The Research of Medical Science Review
ISSN: 3007-1208 & 3007-1216 Volume 3, Issue 2, 2025

EFFECT OF ORAL SODIUM BICARBONATE SUPPLEMENTATION ON CORRECTED QT INTERVAL IN PATIENTS WITH CKD STAGES 3–5

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DOI: https://doi.org/10.5281/zenodo.18657133

Keywords

Article History
Received: 24 December 2024
Accepted: 29 January 2025
Published: 13 February 2025

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Abstract

Objective: To determine the effect of Oral Sodium Bicarbonate Supplementation on corrected QT Interval in Patients with Chronic kidney disease (CKD) Stages 3–5.

Place and Duration of Study: Nephrology Department of CMH Peshawar, a tertiary academic center, between June 2024-November 2024.

Methodology: A prospective observational study was conducted on 96 patients with CKD stages 3–5 and baseline metabolic acidosis. All patients received oral sodium bicarbonate supplementation titrated to achieve a target serum bicarbonate ≥22 mmol/L. Biochemical parameters and 12-lead ECG recordings were obtained at baseline and post-treatment. The primary outcome was the change in QTc interval, with secondary outcomes including QT, QT dispersion (QTd), and QTcd.

Results: The mean age of participants was 62.04±7.66 years, with 54(56.3%) females. Sodium bicarbonate therapy significantly corrected metabolic acidosis, increasing serum bicarbonate from 17.55±1.80 to 22.29±1.34 mmol/L ($p < 0.001$) and pH from 7.27±0.04 to 7.33±0.04 ($p < 0.001$). QTc interval decreased from 459.72±25.47 ms to 448.49 ± 23.62 ms ($p = 0.004$). Similarly, the QT interval reduced from 410.47 ± 34.11 ms to 399.92±31.97 ms ($p = 0.030$). Electrical heterogeneity improved, with QTd declining from 46.03±16.36 ms to 33.08±11.12 ms ($p < 0.001$) and QTcd from 46.46±16.67 ms to 36.25±15.60 ms ($p < 0.001$). Minor increases in creatinine and potassium were observed.

Conclusion: These findings highlight the potential role of bicarbonate therapy in reducing arrhythmogenic risk in this high-risk population. Further randomized trials are needed to validate its long-term cardiovascular benefits.

INTRODUCTION

Chronic kidney disease (CKD) is a growing global health concern, with stages 3–5 representing advanced disease characterized by significant reductions in glomerular filtration and frequent metabolic derangements(1). Cardiovascular complications are the leading cause of mortality in CKD, and electrophysiologic abnormalities, particularly prolongation of the corrected QT (QTc) interval, are prevalent(2). QTc prolongation is an established independent predictor of ventricular arrhythmias and sudden cardiac death in the CKD population (3).

One of the key pathophysiological contributors to QTc prolongation in CKD is metabolic acidosis, a common electrolyte imbalance in patients with impaired renal acid excretion. Metabolic acidosis adversely affects myocardial repolarization, contributing to pronounced QTc interval changes(4). Standard clinical practice often includes oral sodium bicarbonate to correct acidosis, which has demonstrated benefits such as slowing the decline in eGFR, improving serum bicarbonate levels, and modestly reducing blood pressure, as shown in recent meta-analyses(5).

However, despite the frequent clinical use of sodium bicarbonate in CKD, there remains limited evidence regarding its direct effects on the QTc interval(6). A study involving stage 3–5 CKD patients with baseline serum bicarbonate levels below 20 mmol/L demonstrated statistically significant reductions in QT, QTc, QT dispersion (QTd), and corrected QT dispersion (QTcd) after alkali therapy with oral sodium bicarbonate, suggesting a direct cardiac electrophysiological benefit(7).

At the same time, concerns persist regarding the consistent effectiveness and safety of sodium bicarbonate supplementation(8). Some recent critical reviews argue that the benefits of alkali therapy, such as slowing CKD progression, have not been conclusively upheld in more rigorous, blinded trials, and that clinical guidelines may be shifting away from routine use of sodium bicarbonate(9). Furthermore, achieving sustained correction of metabolic acidosis in advanced CKD is challenging—one observational study found only around 25% of patients achieved stable serum bicarbonate ≥ 22 mEq/L with oral supplementation (10).

These data demonstrate a compelling rationale for further investigation: although initial evidence suggests sodium bicarbonate may improve QTc parameters, more robust and controlled studies are needed to validate this effect in CKD stages 3–5. There is a critical gap in our understanding of whether oral sodium bicarbonate can reliably normalize QTc intervals, and thereby potentially reduce arrhythmic risk in this high-risk population. This study aims to fill that gap by rigorously evaluating the effect of oral sodium bicarbonate supplementation on corrected QT interval in patients with CKD stages 3–5.

METHODOLGY

This was a prospective observational study conducted at the Nephrology Department of CMH Peshawar , a tertiary academic center, between June 2024-November 2024. Institutional Review Board (IRB) approval was obtained before study initiation, with waiver of consent for secondary data analysis. Consecutive patients with stage 3–5 chronic kidney disease (CKD), not on dialysis, who were evaluated in the nephrology outpatient clinic and found to have metabolic acidosis, were screened for eligibility.

