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Original Research

Evaluation of hyperkalemia associated with intravenous co-trimoxazole in hospitalized patients in Oman

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Abstract

Co-trimoxazole is a combination of two antimicrobial drugs, (trimethoprim and sulfamethoxazole), that are used to treat a wide variety of infections such as urinary tract infection, pneumocystis pneumonia and traveler's diarrhea. Hyperkalemia is a life-threatening electrolyte disturbance. Objectives: This study aimed to determine the incidence of hyperkalemia and its risk factors among hospitalized patients receiving intravenous co-trimoxazole at Sultan Qaboos University Hospital (SQUH) in Muscat, Oman. Methods: This retrospective observational study included patients that were prescribed intravenous co-trimoxazole and identified using a computerized pharmacy system between January 2010 and December 2020. Patients' demographic and clinical characteristics were retrieved from their electronic medical records. The data were analyzed using descriptive and inferential statistical tests. Results: A total of 420 patients participated in this study. The median age of the patients was 51 (35-65) years and 55.5% were male. Hyperkalemia associated with co-trimoxazole was observed in (40.2%) of the patients. Around (44.2%) of patients who experienced hyperkalemia received a high dose of co-trimoxazole (15-20 mg/kg). Hyperkalemia occurred after the 5th day of co-trimoxazole treatment. Logistic regression analysis showed no relationship between hyperkalemia and age (adjusted odds ratio (AOR) 1.054, p=0.84), sex (AOR 1.167; p=0.471), dose (AOR 0.779; p=0.251), or use of concomitant medications (angiotensin-converting inhibitors, AOR 1.054, p=0.84; angiotensin receptor blockers, AOR 0.564; p=0.734; β-blockers, AOR 0.986; p=0.963; potassium supplements, AOR 0.59; p=0.175; nonsteroidal anti-inflammatory drugs, AOR 0.842, p=0.684; spironolactone AOR 0.748, p=0.629; heparin AOR 0.822, p=0.382; calcineurin inhibitor, AOR 1.537, p=0.406). Conclusion: Co-trimoxazole use was associated with a high incidence of hyperkalemia in this group of patients. No association between hyperkalemia and risk factors was observed. Serum potassium levels should be closely monitored, especially in the first week of co-trimoxazole treatment, to prevent the incidence of hyperkalemia, and clinical staff should adhere to serum monitoring guidelines.

Keywords: co-trimoxazole; intravenous; hyperkalemia

INTRODUCTION

Co-trimoxazole, a combination of two antimicrobial agents (trimethoprim and sulfa-methoxazole), was introduced in 1968 in a ratio of 1:5. These two drugs act synergistically against a wide variety of aerobic bacteria, both Gram-positive and Gram-negative, as well as against certain parasitic infections.[1] Co-trimoxazole is the drug of choice for the treatment of Pneumocystis jirovecii pneumonia. It is also used for certain urinary tract, gastrointestinal, and skin infections, as well as prophylaxis for pneumocystis pneumonia. It is a commonly prescribed antibiotic, owing to its effectiveness and low cost. In Canada and in the United States, co-trimoxazole is the most frequently prescribed antibiotic for urinary tract infections.[2,3]

Trimethoprim reversibly binds to and inhibits dihydrofolate reductase, an enzyme that reduces dihydrofolicacid to tetrahydrofolic acid, thereby decreasing folic acid synthesis. Sulfamethoxazole, a sulfonamide drug, is a structural analog of para-aminobenzoic acid (PABA) that competitively inhibits the synthesis of dihydrofolic acid, thereby preventing its synthesis of folic acid.[4]The absorption of co-trimoxazole through the gastrointestinal tract is rapid and the drug reaches its therapeutic concentration in most bodily fluids and tissues. Therefore, this drug is indicated in a wide range of clinical situations.[5]

Co-trimoxazole is available for oral (PO) and intravenous (IV) preparations. The standard single-strength tablet for oral use contains 400 mg of sulfamethoxazole and 80 mg of trimethoprim. Double-strength tablet, which is more clinically used is also available. An IV preparation with 16 mg trimethoprim and 80 mg sulfamethoxazole per ml is also available. Both IV and PO dosages of 15mg/kg/day trimethoprim produced maximum concentrations during the dose interval within the target range for treatment of infections with different pathogens.

