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Comparison of treatment of hypokalemia with oral administration of potassium chloride vial or oral tablets

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ABSTRACT

Introduction: Treatment of mild to moderate hypokalemia is a high potassium-containing diet and oral pharmaceutical potassium products. However, several medical centers in Iran use injectable dosage forms orally, which is not a confirmed method by reliable guidelines.

Objectives: This study investigated the advantages and side effects of oral tablets versus injection vials of potassium chloride orally.

Patients and Methods: This descriptive-analytical cross-sectional study was performed from March 2022 to June 2022. Thirty patients received tablets ("potassium chloride tablet" group), and thirty patients received injection vials ("potassium chloride vials orally" group) of potassium chloride orally. The variables, including age, gender, clinical side effects, and serum level of potassium, were regularly recorded.

Results: The mean duration of serum potassium normalization was 42.00 hours for the "potassium chloride tablet" group and 84.57 hours for the "potassium chloride vials orally" group. The mean total potassium intake was 127.20 mEq/L in the "potassium chloride tablet" group and 280.03 mEq/L for the "potassium chloride vials orally" group. No significant difference was observed in gastrointestinal complications, including esophagitis, bloating, stomach ache, and nausea. None of the patients have required endoscopy due to esophagitis.

Conclusion: Our result suggested that prescribing oral potassium chloride tablets has superior benefits over injection vials. However, more detailed research is needed to reveal the other aspects of this problem.

Study Registration: This study was retrospectively registered in Research Registry UIN (UIN: reviewregistry1668).

Original Article

Implication for health policy/practice/research/medical education:
In the present study, sixty patients into two groups received tablets and injection vials of potassium chloride orally. The side effects and efficacy of the two dosage forms were compared. We found that potassium chloride tablets are more efficient compared to injection vials.

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Introduction

Hypokalemia defines the serum concentration of potassium as less than 3.5 mEq/L. This disorder is divided into mild (3-3.5 mEq/L), moderate (2.5-3 mEq/L), and severe (≤2.5 mEq/L) subgroups (1). Hypokalemia occurs for various reasons such as inadequate dietary potassium intake, increased gastrointestinal loss, increased renal loss, transcellular shift, hematologic disorders, and hypomagnesemia. Some drugs can also cause hypokalemia by different mechanisms (e.g., aminoglycosides, amphotericin B and diuretics with increased urinary excretion, laxatives with increasing excretion through the gastrointestinal tract and beta two agonists, and insulin with transcellular shift (2,3).

Potassium can be taken intravenously or orally, which has different absorption levels. The absorption of

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potassium from the gastrointestinal tract is mainly by an inactive transfer mechanism and occurs primarily in the small intestine; this transfer follows first-order kinetics and is also concentration-dependent (4).

Treating mild to moderate hypokalemia usually includes oral products or high-potassium-containing diets on the market. In many medical centers in Iran for hypokalemia treatment, potassium chloride injection vials are prescribed orally instead of in oral formulations. It can cause several adverse effects in case of rapid absorption from the gastrointestinal tract. In addition, no guidelines or sources indicate that potassium chloride vials can be used orally (1,4).

It should be noted that the osmolality of the potassium chloride vials is very high; if the dilution process is not performed correctly, the oral use of potassium chloride vials may cause adverse effects similar to the high infusion rate of intravenous injection of the drug. We are still determining this hypothesis. Another concern with taking potassium chloride orally is the complication of esophagitis. Potassium chloride can directly irritate the esophagus and causes esophagitis (5).

Objectives

The present study examines the administration of oral tablet versus injection vial orally in terms of the duration of potassium normalization, the total amount of potassium intake, and adverse complications.

Patients and Methods

Study design

This descriptive-analytical cross-sectional study was performed in Ahvaz Golestan hospital, Iran. Sixty patients over 18 years of age with mild to moderate hypokalemia (2.5-3.5 mEq/L) and normal magnesium levels were selected. Demographic parameters, including age, gender, and clinical side effects, were recorded, and patients were selected through medical files. The patient's potassium levels were recorded every 8 hours. In the medical file assessment, thirty patients received potassium chloride vials orally 12 mL every 8 hours, equivalent to 3 modified-release potassium chloride tablets, and thirty patients received three modified-release potassium chloride tablets every 8 hours as a routine treatment.

