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Potassium supplementation and heart rate: A meta-analysis of randomized controlled trials

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Abstract *Background and aims:* Increasing the intake of potassium has been shown to lower blood pressure, but whether it also affects heart rate (HR) is largely unknown. We therefore assessed the effect of potassium supplementation on HR in a meta-analysis of randomized controlled trials.
Methods and results: We searched PubMed (1966–October 2014) for randomized, placebo-controlled trials in healthy adults with a minimum duration of two weeks in which the effect of increased potassium intake on HR was assessed. In addition, reference lists from meta-analysis papers on potassium and blood pressure were hand-searched for publications. Two investigators independently extracted the data. We performed random effects meta-analyses, subgroup and meta-regression analyses for characteristics of the study (e.g. design, intervention duration, potassium dose and salt type, change in potassium excretion, sodium excretion during intervention) and study population (e.g. gender, age, hypertensive status, pre-study HR, pre-study potassium excretion). A total of 22 trials (1086 subjects), with a median potassium dose of 2.5 g/day (range: 0.9–4.7 g/day), and median intervention duration of 4 weeks (range: 2–24 weeks) were included. The meta-analysis showed no overall effect of increased potassium intake on HR (0.19 bpm, 95% CI: −0.44, 0.82). Stratified analyses yielded no significant effects of potassium intake on HR in subgroups, and there was no evidence for a dose–response relationship in meta-regression analyses.
Conclusion: A chronic increase in potassium intake with supplemental doses of 2–3 g/day is unlikely to affect HR in apparently healthy adults.

Introduction

Elevated resting heart rate (HR) has been identified as a predictor of cardiovascular morbidity and mortality in population-based studies [1–3]. In a meta-analysis of 7 prospective cohort studies a high resting HR was associated with a 40% higher risk of heart failure compared to a low resting HR [3]. HR can be affected by cardiac drug therapy, e.g. use of beta-blockers [3–8], and by non-pharmacological factors such as stress [9], physical activity [10–12], smoking [13], and alcohol use [14,15]. To what extent HR can be modified by diet, however, is largely unknown. García-López et al. [16] showed that baseline adherence to the Mediterranean diet, characterized by high consumption of fruits and vegetables, olive oil, legumes, whole grain cereals, moderate consumption of fish,

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poultry and dairy products, and low consumption of red and processed meats, was associated with a lower average HR. No association was found for repeated measurements of adherence during follow up and no difference in HR was observed among the dietary intervention groups in the PREDIMED trial [16]. Mozaffarian et al. [17], however, showed in a meta-analysis of 30 randomized controlled trials (RCTs) that fish oil significantly reduced HR by 1.6 beats per minute (bpm), particularly in subjects with high pre-study HR and after longer treatment duration.

Increased potassium intake favorably affects BP. A meta-analysis of 21 RCTs in healthy adults showed a 3.5 mmHg lower systolic BP and 2.0 mmHg lower diastolic BP after potassium supplementation (~2 g/day), an effect that was most pronounced in hypertensives and in those with a high sodium intake [18]. In a recent crossover study, we found a 4.0/1.7 mmHg lower 24-h BP in 36 subjects with untreated elevated BP who received 3 g/day of potassium for 4 weeks on top of a fully controlled, reduced-sodium diet (2.4 g per 2500 kcal) [19]. In that study, we noted that potassium supplementation significantly increased 24-h HR by 2.6 bpm, without affecting resting office HR. In a 4-week trial in 21 healthy adults with a high sodium intake, however, no effect of 4 g/day of potassium on 24-h HR was seen [20].

To clarify the role of potassium intake in determining HR, and possible interaction with sodium intake or other factors, we performed a meta-analysis of RCTs of potassium supplementation and HR (mostly as a secondary study outcome) in healthy adults.

Methods

Search strategy

A systematic literature search was performed for RCTs of potassium supplementation evaluating the effect on HR or BP in PubMed (1966 through 31 October 2014), using terms and algorithms as presented in Supplemental Table 1. References from previous meta-analyses and reviews evaluating the effect of potassium on BP were screened for additional publications. No restrictions were imposed on language.

Study selection

An overview of the study selection is given in Fig. 1. After screening titles and abstracts, full-text articles were screened according to predefined criteria. Inclusion criteria were (1) randomized design; (2) effect of increased potassium intake on HR or BP assessed; (3) placebo-controlled study; (4) subjects of 18 years or older; (5) apparently healthy individuals; (6) treatment effect could be appointed to increased potassium intake alone; and (7) intervention period was 2 weeks or longer. After excluding duplicate publications, 34 potential relevant studies remained.

If not reported, authors were contacted to provide HR data. For 12 studies HR data were not obtained, either because (1) no HR measurements were performed [21–23]; (2) HR data were not accessible [24–28]; or (3) no contact could be established with the author [29–32], leaving 22 RCTs [19,20,33–52] that were eligible and included in the meta-analysis.

Data extraction and risk of bias assessment

Two investigators (LG and FJMM) extracted the following data from each study using a standardized extraction sheet: study design; primary outcome of the study; intervention duration; potassium type and dose; data on potassium and sodium excretion; method of HR assessment; data on HR and variance measures; and data on BP. Data on sample size and characteristics of the study population including mean baseline age, sex, hypertensive status, and use of antihypertensive medications were also collected. When the outcome was measured multiple times, data from the latest time point were extracted. Discrepancies were resolved by discussion with a third investigator (JMG). When data were missing, authors were requested or data were calculated using published data. None of the 22 RCTs reported the HR effect estimate with the standard error (SE) of this treatment effect. For 5 RCTs [19,45,48,50,52], HR effects with SEs were available upon author request. For 17 RCTs [20,33–44,46,47,49,51], the HR effect and SE were calculated using published data, of which for one RCT [44] HR data were derived from graphs. If pre-study characteristics were missing, placebo values were extracted if the protocol aimed to maintain usual dietary patterns during the study period. Eventually, for one study [34] data on pre-study HR, for two studies [42,49] data on potassium excretion after potassium supplementation, and for one study [42] data on sodium excretion after potassium supplementation were missing. Mean age was not reported for one study [39] and we took the midpoint of the age range.

We assessed the risk of bias of the included studies as being low, unclear, or high using the Cochrane Collaboration's tool [53], taking into account method of sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment and incomplete outcome data. Selective reporting was not taken into account, because authors were requested for additional HR data equalizing and minimalizing reporting bias between all studies. Studies considered to be high in risk of bias were the studies graded as high in risk for the method of sequence generation, allocation concealment and additionally in one of the blinding procedures or incomplete outcome data.

Statistical analysis

Our primary outcome was the effect of potassium supplementation on HR, as compared to a placebo-controlled situation. For crossover RCTs, the treatment effect was calculated as HR after potassium intervention minus HR after placebo intervention. For parallel RCTs, the treatment effect was calculated as the HR change from baseline to end in the potassium intervention group minus the HR change from baseline to end in the control group. If not obtained, the SE of the HR effect was estimated