Side effect burden of lithium augmentation in geriatric compared to non-geriatric patients with treatment-resistant depression

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Background

Treatment resistance is a frequent challenge in the treatment of Major depressive disorder (Bauer et al. 2014). Lithium augmentation (LA) is an effective strategy for geriatric and non-geriatric patients who do not respond to the initial antidepressant-treatment (Bauer et al. 2014, Nelson et al. 2014). For example, in a recent published prospective cohort study Buspavanich et al. (2018) found superior effectiveness of LA in geriatric compared to non-geriatric patients. However, LA is rarely used in geriatric patients (Pruckner and Holthoff-Detto 2017). One reason may be the fear of increased side effects of the treatment due to somatic comorbidity of geriatric patients (Cooper et al. 2011).

Methods

The aim of the present study is to investigate the side effect burden of LA in geriatric compared to non-geriatric patients with treatment-resistant depression. Severity of depression was measured weekly in 167 acutely depressed patients (ICD10 F32.1-3 and F33.1-3; $n_{\text{age} \geq 65 \text{ years}} = 22$; $n_{\text{age} < 65 \text{ years}} = 145$) at baseline and during four weeks of LA using the Hamilton Depression Rating Scale (HDRS-17). The Patient Rated Inventory of Side Effects (PRISE) was used to assess the presents of side effects in a variety of biologic systems.

Results

Descriptive statistics of geriatric and non-geriatric patients can be found in Table 1.

Table 1 Comparison of characteristics: n(%), mean [standard deviation]

	All Participants N=167	Geriatric Patients n=22	Non-geriatric Patients n=145	p-value
Age (years)	48.35 [13.9]	71.91 [5.6]	44.78 [11.0]	
Gender				0.89
Female	104 (62.3)	14 (63.6)	90 (62.1)	
HDRS-17 ^a baseline	21.75 [5.3]	21.50 [4.6]	21.79 [5.4]	0.93
Sufficient lithium level ^b	150 [89.9]	22 [100]	128 [88.3]	0.09
Lithium level at study endpoint	0.68 [0.2]	0.61 [0.2]	0.69 [0.2]	0.62
Charlson comorbidity score ^d	0.23 [0.8]	0.55 [1.3]	0.19 [0.7]	0.06

Table 2 Mean Differences of side effects for all categories at baseline

Table 3 Item Dizziness on standing

Table 4 Item Chest pain

We used a linear mixed model for statistical analysis to investigate the effect of geriatric patients as an explanatory factor for differences in side effects (dependent variable). We found significantly more side effects in the category heart (estimated differences: 0.53; 95%-CI: 0.16 to 0.91; $F_{1,121} = 8.14$; $p < 0.01$) in geriatric patients compared to non-geriatric patients. We found no significant effect in the other categories of side effects (gastrointestinal, nervous system, eye/ears, skin, genital/urinary, sleep, sexual functioning). Regarding various items of the PRISE we found significantly more side effects of chest pain (estimated differences: 0.28; 95%-CI: 0.11 to 0.46; $F_{1,121} = 10.39$; $p < 0.01$) as well a trend to more side effects of dizziness on standing (estimated differences: 0.53; 95%-CI: -0.02 to 0.45; $F_{1,119} = 3.32$; $p = 0.07$). Regarding other selected items (tremors, frequent urination, diarrhea and nausea) we found no significant effect in any of the models ($p > 0.05$, data not shown).

Discussion

This is the first study investigating side-effect burden of geriatric compared to non-geriatric patients with treatment-resistant depression. We found that geriatric patients reported significantly more side effects of chest pain in compared to non-geriatric patients. Regarding all other side effects there was no significant difference in both groups. Thus, our data suggest that LA is a highly effective and relatively tolerable treatment option in geriatric patients. Our findings contribute to a better risk-benefit assessment for the indication of LA in geriatric patients in clinical care.