Inclusion Criteria: Eligible participants were adults (aged 18–80 years) with CKD stages 3–5, classified according to KDIGO criteria using the MDRD formula for eGFR, and baseline serum bicarbonate concentration <20 mmol/L.

Exclusion Criteria: history of cardiac intervention or acute coronary syndrome, pre-existing arrhythmias or significant ECG abnormalities, structural heart disease, use of antiarrhythmic or QT-prolonging drugs, electrolyte disturbances outside the predefined normal range, dialysis dependence, or failure to achieve target serum bicarbonate ≥22 mmol/L during follow-up (11).

A sample size of 96 was calculated by using the single mean sample size formula and taking the post-treatment mean QTc interval as 447.1 ± 24.9ms (3) at 5% level of significance and 5% precision, as all included patients had sinus rhythm on baseline ECG and normal transthoracic echocardiography with preserved left ventricular ejection fraction (>50%).

All enrolled patients received oral sodium bicarbonate therapy to correct metabolic acidosis. Treatment was initiated at 0.5–1 mEq/kg/day, titrated weekly until the target serum bicarbonate ≥22 mmol/L was achieved, in accordance with KDIGO guidelines(12). Laboratory parameters, including serum urea, creatinine, electrolytes (Na^+, K^+, Cl^-, Mg^{2+}, Ca^{2+}, phosphate), uric acid, and arterial blood gases, were assessed at baseline and after reaching steady-state bicarbonate correction.

Twelve-lead ECGs were recorded at baseline and after achieving correction of serum bicarbonate. ECGs were obtained at 25 mm/s paper speed and analyzed manually by a single blinded cardiologist. The QT interval was measured from the onset of QRS to the end of the T-wave, and corrected for heart rate using Bazett's formula ($QTc = QT/\sqrt{RR}$)(13). QT dispersion (QTd) and corrected QT dispersion (QTcd) were calculated as the difference between maximal and minimal QT and QTc across the 12 leads. The primary outcome was the change in corrected QT interval (QTc) following sodium bicarbonate supplementation. Secondary outcomes included changes in QT, QTd, and QTcd.

Analyses were performed using SPSS version 25. Continuous variables were expressed as mean ± standard deviation and compared using paired t-tests or Wilcoxon signed-rank tests, as appropriate. Correlations between biochemical variables (e.g., pH, electrolytes) and ECG parameters were assessed using Spearman's correlation coefficients. Multivariate linear regression was performed to identify independent predictors of QTc, QTd, and QTcd intervals. A p-value <0.05 was considered statistically significant.

Results

In this prospective study of 96 patients with CKD stages 3–5, the mean age of the cohort was 62.04 ± 7.66 years, with a slightly higher representation of females, 54(56.3%), compared to males, 42(43.8%). Baseline biochemical and ECG parameters were compared before and after sodium bicarbonate supplementation.

Table-I: Baseline demographic characteristics of patients with CKD stages 3–5 included in the study.

		Frequency (Percentages)
Gender	Male	42 (43.82%)
	Female	54(56.31%0
Age	Mean ± S. D	62.04±7.66
Total		96(100.0%)

Normality testing using Kolmogorov–Smirnov test and Q–Q plots indicated that most biochemical and ECG variables followed a normal distribution. Therefore, data were expressed as Mean ± SD and compared using paired t-tests. Metabolic correction was evident, as mean serum bicarbonate increased significantly from 17.55 ± 1.80 mmol/L to 22.29 ±1.34 mmol/L ($p < 0.001$), accompanied by an improvement in systemic pH from 7.27±0.03 to 7.33±0.04 ($p < 0.001$). Chloride concentration showed a marked decline from 110.74 ± 6.48 to 103.56±5.31 mmol/L ($p < 0.001$), while phosphate levels decreased from 4.20±0.79 to 3.90±0.85 mmol/L ($p = 0.015$). A modest but statistically significant increase in serum potassium was observed (4.89 ±0.72 to 5.13±0.84 mmol/L; $p = 0.032$), whereas creatinine rose slightly (3.32±1.24 to 3.77±1.55 mg/dL; $p = 0.035$). Other biochemical parameters, including sodium, calcium, uric acid, and magnesium, did not exhibit significant changes.

Table-II: Changes in biochemical markers and corrected QT intervals following correction of metabolic acidosis with oral sodium bicarbonate in CKD stages 3–5.