Co-trimoxazole affects the metabolism of many common drugs that are frequently prescribed in concurrence with antibiotics, thus necessitating the consideration of the potential risks in patients using such drugs.[7] The major drug interactions with co-trimoxazole include warfarin, methotrexate, phenytoin,

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digoxin, sulfonylureas and oral contraceptives.[7] Although co-trimoxazole is a safe medication that is well-tolerated by many patients, it is associated with several possible adverse reactions, with gastrointestinal and dermatological adverse reactions being the most commonly demonstrated effect.[8,9] Many of these adverse effects are mild and dose-related; however, others are potentially serious and can be life-threatening, including hyperkalemia, serum creatinine elevation, bone marrow suppression, blood dyscrasias, and hepatotoxicity.[10]

Hyperkalemia is a life-threatening metabolic condition characterized by the inability of the kidneys to excrete potassium, impairment of mechanisms that transport potassium from the blood into cells, or a combination of these two factors.[11] Hyperkalemia tends to occur after several days of co-trimoxazole therapy, and its symptoms are usually nonspecific, benign, and present as muscle weakness that develops into flaccid paralysis, paresthesia, or depressed deep tendon reflexes until cardiac rhythm or conduction disorders occur.[12] Certain patient populations have an increased risk of hyperkalemia.

These include advanced age, advanced stages of chronic kidney disease, heart failure, hypertension, diabetes mellitus, and/or a combination of these conditions.[13,14] Additionally, the risk of hyperkalemia progressively increases in patients receiving certain drugs.[15-16]

The Dutch guidelines advise that serum potassium levels should be monitored during co-trimoxazole treatment in patients at high risk of hyperkalemia. The Royal Dutch Pharmacists Association Guideline recommends serum potassium monitoring for patients using co-trimoxazole in combination with potassium-sparing diuretics, angiotensin converting enzyme inhibitors or angiotensin receptor blockers.[17] The Dutch Pharmacotherapeutic Compass also recommended that all patients with risk factors for hyperkalemia should be monitored for hyperkalemia, including patients aged over 70 years, patients with diabetes mellitus or heart failure, patients who use other potassium-elevating medications, and those who receive high doses of co-trimoxazole (15-20 mg/kg) for the treatment of *Pneumocystis jirovecii pneumonia*.[18]

This single-center retrospective observational study was conducted in Turkey in 2021. The records of 64 patients who received co-trimoxazole in the ICU were examined to assess the incidence of hyperkalemia. The incidence of hyperkalemia in the ICU was 49%. Hyperkalemia occurred 6.2±3.8 days after the beginning of co-trimoxazole treatment.[19] In 2020, Adawi et al. found that co-trimoxazole use was associated with a high incidence of hyperkalemia, especially among older patients and those receiving it in combination with other medications.[20] Another study conducted in the Netherlands reported that the incidence of hyperkalemia was 20% in the co-trimoxazole-receiving group, compared to 5% in the ceftriaxone group and low adherence to the Dutch guidelines for monitoring potassium levels in patients receiving co-trimoxazole.[17] A retrospective study conducted at a tertiary care medical center in South Carolina reported that the overall frequency of elevated serum potassium levels was 36%. Hyperkalemia requiring therapeutic intervention occurred in 12 patients in the high-dose group and in two patients in the low-dose group.[21]

Generally, patients who receive IV co-trimoxazole are more vulnerable to adverse reactions, such as hyperkalemia because they usually use concomitant drugs or complain of potassium-altering comorbidities. Hyperkalemia is reported as unexpected finding and represents a common cause for hospital readmissions or emergency department visits.

This study aimed to evaluate the incidence of hyperkalemia with IV co-trimoxazole at Sultan Qaboos University Hospital (SQUH) in Muscat, Oman. The specific objectives were to determine the incidence of hyperkalemia in hospitalized patients receiving co-trimoxazole, to compare the incidence of hyperkalemia in patients receiving low-dose and high-dose co-trimoxazole and at different times after initiation of the drug, and to assess the association between the incidence of hyperkalemia and certain risk factors, such as age, sex, dosage, and the use of concomitant medications.