Inclusion criteria were age over 18, mild to moderate hypokalemia, and average magnesium level. Exclusion criteria were pregnancy, breastfeeding, severe hypokalemia, patients who used drugs that interfered with potassium serum levels, patients who had symptoms of esophagitis before initiating potassium chloride, and participants who were not willing to participate in the study.

The primary outcomes were reaching the duration of potassium normalization (serum potassium levels >4 mEq/L) and the total amount of potassium intake. The secondary outcomes were the symptoms of esophagitis, pain, nausea, and bloating.

Statistical analysis

The quantitative variables were described using the mean and standard deviation, while the qualitative variables were described using the frequency and percentage**.** The comparisons were performed using an independent t-test for quantitative variables, the chi-square test, and Fisher's exact test for qualitative variables. All statistical analyses were performed using SPSS version 25. A P value < 0.05 was considered statistically significant.

Results

A total of 60 patients entered the study. Thirty patients were in the "potassium chloride vials orally" group, and thirty patients were in the "potassium chloride tablet" group. Twelve (40%) of patients were male, and eighteen (60%) of patients were female in the "potassium chloride vials orally" group. Seventeen (56.7%) of patients were male, and thirteen (43.3%) of patients were female in the "potassium chloride tablet" group. There was no significant difference between the two genders (P=0.301).

Twenty-five (83.3%) patients in the "potassium chloride vials orally" group and twenty-two (73.3%) patients in the "potassium chloride tablet" group had mild hypokalemia. Five (16.7%) patients in the "potassium chloride vial orally" group and eight (26.7%) patients in "potassium chloride tablet" group had moderate hypokalemia. The two groups had no significant difference regarding mild and moderate hypokalemia (P=0.532).

The serum potassium level of twenty-eight (93.3%) patients was normalized in both groups. The mean total potassium intake was 280.03 mEq for the "potassium chloride vials orally" group and 127.20 mEq for the "potassium chloride tablet" group. The mean duration of potassium normalization was 84.57 hours for the "potassium chloride vials orally" group and 42.00 hours for the "potassium chloride tablet" group. There was a significant difference between the two groups regarding the meantime of serum potassium normalization (P=0.002) and the mean total potassium intake (P=0.003).

The most common adverse reactions were esophagitis in the "potassium chloride vials orally" group (23.3%) and stomach ache in the "potassium chloride tablet" group (16.7%). Bloating occurred in none of the patients in the "potassium chloride tablet" group. Other adverse reactions are shown in detail (Table 1). None of the patients required endoscopy due to esophagitis.

Discussion

Hypokalemia is found in more than 20% of hospitalized

Table 1. Gastrointestinal complications comparison in "potassium chloride vials orally" and "potassium chloride tablet" groups

Variable		Groups		*P* value
		Potassium chloride tablet, No. (%)	Potassium chloride vials orally, No. (%)	
Esophagitis	+	2 (7.6)	7 (23.3)	145.0
	-	28 (93.3)	23 (76.7)	
	Total	30 (100)	30 (100)	
Bloating	+	0 (0)	1 (3.3)	>0.999
	-	30 (100)	29 (96.7)	
	Total	30 (100)	30 (100)	
Stomach ache	+	5 (16.7)	5 (16.7)	>0.999
	-	25 (83.3)	25 (83.3)	
	Total	30 (100)	30 (100)	
Nausea	+	1 (3.3)	2 (7.6)	>0.999
	-	29 (96.7)	28 (93.3)	
	Total	30 (100)	30 (100)	

patients. Mild or moderate hypokalemia increases the risks of morbidity and mortality in patients with cardiovascular disease (6). Therefore, correction is vital. Potassium chloride can be given in liquid or tablet form to correct mild to moderate hypokalemia (7). Due to the absence of a liquid dosage form, prescribing injection vials of potassium chloride orally is a standard method used in our hospitals. The hyperosmolarity of vials can affect the intestine and shrink the cellular of the gastrointestinal tract.

