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Effect of moderate potassium-elevating treatment in long QT syndrome: the TriQarr Potassium Study

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ABSTRACT

Background In long QT syndrome (LQTS), beta blockers prevent arrhythmias. As a supplement, means to increase potassium has been suggested. We set to investigate the effect of moderate potassium elevation on cardiac repolarisation.

Methods Patients with LQTS with a disease-causing *KCNQ1* or *KCNH2* variant were included. In addition to usual beta-blocker treatment, patients were prescribed (1) 50 mg spironolactone (*low dose*) or (2) 100 mg spironolactone and 3 g potassium chloride per day (*high dose+*). Electrocardiographic measures were obtained at baseline and after 7 days of treatment.

Results Twenty patients were enrolled (10 low dose and 10 high dose+). One patient was excluded due to severe influenza-like symptoms, and 5 of 19 patients completing the study had mild side effects. Plasma potassium in low dose did not increase in response to treatment (4.26±0.22 to 4.05±0.19 mmol/L, p=0.07). Also, no change was observed in resting QTcF (QT interval corrected using Fridericia's formula) before versus after treatment (478±7 vs 479±7 ms, p=0.9). In high dose+, potassium increased significantly from 4.08±0.29 to 4.48±0.54 mmol/L (p=0.001). However, no difference in QTcF was observed comparing before (472±8 ms) versus after (469±8 ms) (p=0.66) high dose+ treatment. No patients developed hyperkalaemia.

Conclusion In patients with LQTS, high dose+ treatment increased plasma potassium by 0.4 mmol/L without cases of hyperkalaemia. However, the potassium increase did not shorten the QT interval and several patients had side effects. Considering the QT interval as a proxy for arrhythmic risk, our data do not support that potassium-elevating treatment has a role as antiarrhythmic prophylaxis in patients with LQTS with normal-range potassium levels.

Trial registration number NCT03291145.

Key questions

What is already known about this subject?

► Potassium-elevating treatment has been suggested as an antiarrhythmic therapy in patients with long QT syndrome (LQTS).

What does this study add?

► Daily intake of 100 mg spironolactone and potassium supplements increased plasma potassium by 0.4 mmol/L. However, this modest increase did not shorten cardiac repolarisation in static or dynamic ECG recordings in LQTS types 1 and 2.

How might this impact on clinical practice?

► Current data do not support that moderate elevation of plasma potassium has a role for long-term antiarrhythmic prophylaxis in patients with LQTS with normal potassium levels.

INTRODUCTION

In patients with congenital long QT syndrome (LQTS), beta blockers effectively prevent syncope and sudden cardiac death.[1] Unfortunately, side effects may prohibit treatment or patients may experience arrhythmic events despite beta-blocker therapy.[1] In patients with recurrent syncope or breakthrough arrhythmias despite beta-blocker treatment, guidelines suggest considering an implantable cardioverter defibrillator (ICD) and/or left cardiac sympathetic denervation.[2 3] As a non-invasive supplement, elevating plasma potassium concentration by spironolactone in combination with potassium supplements has been suggested.[4 5] The first experimental study by Compton *et al*[5] found that repolarisation, both length of QT interval and T-wave morphology, normalised in *KCNH2* (LQTS2) patients when increasing *serum* potassium by ≥1.5 mmol/L. This study was followed by a clinical study by Etheridge *et al* treating eight patients with LQTS2 for 4 weeks. They increased serum potassium by 1.2 mmol/L and found a dramatic shortening of the QTcB from 526 to 423 ms. Still, data remain very limited, and due to the potential risk of hyperkalaemia,[6] the clinical use is limited and not recommended as standard treatment by guidelines.[2 3] In this study, we set to investigate the effect of modestly increasing *plasma* potassium by spironolactone and potassium supplements in clinically relevant doses

on duration of the repolarisation as a proxy for risk of ventricular arrhythmia.

METHODS

Clinical inclusion

Patients with LQTS in active beta-blocker treatment and with a variant in *KCNQ1* or *KCNH2* (*LQTS1* or *LQTS2*) were prospectively included at the Herlev-Gentofte Hospital, Copenhagen University Hospital, as part of the TriQarr project, which explored the mechanism of QT prolongation.[7] When arriving at our clinic, patients took their usual beta blocker. One hour after intake, electrocardiograms were recorded after a minimum of 5 min of rest and during change from supine position to standing—'brisk standing'.[8]

In addition to the usual beta-blocker treatment, the first 10 patients were prescribed 50 mg of spironolactone (50 mg×1, *low dose*) per day. After assessing the effect on potassium levels in the low dose group, the latter 10 patients were prescribed 100 mg spironolactone (50 mg×2) and orally 3 g potassium chloride (750 mg Kaleorid×4 ~40 mmol potassium) per day (*high dose+*). Tablets were administered to patients in a 7-day tablet box, which secured 100% compliance from all patients (tablet counting). After 7 days on potassium-elevating treatment, ECGs at rest and during brisk standing were obtained 1 hour after intake of usual beta blocker. All electrolyte concentrations were reported as plasma concentrations as this has become standard in Danish hospitals.