MATERIALS AND METHODS

Study Setting and Design

The study was conducted at SQUH, a 500-bed tertiary care hospital in Oman that includes different inpatient and outpatient units. The study was retrospective cross-sectional, covering data for 10 years between (January 2010 and December 2020) from all medical records of patients who received co-trimoxazole for therapeutic or prophylactic indications at SQUH.

Data Collection and Variables

Data were collected in a predesigned Excel® form using the Trak Care® system, the electronic patient record (EPR), and the system used by SQUH to store patient information. Patients who received co-trimoxazole were identified using a computerized pharmacy system. Electronic medical records were reviewed to obtain relevant data, including patients' demographic data (age, sex, weight, height, and body mass index (BMI)), drug history including dose, route of administration, and duration of co-trimoxazole, and comorbid medical conditions including cardiovascular disease, diabetes mellitus, hemolysis, hypertension and sepsis. Concurrent medications potentially affect serum potassium levels including β-blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, calcineurin inhibitors, heparin, potassium-sparing diuretics (spironolactone), non-steroidal anti-inflammatory drugs, potassium supplements, and antifungals (ketoconazole). Potassium monitoring was assessed in four time slots: one before initiation of antibiotic therapy (in the first week before starting the drug) and three after initiation of antibiotic therapy (0-48h, 48-120, and after 120h until the end of antibiotic therapy). Since there are no clear criteria for regular serum potassium monitoring in the guidelines, guideline adherence was defined as in this period of 48-120 h when trimethoprim reached the steady-state concentration. Therefore, we chose different times before and after this period to assess the

increase in the potassium levels.

Used Definition

Hyperkalemia was defined as a serum potassium level >5.1 mmol/L according to the reference value at SQUH.

Inclusion Criteria and Exclusion Criteria

Inclusion criteria

The patient selection criteria included all adult patients (≥18 years) with GFR ≥60 mL/min, who received intravenous co-trimoxazole for different indications, whose potassium level was normal at the beginning of administration of IV co-trimoxazole and had documented potassium serum levels at baseline and during follow-up.

Exclusion criteria

Patients whose therapy was <48h, GFR was<60 ml/min, and those who had no recorded potassium baseline and follow-up levels were excluded from the study.

Sample Size

According to previous studies, the incidence of hyperkalemia associated with intravenous co-trimoxazole ranges from 16% to 63%[22,23]. We hypothesized that the incidence of hyperkalemia with co-trimoxazole at SQUH would be 40%. The minimum effective size was calculated with a hyperkalemia rate of 40%, margin of error of 5% and 95% confidence interval**;** and the sample size was estimated to be 363 patients. To compensate for the missing data, the sample size was adjusted upwards to 420 patients.

Statistical Analysis

Descriptive statistics were used to describe the data. Continuous data were described as medians and interquartile ranges for non-normally distributed variables and mean and SD for normally distributed variables. Categorical data were expressed as frequencies and percentages. For the association between hyperkalemia and other categorized characteristics, chi-squared tests was employed. An ANOVA test was performed to assess the changes in the mean potassium level at different times, Bartlett's test was performed to test the equality of variance. Multivariable logistic regression was used to determine the association between the risk factors and the development of co-trimoxazole-induced hyperkalemia. Statistical significance was set at $p< 0.05$. Data were analyzed using Statistical Package for Social Sciences (SPSS) software version 25, IBM Corp. Released 2020, IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY: IBM Corp., USA.

RESULTS

Of the 920 patients reviewed, 235 patients were excluded due to impaired renal function (GFR <60 mL/min/1.73 m2), 200 patients did not have follow-up data, and 65 patients had less than two doses of co-trimoxazole. A total of 420 electronic medical records of patients who fulfilled the inclusion criteria (233 males, 187 females) were examined for the incidence of hyperkalemia. (Figure 1).

