Acetazolamide arterial spin labeling to estimate cerebrovascular reserve in Moyamoya disease and syndrome

Response

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We thank Dr. Mugikura and colleagues for their interest. We agree with them that, like any medical intervention, acetazolamide administration is associated with risk, which must be interpreted relative to benefit. However, it is important to point out that this risk is small. Mugikura et al. in a prior letter (1) cite Japanese literature suggesting that acetazolamide was related to 6 fatalities in 400,000 to 600,000 administrations (0.001 -0.0015%) (2, 3). For reference, the estimated lifetime-adjusted cancer risk from radiation administered during a brain single photon emission tomography (SPECT) examination is at least 100 times greater (4). The only study examining acetazolamide risk in English reported no adverse events in > 1000 studies (5). A more recent study examining MR diffusion changes following acetazolamide in a small cohort of Moyamoya patients could not detect any deleterious effects (6).

In Moyamoya, the most common surgical treatment is external carotid – internal carotid (EC-IC) bypass, a complex procedure with non-negligible risk. Cerebrovascular reserve (CVR) assessment might inform on the optimal timing for surgery (7–9). In this context, where a low-risk diagnostic test identifies patients who may benefit from a higher risk surgical intervention, the risk–benefit ratio is likely justified. If CVR studies are performed, our article highlights that using arterial spin labeling (ASL) MRI instead of SPECT and PET will reduce cancer risk by avoiding the need for radioactivity.
Alternative approaches to acetazolamide for CVR are currently being evaluated. These include breath-holding and carbon dioxide inhalation, and have frequently used blood oxygenation-level dependent (BOLD) as a surrogate CVR marker (10, 11). These approaches can be hard to implement and require patient compliance levels not necessary for acetazolamide studies. Finally, the authors suggest indirectly assessing CVR using contrast-perfusion MRI or the 'ivy sign' on fluid-attenuated inversion recovery (FLAIR). While interesting, this has limitations. We suggest considering ASL instead of GD enhanced MR perfusion, which might avoid the need of repetitive contrast injections. Evaluating the ‘ivy sign’ does not require contrast, but is qualitative and has not been directly compared to CVR. These alternatives to acetazolamide CVR testing hold promise, but must still be validated in larger cohorts.

References

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