.4)                         | 11 (12.9)                           |      |
| Angioectasia            | 2 (7.4)                         | 3 (3.5)                             |      |
| Lymphangiectasia        | 1 (3.7)                         | 9 (10.6)                            |      |
| Follicular hyperplasia  | 1 (3.7)                         | 3 (3.5)                             |      |
| of the terminal ileum   |                                 |                                     |      |
| Red spot                | 1 (3.7)                         | 1 (1.2)                             |      |
| Parasites               | 1 (3.7)                         | 1 (1.2)                             |      |
Potassium deficiency has been shown to lead to muscle weakness. Movement of the whole digestive tract decreases progressively as the deficiency continues, and a simple potassium deficiency has been shown to greatly reduce motility in the smooth muscle organs of the gastrointestinal tract. Hypokalemia has been proposed as a factor affecting bowel motility. Hypokalemia may prolong the capsule SBTT and potentially influence SBCE completion. Thus, we conducted a prospective study to evaluate the effect of hypokalemia on SBCE.

In this study, our aim was to identify possible risk factors for incomplete small-bowel examinations in SBCE by analyzing data from 112 consecutive SBCE procedures performed in our hospital.

First, in our prospective analysis of the effects of hypokalemia on SBCE, we demonstrated that hypokalemia is associated with incomplete SBCE procedures. The SBCE completion rate was lower in the hypokalemia group than that in the normal potassium group (55.6% vs. 76.5%, \( P = 0.036 \)). This finding suggests that potassium deficiencies should be rectified before performing SBCE procedures to increase the completion rate.

Moreover, the overall diagnostic yield of SBCE, which ranged from 66% to 80%, was not significantly different between the hypokalemia and normal potassium groups and was similar to the yields reported in previous studies.\(^{[7,27]}\)

Our study had several limitations. First, it was designed as a small, single-center, non-randomized controlled study. Second, as the number of patients was very small, we did not account for patients with moderate or severe hypokalemia who were treated with oral supplementation in the analysis. Third, we did not account for inpatient status, bedridden status, and constipation when enrolling patients. Fourth, potassium measurement was evaluated after (not before) bowel preparation and before the capsule was ingested. Finally, SBTT could not be accurately measured in the cases of incomplete SBCE. We chose to censor the SBTT at the last small-bowel image instead of excluding patients with incomplete SBCEs from the SBTT comparisons. This approach ensured that incomplete cases were represented in the SBTT comparisons for both groups. The maximum SBTT values from incomplete examinations in the hypokalemia and normal potassium groups were 752 min and 899 min, respectively.

Our study aimed to increase awareness and knowledge regarding hypokalemia during SBCE. Additional large, multicenter, prospective studies must be conducted to further assess the effect of hypokalemia on SBCE.

**CONCLUSION**

Hypokalemia is associated with incomplete SBCE procedures. Physicians should test for hypokalemia, which can occur after bowel preparation. Potassium deficiencies should be rectified before performing SBCE procedures to increase the completion rate.

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**Conflicts of interest**

There are no conflicts of interest.

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