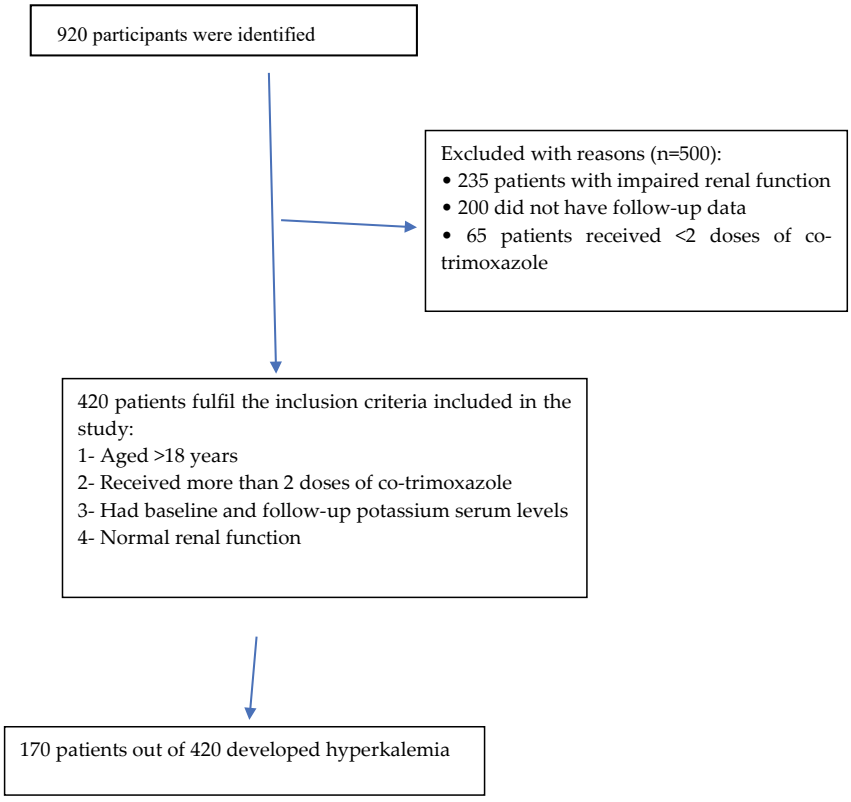

Figure 1. A flow chart of the screening process

Patient's Demographics

The characteristics of the study population are summarized in Table 1. The median age of the patients was 51 years (35-65), and 55.5% were men, with the majority (40%) age group of 60-80 years old. Patients treated with ACEi/ARBs, β-blockers, NSAIDs or potassium-sparing diuretic use concomitantly with co-trimoxazole was 5.5%, 1.2%, 16.4%, 6.9%, and 3.8%, respectively. The most common underlying conditions were sepsis, and hypertension, with percentages of 24.3% and hypertension 23.1%, respectively. A total of 264 (62.9%) patients were prescribed co-trimoxazole at a low dose of 5-10 mg/kg trimethoprim, while the remaining patients received a high dose of 15-20 mg/kg trimethoprim.

Distribution of the Potassium level

Table 2 shows the changes in average serum potassium levels before drug initiation and during the three follow-up measurement points. The mean of the baseline serum potassium was 4.1± 0.4 mmol/L and the mean follow-up of potassium level after 5 days was 4.81± 0.8 mmol/L with 0.68 mmol/L higher than at baseline. ANOVA revealed a highly significant difference between at least two groups (F=77.209, p<0.001). The least significant difference (LSD) showed that there was a highly significant difference between all pairs of comparisons and that the mean of the baseline (4.1, p<0.001) was significantly lower than the three other mean (4.4, 4.6, 4.8, p<0.001).

Table 1. Patients' Characteristics

Characteristics	**Value**
Number of patient	420
Age, median (IQR), years	51.0 (35-65)
Gender, n (%)	
Male	233 (55.5%)
Female	187 (44.5%)
Co-trimoxazole dosage, n (%)	
High dose, 15-20 mg/kg	156 (37.1%)
Low dose, 5-10 mg/kg	264 (62.9%)
Concomitant medications, n (%)	
ACEi	23 (5.5%)
ARBs	5 (1.2%)
β -Blocker	69 (16.4%)
Ketoconazole	2 (0.2%)
Potassium supplements	40 (9.5%)
NSAIDs	29 (6.9%)
Calcineurin inhibitors	18 (4.3%)
Spironolactone	16 (3.8%)
Heparin	162 (38.6%)
Underlying diseases, n (%)	
HF	53 (12.6%)
DM	67 (16%)
HTN	97 (23.1%)
Sepsis	102 (24.3%)
Hemolysis	19 (4.5%)

ACEi: angiotensin-converting enzyme inhibitors; ARBs: Angiotensin receptor blockers; NSAID: Non-steroidal anti-inflammatory drugs; HF: Heart failure; DM: diabetes mellitus; HTN: Hypertension

