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Opinion

Better Mood, Better Outcomes in Stroke Elderly Patients?

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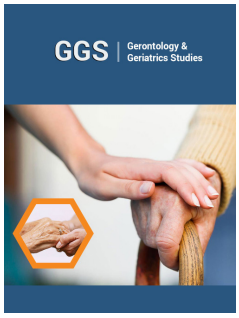

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Opinion

Stroke is one of the main global causes of death and disability-adjusted life-years around the world [1]. Most of community-dwelling elderly stroke survivors need special care on their daily living [2]. Stroke treatment in elderly patients is complex. Many randomized clinical trials exclude these individuals for their multiple geriatric syndromes, functional status and comorbidities [3]. Nowadays, prevention is the principal intervention, in particular lifestyle changes and control of chronic diseases. Ischemic stroke treatment is focused on early management; recognition of eligible patients for intravenous thrombolysis or mechanical thrombectomy, early rehabilitation and initiation secondary stroke prevention. Classically, antiplatelet and anticoagulants are prescribed for secondary stroke prevention due to their inhibition of thrombus formation [4]. Although, rehabilitation is a focal treatment for disability and motor recovery, there is major interest in supportive novel treatment pathways. One that has been booming recently is the serotonin signaling system and the selective serotonin reuptake inhibitors (SSRIs) administration after an acute ischemic stroke.

Descriptions of cellular pathways for neurogenesis and clinical recovery manifestations have been studied. At a cellular level, neurogenesis is a rare term attributed or used for drugs now a day. Thus, theories have recognized and reviewed SSRIs efficacy for these traits. Neurotrophic growth factors have been implicated. Their expression in peri-infarct matter leads to migration and maturation of neurons from the sub granular zone in the hippocampus. Brain derived neurotropic factor induction enhances neuroplasticity. In addition, SSRIs incite a reinstatement of neuronal organization by inhibition of overexcited neuronal circuits caused by stroke. Moreover, inhibition of serotonin reuptake and higher levels of neurotransmitter in the synaptic cleft, modulate glutamate, calcium and γ-aminobutyric acid transmission for long-term potential restoration [5,6].

SSRIs are extensively used around the world and very common in the elder population. Mostly, small clinical trials suggest encouraging outcomes in different domains such a motor skills, depression and mortality. Consistency has not permitted SSRIs to be included as a routinely practice for ischemic stroke. For the moment, there are no clear indications to prescribe them regularly. Additionally, studies that focus on aging patients are scarce or non-existent. Should there be broadened awareness for SSRIs during evaluation of elderly stroke patients?

Post-stroke depression appears in 30% of patients, and as we know, it can bring detrimental outcomes on quality of life, independence, and mobility. Meta-analysis shows consistent results for prevention. In 2020, Zhou et al. [7] included 3768 patients without depression from 4 trials, the analysis revealed positive outcomes in prevention of post-

stroke depression (RR 0.78 [95% CI 0.67-0.90; p .001) and low heterogeneity (I2=23%) [7]. Previous systemic reviews have also yield encouraging results [8].

Clinically, the most debated effect for SSRIs is motor recovery. One of the first double blinded placebo-controlled studies to demonstrate effectiveness was the FLAME study (Fluoxetine for motor recovery after acute ischemic Stroke), where the antidepressant group had a significant improvement in comparison to the placebo group in the Fugl-Meter motor scale (mean 34.0 points [95% CI 29.7-38.4] vs 24.3 points [19.9-28.7]; p .003) [9]. Systemic reviews have assessed the use of SSRIs. The overall results do not identified benefits. When high bias studies are included, improvement is demonstrated. However, as previously mentioned, age is not often accounted for. We could only find that a systemic review by Mead et al. [10] mentioned that mostly recruited patients were in the range of 60-70 years. Although, a high risk of bias is described, evidence of favorable outcomes is shown [10]. Interestingly, a study showed reduction in 30-day all-cause mortality with the administration of early treatment (first 5 days after the event) [11].

Evidence in the elderly to support the administration of SSRIs is scarce as previously mentioned. Could the described potential benefits of SSRIs out weight the side effects? For its low cost, should antidepressant treatment be initialized in selected candidates? Should the suspension occur only in the event of an adverse reaction? As SSRIs have shown to be safe, small doses could be initiate and titrated until clinical benefit. The choice must be individualized based in patient's profile. However, in a geriatric perspective, the fewer the anti-cholinergic effects the better. Anti-cholinergic activity leads easier adverse reactions (dry mouth, urinary retention, constipation, etc.) leads to worse outcomes. Uncertainty may rise on the duration of treatment, based on post-stroke depression analysis, at least for 8 weeks could be beneficial.

At last, utilization of SSRIs on specific demographic areas or third world countries such as ours, may bring an additional tool for patient recovery. Further trials will define improvements and long-term answers for the elderly population, but for now, as the lines of investigation are open, consideration for SSRIs may be exciting.

Conflict of Interest

Authors have nothing to disclose with regard to commercial support.

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