ECG measurements

Continuous ECG monitoring was conducted by 12-lead Holter monitoring (Life card CF, Spacelabs Healthcare) through all sessions. Holter ECGs were uploaded into the Sentinel Cardiology Information Management System. In this study, we tried to apply the brisk standing test to investigate the role of increasing potassium during heart rate accelerations and potentially measure a difference. QT intervals were measured by PM and JT, blinded using the tangent principle[9] at *baseline*, defined as the last electrical cycle before standing up and at *max HR*, defined as the single beat with the fastest heart rate. The tangent method was used both before and after treatment and chosen for its low interobserver variability, although this method could theoretically underestimate a beneficial effect of treatment.

To assess automatic QT measurement, the recordings were split into 10 s ECG sampled at 500 Hz and analysed using V.243 of the 12SL algorithm (GE Healthcare, Milwaukee, Wisconsin, USA), which superimposes all 12 leads to measure the QT interval from earliest onset to latest offset in any lead. All QT intervals were corrected using Fridericia's formula, $QTcF=QT/(RR)^{1/3}$, and Bazett's formula, $QTcB=QT/(RR)^{1/2}$.

Morphology of the T wave

T-wave Morphology Combination Score (MCS) and its subcomponents (flatness, asymmetry and notches) were measured with QT Guard Plus (GE Healthcare). MCS is a unitless marker, combining the asymmetry, flatness and notching of the T wave into a combined score.[10] The normal T wave has an MCS of 0.71±0.24, and a higher MCS indicates a deviation from the normal T wave associated with blockage or loss of function of the cardiac repolarisation. The MCS score has previously been described in detail.[10]

Statistics

Continuous variables were expressed as mean±SD measurements of heart rate, and QT intervals were expressed as mean±SEM and compared before versus after treatment using a paired t-test. Differences in categorical variables were calculated using Fisher's exact test. An intraclass correlation coefficient (ICC) was calculated (two-way, single measures and absolute agreement) to assess interobserver variability. An ICC >0.70 was considered *excellent*. For all analyses, a p value of <0.05 was considered statistically significant. R V.3.6.1 was used for all analyses.[11]

RESULTS

A total of 20 patients were included: 10 in the low dose and 10 in high dose+ (table 1). The mean age of the whole cohort was 39±10 and 17 (85%) were women. One patient in the low dose group experienced severe influenza-like symptoms on day 3; spironolactone was discontinued, and the patient was excluded from clinical testing analyses. None of the patients reported any cardiac events or symptoms during the treatment period.

Low dose

Of the 10 patients, 3 (30%) were LQTS1 and 7 (70%) were LQTS2 patients (list of specific mutations in online supplemental table 1). Eight (80%) were women and the mean age was 37±12 at the time of the study. Five (50%) of the patients had a family history of sudden cardiac death before 60 years of age, and one (10%) had a history of syncope or ventricular tachycardia. Seven (70%) patients were in treatment with metoprolol 86±24 mg/day, and three were treated with atenolol 33±14 mg/day.

At baseline visit, systolic blood pressure was 121±12 mm Hg, which was significantly reduced to 112±12 after 7 days of study treatment (p=0.018) (table 2 and online supplemental figure 1).

There was no increase observed in plasma potassium after 7 days of 50 mg spironolactone (4.26±0.22 to 4.05±0.19 mmol/L, p=0.07) but a borderline decrease (figure 1). Unfortunately, the potassium test of one low dose patient haemolysed; thus, only eight tests were used in this preanalysis/postanalysis of potassium.

The low dose spironolactone did also not affect plasma sodium (141.7±0.26 to 140.1±2.1 mmol/L, p=0.11) (figure 1), magnesium (0.87±0.04 to 0.84±0.06 mmol/L, p=0.2) or glucose (5.1±0.5 to 5.5±0.8 mmol/L, p=0.2). The eGFR was significantly reduced from 106±17 to 97±18 (p=0.043).

