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Testing the potential of antihypertensive drugs for spinal pain treatment

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Motivation and Aim: Current treatment for spinal (neck and back) pain commonly turns out to be ineffective, making the search for new medications an important research goal. While developing a new drug takes years and substantial expense, the repurposing of existing medications can improve efficiency of this process. In this sense, testing the potential of antihypertensive drugs for spinal pain treatment may be promising, since the link between hypertension and back pain has been described elsewhere [1]. In this study, we aimed to assess the effect of four classes of cardiovascular medications (beta-blockers, calcium channel blockers, angiotensin-converting enzyme inhibitors, and statins) on spinal pain and answer the question of whether they can be useful for its treatment or prevention.

Methods and Algorithms: As the input data we used publicly available results of genome-wide association studies (GWAS) conducted in White Europeans for systolic blood pressure (N = 757,601) [2], low-density lipoprotein cholesterol (N = 173,082) [3], and spinal pain (N = 1,028,947) [4]. The first two were considered as exposures, and the latter was an outcome in Mendelian randomization (MR) analyses. All data passed quality control and unification in the GWAS-Map platform [5]. We followed the pipeline proposed by Gill and coauthors [6] to estimate the causal effect. In brief, we utilized the inverse-variance weighted MR approach [7], instrumental variables for beta-blockers, calcium channel blockers, and angiotensin-converting enzyme inhibitors preselected in resent work [6] and we found the instrumental variable for statins using PLINK v1.90b6.24 [8], the DrugBank [9], GeneCards and GeneHanser [10] databases. Effect of statin use on levels of low-density lipoprotein cholesterol was taken from the randomized clinical study [11]. For MR analyses we set the threshold for statistical significance at p-value < 0.0125 after correction for multiple testing. Additionally we estimated the detectable MR effect for each medication assuming 80 % statistical power.

Results: We observed no statistically significant effect on spinal pain for any of the four medication classes. However, point estimates for the MR analyses of beta-blockers were suggestively significant and demonstrated a protective effect on spinal pain (OR = 0.84 [95 % CI 0.72–0.98], *p*-value = 0.026). In contrast, point estimates for the MR analyses of calcium channel blockers suggested a detrimental effect on spinal pain (OR = 1.12 [95 % CI 1.02–1.24], *p*-value = 0.020) but this was not statistically significant after accounting for multiple testing. For other drugs MR results showed wide 95 % CIs (OR = 0.91 [95 % CI 0.49–1.71], *p*-value = 0.78 for and OR = 1.11 [95 % CI 0.96–1.27], *p*-value = 0.16 for statins) reflecting imprecise estimates and were not statistically significantly associated with spinal pain. In power calculations we estimated the detectable effects for beta-blockers, calcium channel blockers, angiotensin-converting enzyme inhibitors, and statins to be OR = 0.81, OR = 1.10, OR = 0.37, and OR = 0.80, respectively.

Conclusion: A protective effect of beta-blockers on spinal pain was suggested in the current study, consistent with findings from observational and bioinformatic studies of diverse pain phenotypes. The detrimental effect of calcium channel blockers on spinal pain identified in this work must be interpreted in the context of conflicting directions of effect on other pain traits in observational and bioinformatic studies.

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