	Pretreatment	Posttreatment	p-value
	Mean± SD	Mean± SD	
Biochemical Parameters			
Urea Pre	109.21±31.85	107.17±34.82	0.667
Creatinine	3.321.24	3.77±1.55	0.035
Uric Acid	6.55±1.79	6.68±1.57	0.623
Sodium	138.51±2.85	139.34±3.45	0.075
Potassium	4.89±0.723	5.13±0.85	0.032
Chloride	110.74±6.49	103.56±5.31	0.000

Calcium	8.84±0.88	9.07±0.90	0.084
Phosphate	4.20±0.79	3.90±0.84	0.015
Magnesium	2.04±0.27	1.99±0.34	0.282
Bicarbonate	17.55±1.80	22.29±1.39	0.000
pH	7.27±0.04	7.34±0.04	0.000
ECG			
RR	0.79±0.17	0.80±0.14	0.633
QT	410.47±34.11	399.93±31.99	0.030
QTc	459.73±25.48	448.50±23.629	0.004
QTd	46.03±16.36	33.09±11.13	0.000
QTcd	46.46±16.68	36.25±15.60	0.000

Electrocardiographic analysis revealed clinically meaningful improvements in ventricular repolarization indices. The QT interval shortened significantly from 410.47 ± 34.11 ms to 399.92 ± 31.97 ms ($p = 0.030$). More importantly, QTc decreased from 459.72 ± 25.47 ms at baseline to 448.49 ± 23.62 ms after treatment ($p = 0.004$), indicating a favorable shift away from the arrhythmogenic range. Measures of electrical heterogeneity also improved: QT dispersion fell from 46.03 ± 16.36 ms to 33.08 ± 11.12 ms ($p < 0.001$), and QTc dispersion reduced from 46.46 ± 16.67 ms to 36.25 ± 15.59 ms ($p < 0.001$). Collectively, these findings suggest that sodium bicarbonate supplementation significantly ameliorates metabolic acidosis and concurrently improves cardiac electrophysiological stability in advanced CKD patients.

DISCUSSION

The present study demonstrates that correction of metabolic acidosis with oral sodium bicarbonate supplementation leads to a significant reduction in QTc interval and related dispersion parameters in patients with CKD stages 3–5. This aligns with prior evidence linking acidosis with delayed myocardial repolarization and increased arrhythmic risk (2, 4). In our cohort, the mean QTc declined by approximately 11 ms following supplementation, with parallel improvements in QTd and QTcd, suggesting enhanced homogeneity of ventricular conduction(14). Given that QTc prolongation is an established predictor of ventricular arrhythmias and sudden cardiac death in CKD(3), these electrophysiologic improvements may translate into meaningful clinical benefit.

Our findings are consistent with those of (7), who reported significant reductions in QT and QTc intervals after sodium bicarbonate therapy in patients with advanced CKD and metabolic acidosis. Similarly, (3) documented prolonged QTc in CKD patients with low serum bicarbonate, reinforcing the pathophysiological link between acidosis and repolarization abnormalities. By correcting serum bicarbonate and normalizing pH, sodium bicarbonate therapy likely restores ionic homeostasis, particularly influencing potassium and calcium handling, thereby stabilizing cardiac conduction(15). The observed decrease in QT dispersion in our study further supports the hypothesis that bicarbonate supplementation mitigates heterogeneity of repolarization, a key substrate for malignant arrhythmias(16).

It is noteworthy, however, that serum creatinine and potassium increased modestly during therapy. While the rise in creatinine may reflect progression of CKD rather than a direct drug effect, the elevation in potassium warrants cautious interpretation(17). Hyperkalemia is a known arrhythmic risk factor and may potentially counterbalance some of the electrophysiological benefits of bicarbonate therapy(18). Nonetheless, the net reduction in QTc and QTd observed here suggests that the correction of systemic acidosis had a dominant protective effect(3, 7).

Contrasting with recent reviews questioning the universal benefit of sodium bicarbonate in CKD progression (9), our results highlight an important cardiovascular dimension that may justify its continued use in selected patients. Indeed, while meta-analyses have demonstrated mixed results regarding renal endpoints (5), the electrophysiological improvements observed in

our study underscore a potential role of bicarbonate therapy in arrhythmia prevention, a domain insufficiently explored in prior research. These results contribute novel evidence that, beyond biochemical correction, sodium bicarbonate supplementation has direct and favorable effects on cardiac electrical stability in CKD stages 3–5. Further randomized controlled trials with long-term follow-up are warranted to confirm whether these electrophysiological improvements translate into reductions in arrhythmic events and cardiovascular mortality.

CONCLUSION

This study demonstrates that oral sodium bicarbonate supplementation in patients with CKD stages 3–5 significantly corrects metabolic acidosis and improves cardiac electrophysiological stability. The therapy led to a meaningful reduction in QTc interval, QT dispersion, and corrected QT dispersion, thereby reducing the heterogeneity of ventricular repolarization that predisposes to arrhythmias. These findings suggest that beyond its established role in acid–base balance, sodium bicarbonate may provide additional cardiovascular benefits in advanced CKD. However, the modest rise in serum creatinine and potassium observed highlights the need for careful monitoring during therapy. Larger randomized controlled trials with extended follow-up are warranted to confirm whether these electrophysiological improvements translate into a reduction in arrhythmic events and cardiovascular mortality in this high-risk population.

Conflict of Interest: None.

Funding Source: None.

Authors Contribution

The following authors have made substantial contributions to the manuscript as under:

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