Table 1 Baseline characteristics

	Low dose Spironolactone 50 mg	High dose+ Spironolactone 100 mg+3 g potassium chloride
	N=10*	N=10
Female sex, n (%)	8 (80)	9 (90)
Age (years), mean±SD	36.9±11.9	41.5±6.9
BMI, mean±SD	24.7±2.6	23.2±5.5
Spironolactone dose (mg/kg)	0.73±0.14	1.57±0.27
Genetics, n (%)		
LQTS1	3 (30)	5 (50)
LQTS2	7 (70)	5 (50)
Proband, n (%)	2 (20)	6 (60)
ICD, n (%)	0 (0)	2 (20)
Syncope/VT, n (%)	1 (10)	4 (40)
Sudden cardiac death in family before 60 years of age, n (%)	5 (50)	1 (10)
Beta-blocker treatment		
Metoprolol, n (%)	7 (70)	6 (60)
Dose (mg), mean±SD	86±24, 70	96±40
Atenolol, n (%)	3 (30), 73	3 (30), 67
Dose (mg), mean±SD	33±14	50±0
Nebivolol, n (%)	0 (0)	1 (10)
Dose (mg),mean±SD		2.5±0

*Including the patient who did not complete treatment due to side effects.
BMI, body mass index; ICD, implantable cardioverter defibrillator; VT, ventricular tachycardia.

ECG findings

At baseline, the heart rate was 50±2 beats/min, which was not significantly different from the heart rate after 1 week of treatment, 55±2 beats/min (p=0.11). No difference in QTcF was observed comparing before (478±7 ms) versus after (479±7 ms) (p=0.9) treatment with spironolactone. The QTcF observed at max heart rate during brisk standing (figure 2) also did not change in response to treatment before (542±8 ms) versus after (536±9 ms) (p=0.4) (figure 3). Individual changes in QTcF and heart rate are depicted in online supplemental figure 2. QTcFs depicted based on genetic variant are found in online supplemental figure 3. QT intervals were corrected using Bazett's formula in online supplemental figure 4.

Similar results were found using automatic measurement of heart rate: before 53±2 vs 57±two bpm after (p=0.06), QTcF: before 492±8 vs 494±10 ms after (p=0.8) and MCS score: before 1.55±0.20 vs 1.50±0.17 after (p=0.7).

High dose+

Of the 10 patients treated with high dose+, five (50%) patients were LQTS1 and five (50%) patients were LQTS2. Nine (90%) were women and the mean age was 42±7 at the time of study. Two (20%) were ICD carriers and four (40%) had history of syncope or ventricular tachycardia. One (10%) of the patients had a family history of sudden cardiac death before 60 years of age. Six (60%) patients were treated with metoprolol at a dose of 96±40 mg/day; three (30%) were treated with atenolol at a dose of 50 mg/day; and one (10%) patient was treated with nebivolol 2.5 mg/day.

At baseline visit, systolic blood pressure was 117±9 mm Hg, which was significantly reduced to 111±10 mm Hg after 7 days of high dose+ treatment (p=0.022) (table 2).

Plasma potassium was significantly increased from 4.08±0.29 to 4.48±0.54 mmol/L (p=0.001) (figure 1). Conversely, plasma sodium was significantly lowered from 141.2±1.5 to 139.6±1.5 mmol/L (p=0.005). Also, eGFR was significantly reduced from 99±15 to 87±14 (p=0.003). There were no changes in magnesium from 0.83±0.06 to 0.81±0.06 mmol/L (p=0.3), or glucose from 5.1±0.5 to 5.1±0.7 mmol/L (p=0.9).

ECG findings

At baseline, the heart rate was 51±2 beats/min, which was similar after 1 week of treatment, 54±2 beats/min (p=0.4). No difference in QTcF was observed comparing before (472±8 ms) versus after (469±8 ms) (p=0.6) treatment with high dose+. The QTcF observed at max heart rate during brisk standing also did not change in response to treatment before (520±10 ms) versus after (523±13 ms) (p=0.7).

Similar results were found using automatic measurement of heart rate: before, 54±1 beats/min, vs after, 56±2 beats/min (p=0.5); QTcF: before, 485±8 ms, vs after, 483±7 ms (p=0.7); and MCS score: before, 1.57±0.24, vs after, 1.65±0.24 (p=0.4).

Interobserver variability

An intraclass correlation of 0.85 (95% CI 0.76 to 0.90) was calculated, showing excellent agreement between readers.

Side effects of treatment

Of the nine patients in the low dose group completing 1 week of treatment, one patient reported fatigue in response to treatment. Of the 10 patients in the high dose+ group, four patients (40%) experienced mild side effects: fatigue (n=1), headache(n=1), nausea (n=1) and influenza-like symptoms (n=1).