There is a specific instruction for the oral administration of vancomycin injection vials. The administration section of this drug states how much vancomycin can be given to the patient with fruit juice and how much can be given with water. However, potassium chloride, such as vancomycin, is not stated that its vial can be given orally to the patient; no other reference or guideline mentions this issue. The bioavailability of drugs varies according to the administered route (8). For example, vancomycin must be given intravenously for most infections except for treating *Clostridium difficile* because of its poor oral bioavailability (9). Additionally, gastrointestinal abnormalities and some systemic diseases can affect the bioavailability of orally administered drugs (10); an increased plasma and renal clearance of dicloxacillin were observed in a patient with cystic fibrosis (11). Diabetes mellitus can consequently influence oral drug performance because it affects gastrointestinal function (12). Rifampin and ethambutol plasma concentrations were significantly low in HIV/AIDS patients (13). In a case report, oral vancomycin had significantly higher absorption in a patient who had colitis (14), since one of our patients with inflammatory bowel disease, experienced severe abdominal pain three hours after taking oral potassium chloride tablets. Therefore, there are concerns about the oral intake of potassium chloride and that its absorption could be affected by underlying diseases and pathological conditions that can be fatal or ineffective.

Several studies have pointed out the side effects of potassium chloride tablets; in one study in 1965, potassium chloride oral tablets were responsible for a striking increase in ulcerative lesions of the small intestine (15). In another study, a patient with rheumatic heart disease, potassium chloride oral formulation produced severe esophageal ulceration (16). In general, oral formulations most commonly correlate with gastrointestinal irritation, including vomiting and diarrhea (17). However, until now, there was no previous study that investigated the side effects of potassium chloride injection vials orally. We compared adverse complications, including esophagitis, pain, nausea, and bloating of each dosage form of the drug orally (tablets and injection vials), and no significant differences were observed.

Our statistical data analysis showed that prescribing an oral tablet formulation can significantly reduce the duration of hypokalemia treatment and total potassium intake. The result clearly favors the "potassium chloride tablet" group rather than the "potassium chloride vials orally" group. This study has been conducted for the first time; hence, to improve the accuracy of the results, more studies are required.

Conclusion

Our result suggested that prescribing oral potassium chloride tablets has superior benefits over injection vials. Based on this fact, the administration of tablet formulations can reduce the cost and time of medical centers. None of the mentioned formulations are superior to each other in terms of gastrointestinal adverse reactions.

Limitations of the study

The patients receiving tablets in our study received 24 mEq of potassium chloride every 8 hours. This amount was equivalent to three modified-release tablets (one modified-release tablet is equal to 8 mEq of potassium chloride); many of the patients who received the tablets

could not tolerate the receiving of this dose of large tablets daily and had low adherence to therapy. This problem took much work to manage.

Authors' contribution

Conceptualization: Farzaneh Hematian.
Data curation: Hosein Jafari.
Formal analysis: Farzaneh Hematian, Reza Ganji, Ahmad Nezhadisalami.
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Project administration: Farzaneh Hematian.
Resources: Farzaneh Hematian, Leila Sabetnia.
Supervision: Farzaneh Hematian.
Validation: Farzaneh Hematian, Leila Sabetnia.
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Writing–original draft: Hosein Jafari and Farzaneh Hematian.
Writing–review and editing: Farzaneh Hematian, Reza Ganji, Leila Sabetnia, Ahmad Nezhadisalami.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

The research conducted in this study adhered to the principles outlined in the Declaration of Helsinki and was approved by the Ethics Committee of Ahvaz Jundishapur University of Medical Sciences (Ethical code No. IR.AJUMS.REC.1400.542). Prior to any intervention, all participants provided written informed consent. The study was retrospectively registered in Research Registry UIN (UIN: reviewregistry1668). The study was extracted from Hosein Jafari's Pharmacology thesis in the department of clinical pharmacy at this university (Thesis #U-00252). The authors have fully complied with ethical issues, such as plagiarism, data fabrication, and double publication.

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