Raloxifene as an Adjuvant Therapy for Patients with Schizophrenia

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■ Background and importance

Raloxifene may be useful as an adjunctive treatment schizophrenia. This meta-analysis aimed to evaluate the effectiveness and safety of adjunctive raloxifene in patients with schizophrenia.

■ Material and methods

We comprehensively searched PubMed, Embase, and Cochrane databases for RCTs published until May 31, 2024. The criteria for the selected articles were based on the PICO principles (participants, interventions, comparisons, and outcomes). We used a combination of Medical Subject Headings and keywords (raloxifene) AND (schizophrenia). Studies were not limited to those published in English. Randomized controlled trials investigating the effectiveness and safety of adjunctive raloxifene for treating schizophrenia were included. The outcome measure was psychotic symptom severity using the Positive and Negative Syndrome Scale (PANSS). Mean differences (MDs) and their 95% confidence intervals (CIs) were calculated using random effects models.

■ Results

Nine studies were included in the final analysis. Compared with the placebo group, raloxifene as an adjunctive therapy significantly improved the positive, negative, general, and total PANSS scores, MD = -1.30 (95% CI = -2.39 to -0.20; I^2 = 52%; p = 0.02), MD = -1.69 (95% CI = -3.19 to -0.20; I^2 = 68%; p = 0.03), MD = -3.90 (95% CI = -6.59 to -1.21; I^2 = 69%; p = 0.005), and MD = -7.12 (95% CI = -11.89 to -2.36; I2 = 74%; p = 0.003), respectively.

Subgroup analysis

We conducted a subgroup analysis of different doses of raloxifene, duration, and menopausal status in women. Regarding total symptoms, the PANSS total scores of the raloxifene group were not significantly different from those of the placebo group at ≤ 12 weeks. However, at intervention durations of > 12 weeks, the raloxifene group showed greater improvement in PANSS positive and general scores than the control group (MD = -8.07, 95% CI = -12.7 to -3.44; I^2 = 58%).

■ Conclusion and Relevance

This meta-analysis shows that adjunctive raloxifene is effective and safe in patients with mild-to-moderate schizophrenia, specifically improving PANSS-positive, general, and total scores. Future studies with larger sample sizes are required to confirm these findings.

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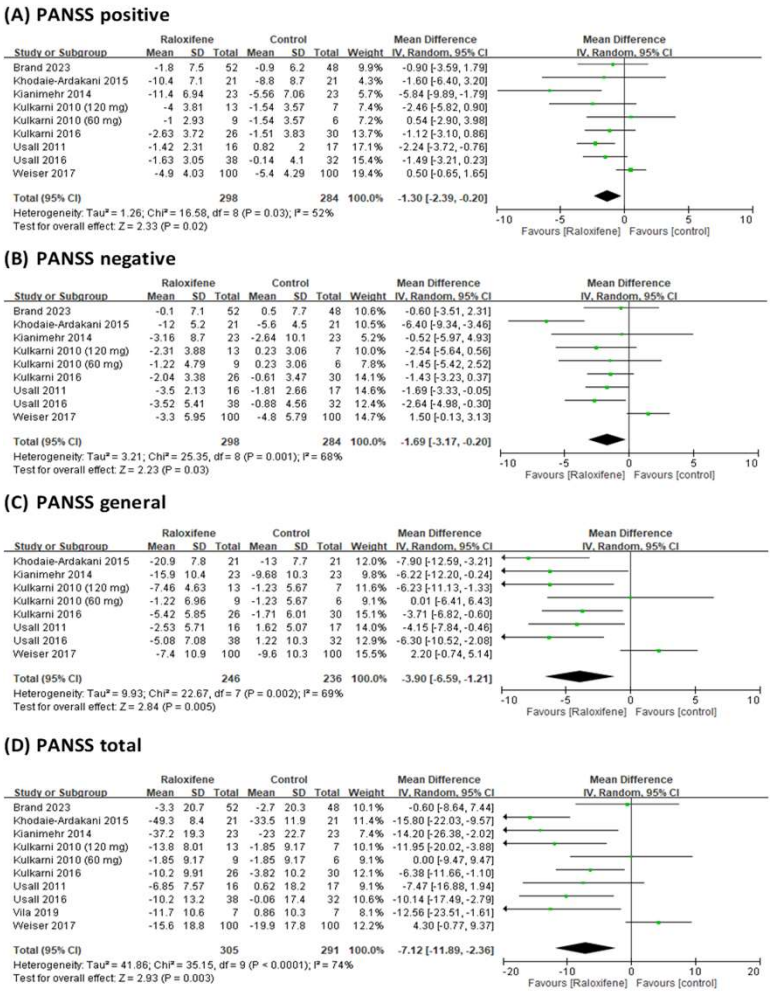

Figure 1. Forest plots for a between-group meta-analysis comparing psychiatric symptoms in patients with schizophrenia receiving or not receiving raloxifene as an adjunctive therapy.

Table 1. Results of subgroup meta-analysis of the treatment effect of adjunct raloxifene in patients with schizophrenia.

Outcomes	No. of studies	MD (95% CI)	Heterogeneity (I^2)
PANSS positive			
Duration > 12	2	-0.39 (-2.33 to 1.55)	72%
Duration ≤ 12	6	-1.78 (-2.86 to -0.71)	14%
Postmenopausal women	5	-1.48 (-3.05 to 0.09)	70%
Mixed	3	-1.10 (-2.61 to 0.42)	0%
PANSS negative			
Duration > 12	2	-0.48 (-4.54 to 3.57)	88%
Duration ≤ 12	6	-2.14 (-3.15 to -0.78)	43%
Postmenopausal women	5	-1.13 (-2.79 to 0.53)	60%
Mixed	3	-2.72 (-5.93 to 0.48)	79%
PANSS general			
Duration > 12	2	-1.91 (-10.23 to 6.42)	90%
Duration ≤ 12	5	-4.68 (-6.46 to -2.91)	0%
Postmenopausal women	5	-3.31 (-6.74 to -0.12)	72%
Mixed	2	-5.42 (-9.46 to -1.39)	53%
PANSS total			
Duration > 12	3	-5.54 (-17.05 to 5.97)	86%
Duration ≤ 12	6	-8.07 (-12.7 to -3.44)	58%
Postmenopausal women	6	-6.84 (-13.04 to -0.62)	74%
Mixed	3	-7.85 (-15.98 to 0.29)	79%