DISCUSSION

Our study systematically investigated the impact of moderate potassium-elevating treatment in patients with

Table 2 Clinical testing before and after treatment with potassium-elevating treatment in addition to usual treatment

Treatment regime	Low dose Spironolactone 50 mg N=9			High dose+ Spironolactone 100 mg +3 g potassium chloride N=10		
Time and comparison	Before treatment	After treatment	P value before versus after	Before treatment	After treatment	P value before versus after
Blood pressure						
Systolic (mm Hg), mean±SD	117.9±12.0	111.9±12.3	0.018	117.0±9.3	110.7±9.9	0.022
Diastolic (mm Hg), mean±SD	74.7±10.9	70.6±9.5	0.10	68.3±6.9	66.4±7.1	0.30
Blood tests						
Potassium (mmol/L), mean±SD	4.26±0.22	4.05±0.19	0.072	4.08±0.29	4.48±0.54	0.001
Sodium (mmol/L), mean±SD	141.7±2.6	140.1±2.1	0.11	141.20±1.48	139.60±1.51	0.005
Magnesium (mmol/L), mean±SD	0.87±0.04	0.84±0.06	0.18	0.83±0.06	0.81±0.06	0.29
Glucose (mmol/L), mean±SD	5.11±0.50	5.50±0.75	0.17	5.09±0.54	5.06±0.74	0.89
eGFR (mL/min/1.73 m^2), mean±SD	105.6±16.9	97.4±18.3	0.043	99.0±14.6	86.6±14.2	0.003
ECG measures—Manuel						
HR, baseline, mean±SEM	50.1±2.3	55.0±1.8	0.11	51.4±2.2	53.7±2.0	0.42
HR at max heart rate, mean±SEM	83.1±2.7	82.0±4.0	0.58	73.7±3.0	78.4±3.6	0.27
ΔHR, max heart rate, mean±SEM	33.0±2.4	27.0±1.9	<0.001	22.3±2.4	24.7±3.0	0.28
Time from baseline to max heart rate (s), mean±SEM	9.9±0.8	8.9±0.8	0.06	9.4±0.8	10.5±1.1	0.33
Fridericia's correction						
QTcF, baseline, mean±SEM	477.9±7.2	478.5±7.3	0.94	471.9±8.1	468.9±8.0	0.66
QTcF, max heart rate, mean±SEM	542.2±8.0	536.0±9.4	0.39	519.9±10.1	523.0±12.5	0.65
ΔQTcF, max heart rate, mean±SEM	64.4±3.5	57.4±3.7	0.11	48.0±5.5	54.1±8.6	0.41
Bazett's correction						
QTcB, baseline, mean±SEM	463.5±9.7	471.5±7.7	0.062	459.8±10.7	460.1±9.5	0.98
QTcB, max heart rate, mean±SEM	571.9±11.3	564.4±11.3	0.20	537.8±12.9	546.5±15.3	0.47
ΔQTcB, max heart rate, mean±SEM	108.4±5.8	93.0±6.0	0.016	78.0±7.7	86.4±11.8	0.36
Automatic—12SL						
HR, baseline, mean±SEM	52.5±2.3	57.3±1.8	0.06	53.6±1.2	55.5±1.7	0.45
QTcF, baseline, mean±SEM	490.2±8.1	492.9±9.7	0.73	484.9±7.9	483.2±7.4	0.66
QTcB, baseline, mean+SEM	479.2±10.4	488.9±9.6	0.20	475.6±6.8	476.7±7.5	0.80
MCS, baseline, mean±SEM	1.551±0.196	1.499±0.167	0.73	1.570±0.237	1.651±0.236	0.35

eGFR, estimated glomerular filtration rate; max, maximum.

LQTS. In our relatively young primarily female cohort, 50 mg of spironolactone did neither increase plasma potassium nor shorten cardiac repolarisation. Treating with 100 mg of spironolactone and potassium supplement, we were able to significantly increase plasma potassium by 0.4 mmol/L—but this modest potassium increase had no shortening impact on the repolarisation. Using the QT interval as a proxy for arrhythmic risk, it is therefore questionable if modestly increasing plasma potassium within normal range has any clinical relevance as long-term antiarrhythmic therapy.

In 2001, Etheridge *et al*[4] published groundbreaking results, showing great benefits of potassium-elevating treatment in LQTS2 patients. In the study, eight patients, including four children (<16 years), were treated with a mean dose of 250 mg spironolactone (up to 400 mg)+mean dose of 220 mmol potassium supplements for 4 weeks. This resulted in an increase of serum potassium from 4.0 mmol/L to 5.2 mmol/L, which remarkably shortened the QTcB from 526 ms to 423 ms.