Table 2. Potassium level at different time

Serum potassium(K) level	Mean (mmol/L)	Standard deviation	*p*-value
before drug	4.1	0.4	<0.001
0-48 h after drug	4.4	0.5	<0.001
48-120 h after drug	4.6	0.6	<0.001
>120 h after drug	4.8	0.8	<0.001

The incidence of hyperkalemia

Figure 2. indicates the incidence of hyperkalemia in three different time slots after initiating co-trimoxazole, showing that the highest incidence of hyperkalemia occurred five days after starting co-trimoxazole therapy. Hyperkalemia (potassium serum concentration >5.1 mmol/ L) was observed in 170 (40.5%) patients, of whom, 69 (44.2%) were in the high dosing group. One hundred and one (59.4%) patients who developed hyperkalemia received concurrent medications known to increase serum potassium levels (Figure 3). Table 3 compares the incidence of hyperkalemia between the low-dose and high-dose IV co-trimoxazole among different co-administered medication groups. Receiving IV co-trimoxazole in combination with β-blockers or heparin was associated with a higher incidence of hyperkalemia. However, this difference was not statistically significant between the co-trimoxazole and co-administered medications. The associations between hyperkalemia and the risk factors are summarized in Table 4. No statistically significant associations were found between hyperkalemia and age, sex, dose, concomitant medications or diseases in patients receiving IV co-trimoxazole. This could be attributed to the limited sample size in our study, which showed that the study was underpowered for secondary analyses.

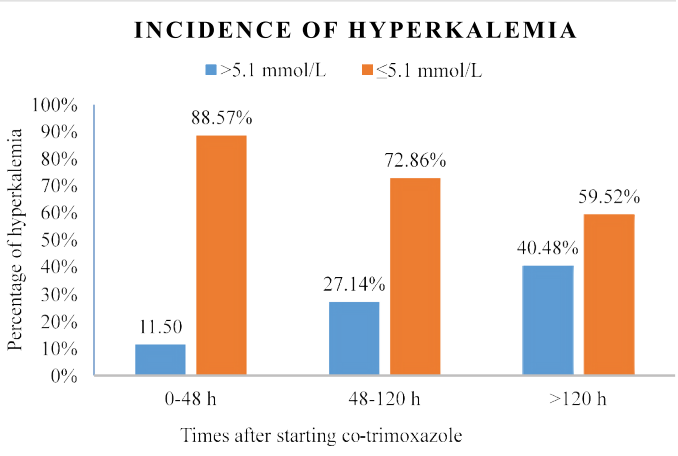

Figure 2. Incidence of hyperkalemia over time after administration co-trimoxazole

