INTERNATIONAL JOURNAL of MEDICAL STUDENTS

ORIGINAL RESEARCH

71. Effects of Non-Nutritive Sweetener Mixers compared to Carbohydrate Mixers on Alcohol Pharmacokinetics and Patient-Reported Outcomes: A Systematic Review and Meta-Analysis

Shwetha Shenod,[1] Dhanikha SV,[1] Hari Sudhan S.[1]

[1] PSG Institute of Medical Sciences and Research, Coimbatore, India

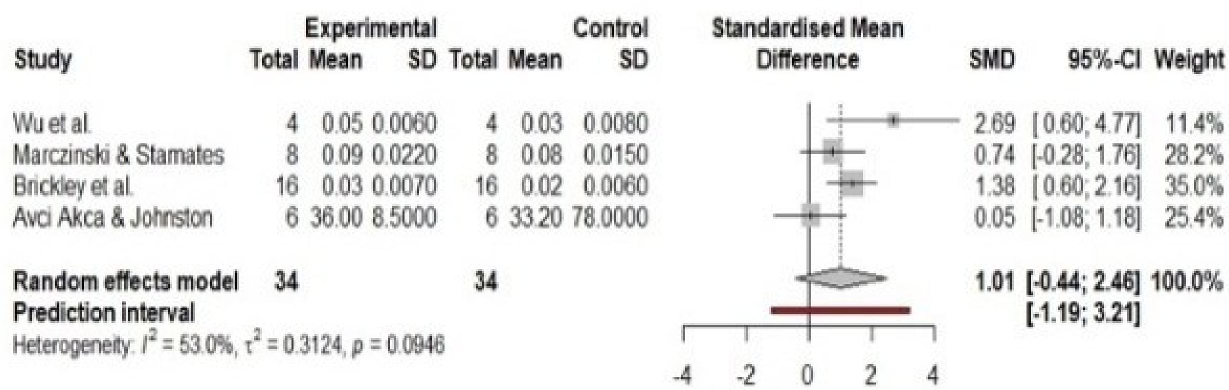
Background: Alcohol-associated accidents pose a major global health burden, accounting for 4.7% of all deaths and 4.6% of total disability-adjusted life years. Alcohol impairs psychomotor performance, driving ability, and risk perception. These acute outcomes are largely determined by alcohol absorption and metabolism, which in turn is influenced by gender, body composition, enzyme polymorphisms, drinking state, and co-consumed mixers. While carbonation and caffeinated mixers have shown to alter the pharmacodynamics of alcohol, the effects of non-nutritive sweetener (NNS) mixers remain underexplored. Given the increasing prevalence in the use of NNS mixers, clarifying their impact on alcohol pharmacokinetics and subjective intoxication and related outcomes is critical.

Methods: A systematic review and meta-analysis of studies obtained from three databases (PubMed, EMBASE, Scopus) was conducted in accordance with PRISMA guidelines. Primary outcomes assessed were breath or blood alcohol concentration (BrAC/BAC) and gastric emptying ($t_{1/2}$, t_{lag}). Secondary outcomes included subjective ratings of intoxication and related psychomotor tests. Risk of bias was assessed using the RoB2 tool. Standardized mean differences (SMD) was calculated for BrAC Cmax. Subgroup analysis were performed separately for the breathalyzer used, standardized ethanol dosing, and non-nutritive sweetener composition. Heterogeneity was quantified using I^2 statistic, and sensitivity and publication bias analyses were performed when required adjusting for the small sample size.

Results: Five studies were reviewed, of which four (34 NNS vs. 34 carbohydrate (CHO)) contributed to meta-analysis. All included studies were rated as having an overall risk of bias of "*some concerns*". NNS mixers were associated with higher not statistically significant peak BrAC (SMD = +1.01, 95% CI = -0.44 to 2.46, p = 0.097; I^2 = 53%). Subgroup analyses done for the type of breathalyzer used (p=0.1), standardized ethanol dose (p=0.80), non-nutritive sweetener content (p= 0.17) were not significant. Sensitivity analysis showed that the study by *Akca et al.* had a strong influence on the overall results. Gastric half-emptying time ($t_{½}$) with NNS mixers were observed to be shorter than with CHO mixers in two studies. *Marczinski & Stamates* found that alcohol with NNS mixers slowed reaction times and increased inhibition failures, indicating impaired cognitive control. Despite *Brickley et al.* observing no significant subjective differences between NNS and CHO mixers, there was a trend toward poorer vehicle control and greater risk-taking in men. *Acka et al.* reported expected alcohol-related changes in intoxication and alertness with no significant differences between mixer types.

Conclusion: Current evidence suggests that NNS mixers may accelerate gastric emptying and raise peak alcohol levels compared to CHO mixers, without proportionally increasing subjective patient-reported or similarly reported intoxication levels. This mismatch between physiological and perceived impairment highlights potential safety risks and underscores the need for further research on diet mixer use.

Figure 1. Forest Plot of Meta-Analysis for Change in BrAC Cmax in NNS Mixers Versus CHO Mixers



ISSN 2076-6327

This journal is published by Pitt Open Library Publishing