In our 10 patients treated with spironolactone high dose+, plasma potassium increased from 4.1 mmol/L

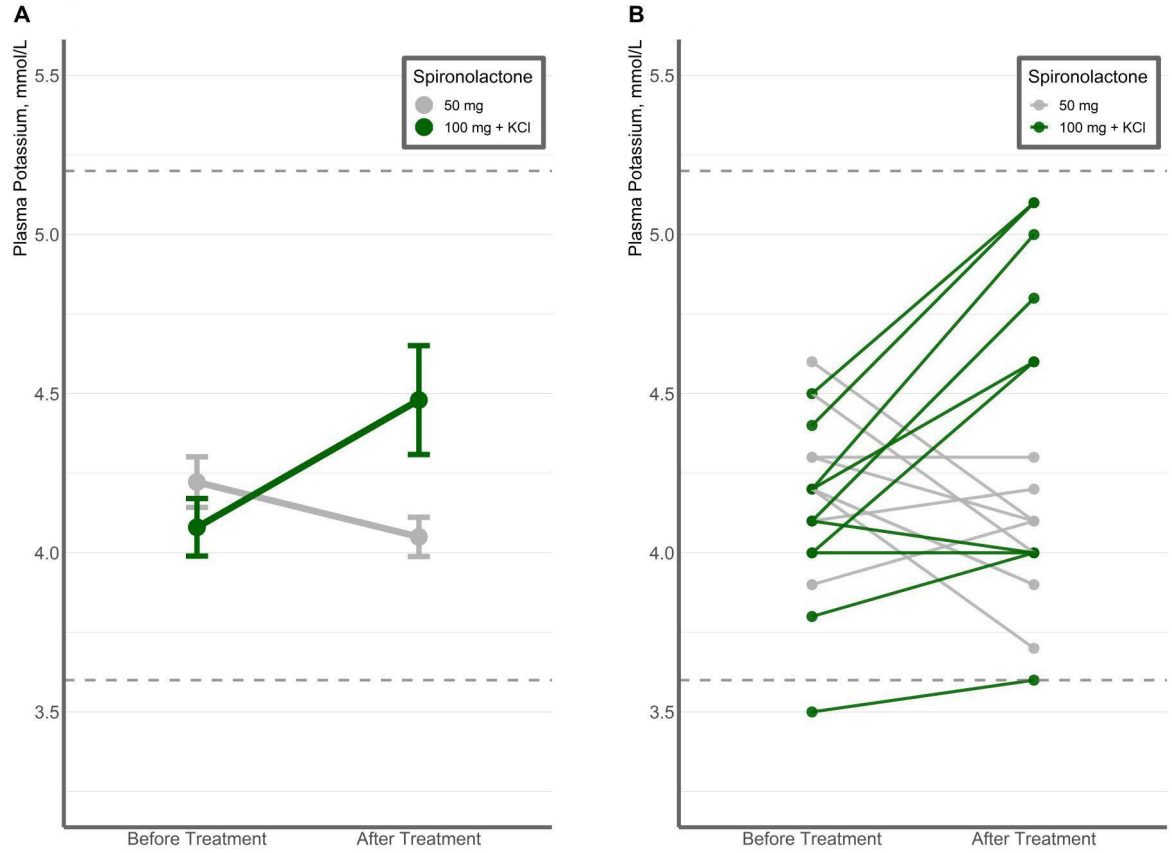

Figure 1 Mean (A) and individual (B) changes of plasma potassium in response to potassium-elevating treatment. Adding 50 mg spironolactone to the usual beta-blocker treatment did not change plasma potassium levels, but 100 mg spironolactone and potassium chloride significantly increased plasma potassium from 4.08 to 4.48 mmol/L.

to 4.5 mmol/L but did not shorten the repolarisation at rest. As brisk standing, inducing a sudden brief tachycardia, has been suggested as a diagnostic test for LQTS,[8] we included this method in our study. In response to brisk standing, heart rate increased by 22–25 beats/min, but from slightly different resting heart rates. To assess impact on repolarisation, and not only to capture differences in response to heart rate changes, the more conservative Fridericia's correction was preferred. Still, no differences in QTcF at maximum heart rate were found, demonstrating that also the ability to adapt repolarisation in response to rapid changes in heart rate was unaffected by potassium-elevating treatment. To further elaborate on the impact of treatment, Bazett's correction (QTcB), automatic measures of QTcF and T-wave morphology were also assessed—finding similar negative results.

Besides a potentially beneficial effect on repolarisation, four other important factors should be considered if potassium-elevating treatment could be used for antiarrhythmic prophylaxis: (1) risk of hyperkalaemia, (2) antiarrhythmic potential, (3) effect on blood pressure and (4) feasibility.