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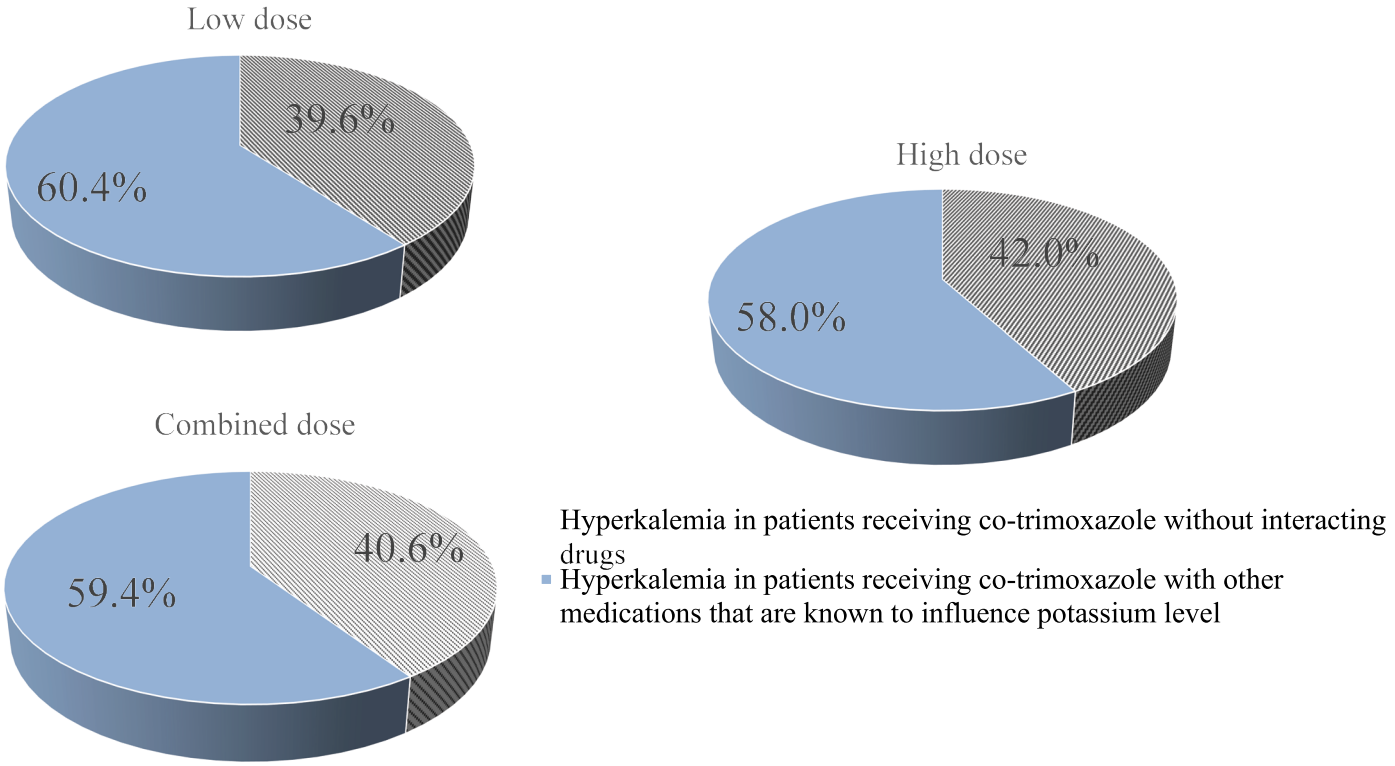

Figure 3. Presence of hyperkalemia in patients receiving co-trimoxazole with and without other medications

Table 3. Incidence of hyperkalemia among different co-administered medications groups

Incidence of hyperkalemia among different co-administered medication groups	**Total N=146**	**Low dose** (5-10 mg/kg) **N=90**	**High dose** (15-20 mg/kg) **N=56**	**p-value**
ACEi	9 (8.9%)	7 (11.5%)	2 (5.0%)	0.116
ARBs	1 (1.0%)	1 (1.6%)	0 (0.0%)	0.613
β -blockers	27 (26.7%)	16 (26.2%)	11 (27.5%)	0.919
Ketoconazole	1 (1.0%)	0 (0.0%)	1 (2.5%)	0.371
Potassium supplement	11 (10.9%)	7 (11.5%)	4 (10.0%)	0.185
NSAIDs	11 (10.9%)	6 (9.8%)	5 (12.5%)	0.48
Sprinolactone	5 (5.0%)	4 (6.6%)	1 (2.5%)	0.272
Heparin	72 (71.3%)	44 (72.1%)	28 (70.0%)	0.511
Calcineurin inhibitor	9 (8.9%)	5 (8.2%)	4 (10.0%)	0.512

ACEi: Angiotensin-converting enzyme inhibitors, ARBs: Angiotensin receptor blockers, NSAID, Non-steroidal anti-inflammatory drugs. Significance value p<0.05

Table 4. Multivariate logistic regression analysis for factors associated with hyperkalemia in patients receiving I.V co-trimoxazole

		Hyperkalemia Present Fr (%) n= 170	Hyperkalemia Absent Fr (%) n= 250	p-value
Age Group	13 - 39	52 (30.6)	86 (34.4)	0.303
	40 - 60	61(35.9)	80 (32.0)	0.84
	>60	57 (33.5)	84 (33.6)	
Gender	Male	100 (58.8)	133 (53.2)	0.471
	Female	70 (41.2)	117 (46.8)	
Co-trimoxazole dose	Low (5-10 mg/kg)	101 (59.4)	163 (65.2)	0.251
	High (15-20 mg/kg)	69 (40.6)	87 (34.8)	