After the study by Etheridge *et al*[4] was published, Goldenberg and Moss[6] set up a randomised trial with the suggested doses, but the study was terminated early due to risk of hyperkalaemia. Unfortunately, the data from the trial was never published but only mentioned in a correspondence letter.[6] Therefore, as a compromise, our study aimed to use doses that would be feasible to initiate without intense monitoring of potassium concentration. In our cohort, 50 mg of spironolactone did not increase plasma potassium, which was only accomplished in the treatment group taking 100 mg and potassium supplements. The increase was only one-third of the increase reported in the study by Etheridge *et al*, which correspond well with the smaller doses used. Although the increase in plasma potassium varied from patient to patient—no patients in our study developed hyperkalaemia as the maximum concentration was 5.1 mmol/L. In contrast, Etheridge *et al* reported that 3/8 developed serum potassium ≥5.5 mmol/L. Importantly, in this study plasma potassium is used, which is measured approximately 0.4 mmol/L lower compared with *serum* potassium used in previous studies.[12]

The concept of using potassium-elevating treatment suggested by Etheridge *et al* was based on a Xenopus oocytes study, describing a paradoxically linear correlation between increasing *HERG* current amplitude and increasing *extracellular* potassium concentration.[13] However, shortening of the QT interval is merely a proxy of arrhythmic risk, and no current data support that potassium-elevating treatment, in patients with a potassium concentration within normal range, translate into a lower risk of arrhythmias. Importantly, the correlation

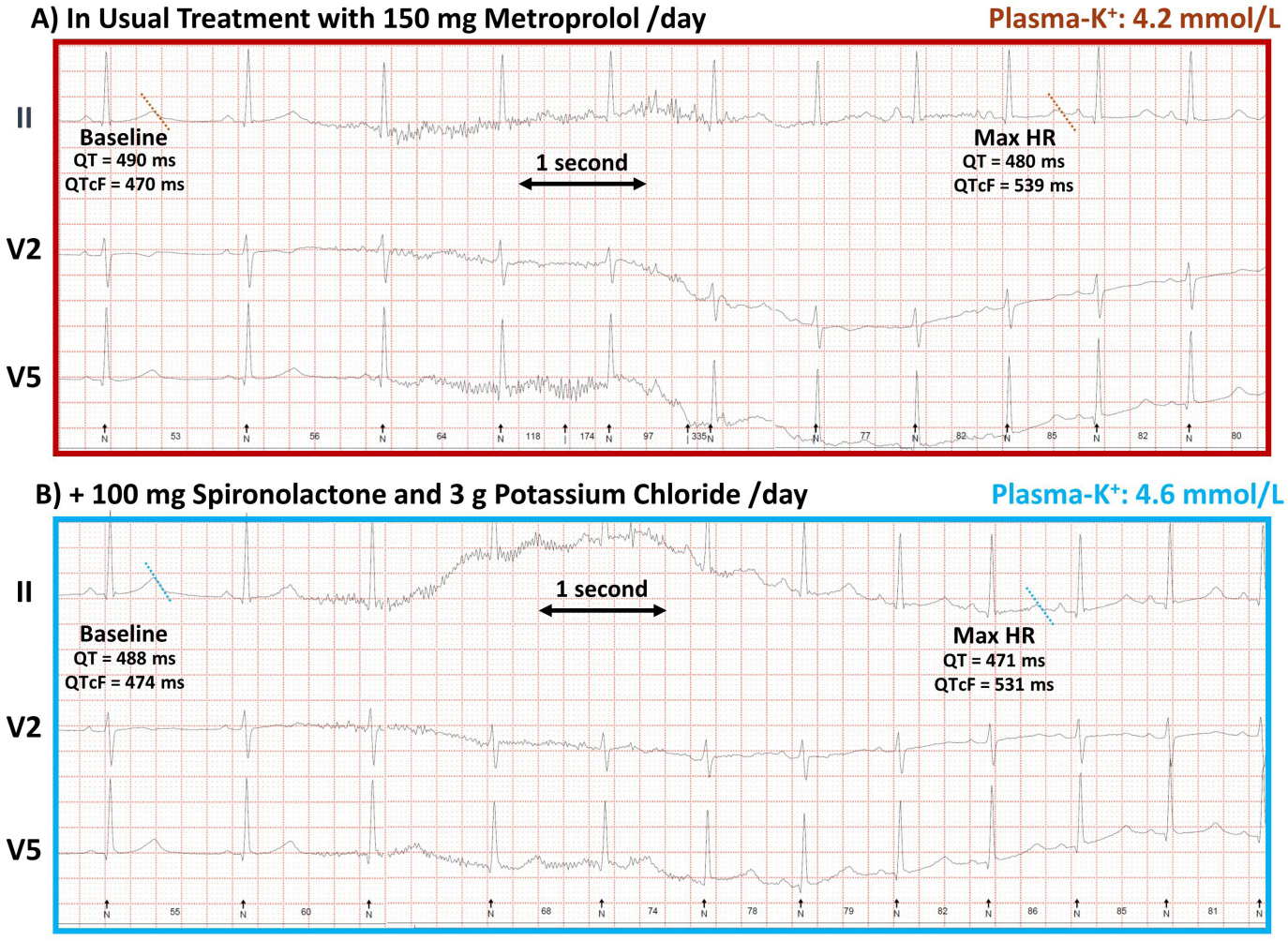

Figure 2 ECG examples of a patient treated with 100 mg spironolactone and 3 g potassium chloride in addition to usual beta-blocker treatment. QT intervals are shown at rest and at maximum heart rate during standing. (A) ECG recording in usual beta-blocker treatment and (B) ECG after 1 week of potassium-elevating treatment.

between potassium concentration and ventricular arrhythmias has recently been investigated by Pezhouman *et al* in rabbit hearts.[14] They found a sigmoid correlation between ventricular arrhythmias and potassium concentration—suggesting a limited antiarrhythmic potential of elevating serum potassium concentration higher than ~4.0 mmol/L.[14]

Hypokalaemia is a well-known risk factor for arrhythmias in patients with LQTS and guidelines recommend correction of electrolyte abnormalities if the patients develops, for example, diarrhoea or vomiting.[2] Therefore, it would be fair to speculate that potassium-elevating treatment may prevent episodes of hypokalaemia—indirectly serving as a antiarrhythmic treatment. Still, this theoretical effect would need to be tested against a pill-in-the-pocked approach with orally administered potassium supplement—carefully considering effect versus side effects and feasibility.

In current guidelines,[2 3] beta blockers are the first-line treatment, and a potential role for potassium-elevating treatment would be as supplement to this. However, with both beta blockers and spironolactone—both lowering blood pressure—the risk of hypotension should be considered. Unfortunately, Etheridge *et al*[4] did not report blood pressure at baseline or after treatment, despite one patient developing orthostatic dizziness. In our cohort, a significant drop in systolic blood pressure was found in both treatment groups, but none reported dizziness as a side effect, which may be explained by the young age in our cohort. On the other hand, 6/20 patients developed other side effects, and though only one patient self-discontinued treatment due to severe influenza-like symptoms, long-term treatment would be prohibitive in a non-neglectable number of patients. Additionally, as previously demonstrated in patients with heart failure, both our treatment groups had a significant reduction of eGFR in response to potassium-elevating treatment, which could have long-term complications in patients with LQTS with chronic kidney failure.[15]

Finally, it is important to consider feasibility in a real-world setting. Our high dose+ group, experiencing an 0.4 mmol/L increase in plasma potassium, was given six extra tablets per day (4×750 mg kaleorid +2× 50 mg spironolactone=42 tables total for the week)—on top of regular