ACEi	No	161 (94.7)	236 (94.4)	
	Yes	9 (5.3)	14 (5.6)	0.734
ARB	No	169 (99.4)	246 (98.4)	
	Yes	1(0.6)	4 (1.6)	0.641
β -blocker	No	143 (84.1)	208 (83.2)	
	Yes	27 (15.9)	42 (16.8)	0.963
Ketoconazole	No	169 (99.4)	250 (100.0)	
	Yes	1 (0.6)	0 (0.0)	1.000
Potassium supplement	No	159 (93.5)	221 (88.4)	
	Yes	11 (6.5)	29 (11.6)	0.175
NSAID	No	159 (93.5)	232 (92.8)	
	Yes	11 (6.5)	18 (7.2)	0.684
Spironolactone	No	165 (97.1)	239 (95.6)	
	Yes	5 (2.9)	11 (4.4)	0.629
Heparin	No	98 (57.6)	160 (64.0)	
	Yes	72 (24.2)	90 (36.0)	0.382
Calcineurin inhibitors	No	161(94.7)	241 (96.4)	
	Yes	9 (5.3)	9 (3.6)	0.406
HF	No	153 (90.0)	214 (85.6)	
	Yes	17 (10.0)	36 (14.4)	0.070
DM	No	142 (83.5)	211 (84.4)	
	Yes	28 (16.5)	39 (15.6)	0.491
HTN	No	134 (78.8)	189 (75.6)	
	Yes	36 (21.2)	61 (24.4)	0.175
Sepsis	No	122 (71.8)	196 (78.4)	
	Yes	48 (28.8)	54 (21.6)	0.146
Hemolysis	No	162 (95.3)	239 (95.6)	
	Yes	8 (4.7)	11 (4.4)	0.865

ACEi: Angiotensin-converting enzyme inhibitors, ARBs: Angiotensin receptor blockers, NSAID: Non-steroidal anti-inflammatory drugs, HF: Heart failure, DM:diabetes mellitus, HTN: Hypertension.

As seen in Figure 3, hyperkalemia (potassium serum concentration >5.1 mmol/ L) was observed in 170 (40.5%) patients, of whom, 69(44.2%) were in the high dosing group. One hundred and one (59.4%) of the patients who developed hyperkalemia were receiving concurrent medications known to increase potassium serum levels.

DISCUSSION

This study found that 40% of patients who received co-trimoxazole for prophylactic or treatment purposes developed hyperkalemia after five days of therapy. The mean potassium level increased significantly by 0.68 mmol/L from baseline. There was no association between co-trimoxazole-induced hyperkalemia and age, sex, dose, concomitant medication or diseases that are considered risk factors for hyperkalemia.

The incidence of hyperkalemia

In the current study, 170 of 420 (almost 40%) patients who received co-trimoxazole developed hyperkalemia which demonstrates that hyperkalemia is a common adverse effect of co-trimoxazole. Studies that compared the incidence of hyperkalemia associated with co-trimoxazole and other antibiotics showed that the use of co-trimoxazole was associated with a substantially greater risk of hyperkalemia.[24,17] The results of our study are consistent with those of studies conducted by Celeste. et al in the USA and by Mengi T et al. in Turkey where the incidence of hyperkalemia were 36% and 47%, respectively.[21,22]

Regarding the incidence of hyperkalemia associated with different types of co-administered medications, our study showed that a combination of co-trimoxazole and heparin or β-blockers showed the highest incidence of hyperkalemia (71.3.0%) (26.7%); a similar finding was reported by Al-Adawi et al.[20] However, several studies showed contradictory results regarding the incidence of hyperkalemia and concomitant administration of ACEi/ARBs, β-blockers, or potassium-sparing diuretics with co-trimoxazole.[10,24]

The findings of this study were not statistically significant in terms of sex or age. The incidence of hyperkalemia was slightly higher in males (58.8%) than in women (41.2%), which is consistent with the results reported by Al-Adawi et al.[21] Additionally, Mori et al. found no statistically significant relationship between hyperkalemia and patient sex.[23] Based on studies conducted in male mice, the plasma potassium concentration was found to be increased by testosterone and amiloride.[25]

Our findings showed that the percentage of hyperkalemia was slightly higher in the age group of 40-60 years (35.9%) than in the >60 years age group (33.5%). These results contradict the findings of other studies that reported the highest percentage of hyperkalemia among patients of advanced age.[20,23] These contradictory results can be explained by the presence of other confounding risk factors associated with an increased percentage of hyperkalemia, such as the presence of underlying diseases in the middle-aged group.