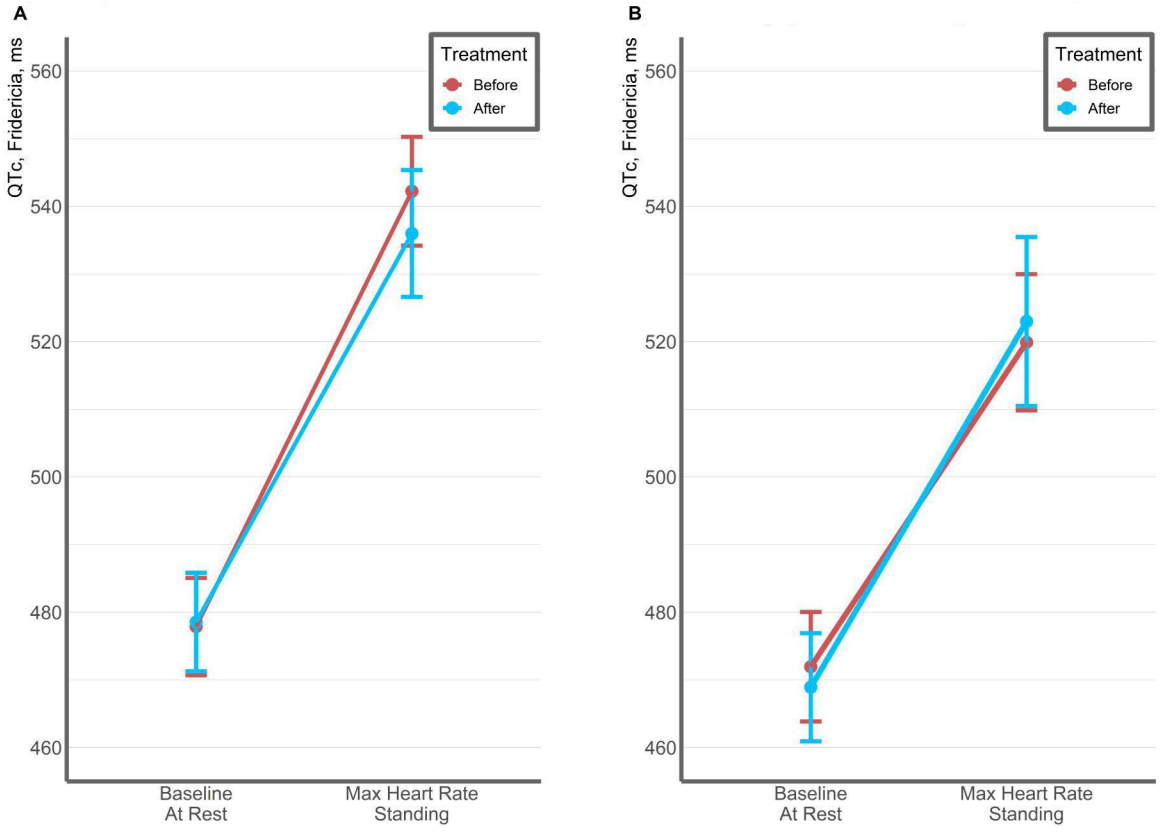

Figure 3 Effect of potassium-elevating treatment in different doses on QTcF interval at rest and at maximum heart rate during brisk standing. (A) The QTcF response to brisk standing is shown on the left, before versus after treatment with 50 mg spironolactone. (B) The QTcF response to brisk standing is shown on the right, before versus after treatment with 100 mg spironolactone +3 g potassium chloride.

treatment. All 19 patients completing our study reported full compliance, but our study period was also limited to only 7 days. In Denmark, the available potassium supplement 'kaleorid' 750 mg contains 10 mmol potassium. To meet the suggested doses from previous studies, patients would need to intake ~20 kaleorid and spironolactone tablets per day in addition to regular medication.

It is highly questionable if such drug loads are feasible as long-term treatment, especially considering that Waddell-Smith *et al* found that 50% of patients with LQTS had suboptimal beta-blocker compliance and only 13% had ideal compliance.[16] At the same time, most arhrythmic events have been found to occur in the non-compliant patients.[17] Taking into account, the questionable effect of moderate doses of potassium-elevating drugs, risk of hyperkalaemia and side effects—efforts are possibly better spent at securing a high beta-blocker compliance in patients with normal electrolyte balance than to experiment with a new complicated regime that may compromise compliance.

Limitations

Although this is the largest study on potassium-elevating treatment in LQTS, we were limited by a low number of participants. Compared with previous studies, patients had shorter baseline QT intervals. Our cohort may therefore more accurately represent the modern patients with LQTS but may have underestimated the shortening effect of treatment on repolarisation of a more malignant cohort. Optimally, patients would have had hypokalaemia at baseline before increasing potassium levels as this would have potentially shown a greater effect on the QT interval. Hence, larger studies on patients with LQTS are needed to show the benefits of potassium-elevating treatment not only in relation to QT-interval duration and safety but also for assessment of the effect on arrhythmia.

Also, our study included only 1 week of treatment, and no restrictions were made regarding food containing more or less potassium. Also, no control group was included as the previous study did not find an effect on repolarisation in controls—even in much higher doses.[5] Therefore, it was not considered ethically acceptable to administer up to 49 tablets (beta blocker +spironolactone+potassium chloride) to healthy participants in just 1 week.

Last, treatment with the beta1 selective beta blockers, metoprolol and atenolol, have for many years been standard in Denmark. Therefore, it may be hypothesised that the amount of potassium increase is underestimated[18] as compared with treatment with the non-selective nadolol, which is recommended as antiarrhythmic treatment by several newer studies.[19–21]

CONCLUSION

In this study, we tested the effect of potassium-elevating treatment on repolarisation in patients with LQTS. We demonstrate that 100 mg spironolactone and potassium supplements increased plasma potassium by 0.4 mmol/L without any cases of hyperkalaemia. However, this modest increase did not shorten cardiac repolarisation in static or dynamic ECG recordings. In addition, more than one-fourth experienced side effects. Considering that potassium-elevating treatment has been suggested as anti-arrhythmic treatment solely based on shortening of the repolarisation, our data do not support that moderate elevation of plasma potassium has a role for long-term antiarrhythmic prophylaxis in patients with LQTS with normal potassium levels.

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