The Level of hyperkalemia after initiation of co-trimoxazole therapy

In this study, we assessed serum potassium from day 1 to day 7 after co-trimoxazole therapy. Our findings indicated that serum potassium levels peaked on the 5th day after starting co-trimoxazole therapy. Our results suggest that serum potassium levels should be evaluated within 1 - 2 weeks in patients treated with co-trimoxazole, especially those at risk of developing hyperkalemia. Previous reports have shown that hyperkalemia developed 5-12 days after the initiation of co-trimoxazole.[10,26]

Regarding the rise in the mean potassium level, our finding reported that the change in the mean plasma potassium concentration significantly increased from baseline level (4.13± 0.44 mmol/L to 4.81± 0.80 mmol/L, p<0.01) with 0.68 mmol/L higher than at baseline. Our results are consistent with of those previous studies. Kowaliski et al. evaluated the change in mean potassium levels from baseline to the end of therapy in patients receiving co-trimoxazole and in a control group. They reported a statistically significant increase in the mean potassium level in the co-trimoxazole group (4.2± 4.5 mmol/L, mean change 0.3± 0.5; p=0.002).[27]

Risk factors for hyperkalemia

Regarding risk factors for hyperkalemia, we used multivariate logistic regression to assess the relationship between hyperkalemia and certain risk factors. Our study failed to find any association between age, sex, dose, and concomitant medication use. This result contradicts the findings of Al-Adawi et al., who found a statistically significant correlation between co-trimoxazole advanced age and the use of (ACEi/ARBs) as concomitant medications.[20] Similarly, Gentry et al. reported that ACEi use was an independent variable associated with hyperkalemia.[11] The small number of patients who received ACEi/ARBs in our study (n=10 of 170) could be the reason for the deviation from the published literature, which reported that the use of concomitant medication was a risk factor for developing hyperkalemia. Moreover, Megni et al. reported that the use of ACEi/ARBs, β-blockers or potassium-sparing diuretics was not a risk factor for hyperkalemia.[28]

Strength and merits of the study

This study was designed to determine the incidence of hyperkalemia in patients aged ≥ 18 years who received intravenous co-trimoxazole at SQUH in Oman. To the best of our knowledge, this is the first study to report the incidence of co-trimoxazole- induced hyperkalemia in Oman.

Limitations of the study

This study has a few limitations. First, because this was a single-center study, the results obtained from SQUH cannot be generalized to other centers. Second, because of the retrospective nature of the study, a causal relationship could not be determined, and we were only able to predict an association. Third, data from electronic patient records were the only source of information; thus, the judgment was based solely on these data, without other verification or additional references. Finally, the small sample size may have meant that the study was underpowered for comparison. Therefore, these results should be cautiously interpreted.

CONCLUSION

This study showed that the use of intravenous co-trimoxazole was associated with an increased incidence of hyperkalemia in adult patients. Hyperkalemia occurred six days after the initiation of co-trimoxazole treatment. Co-trimoxazole raised the mean potassium level by 0.68 mmol/L after 5 days of treatment. A slightly higher incidence of hyperkalemia was observed in patients receiving co-trimoxazole with other medications known to influence potassium levels. Age, sex, dose, and concomitant medication use were not independent risk factors for hyperkalemia, owing to the limited sample size.

Recommendations and Future Directions

The findings of this study should be presented to policymakers for further improvements in monitoring practices, including the implementation of educational programs regarding adverse reactions and drug interactions of commonly prescribed medications targeting both physicians and pharmacists, revision of existing monitoring guidelines at health centers, and assessment of adherence to both national and international monitoring guidelines. Therefore, serum potassium levels should be closely monitored, particularly during the first week of co-trimoxazole treatment. This was a retrospective single-center study; therefore, the findings cannot be generalized. Therefore, we emphasize the need for more homogeneous multicenter prospective studies that provide more patient data and cohort characteristics to confirm our findings.

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ETHICAL APPROVAL:

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Sultan Qaboos University Medical Research Ethics Committee (MREC # 2390)

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