

Nortriptyline plus interpersonal psychotherapy was effective in major depression in older adults

Reynolds CF 3rd, Frank E, Perel JM, et al. *Nortriptyline and interpersonal psychotherapy as maintenance therapies for recurrent major depression. A randomized controlled trial in patients older than 59 years.* *JAMA* 1999 Jan 6;281:39–45.

Question

In older patients with major depression, how effective are nortriptyline hydrochloride and interpersonal psychotherapy (IPT) in preventing recurrence of depressive episodes?

Design

Randomised controlled trial with 3 years of maintenance treatment.

Setting

Geropsychiatric research clinic in Pittsburgh, Pennsylvania, USA.

Patients

180 patients who were ≥60 years of age (mean age 68 y, 75% women) and met criteria for recurrent non-psychotic unipolar major depression according to the Schedule for Affective Disorders and Schizophrenia-Lifetime version. Other inclusion criteria were at least in their second lifetime episode, interepisode wellness interval of ≤3 years, Hamilton Depression Rating Scale score ≥17, and Folstein Mini-Mental State Examination score ≥27. Of 107 patients who successfully completed acute treatment, continuation therapy, and began maintenance therapy (124 randomised), 96 patients (90%) completed the study.

Intervention

Patients were allocated to nortriptyline hydrochloride, 80–120 ng/ml (n=24), placebo (n=29), IPT (n=21), or nortriptyline and IPT (n=22).

Main outcome measures

Recurrence of depressive episodes at 3 years.

Main results

Combined treatment with nortriptyline and IPT led to the lowest recurrence rate and was superior to placebo ($p < 0.001$), to IPT alone ($p = 0.003$), and probably to nortriptyline alone ($p = 0.06$) (table). Lower recurrence rates occurred with nortriptyline alone compared with placebo ($p < 0.001$) but not with IPT alone ($p = 0.16$) (table). IPT was superior to placebo ($p = 0.03$) (table). Patients ≥70 years of age had the greatest rate of recurrence in the first year; combined treatment was the most effective in preventing recurrence in this age group.

Conclusion

Nortriptyline and interpersonal psychotherapy prevented recurrences of major depressive episodes in older adults.

*Depressive episode recurrence rates at 3 years for nortriptyline, interpersonal psychotherapy (IPT), and placebo**

Comparison	Event rates	RRR (95% CI)	NNT (CI)
Nortriptyline and IPT v placebo	20% v 90%	78% (56 to 90)	1 (1 to 2)
Nortriptyline and IPT v IPT	20% v 64%	67% (33 to 87)	2 (2 to 6)
Nortriptyline and IPT v nortriptyline	20% v 43%	53% (-7.3 to 81)	Not significant
Nortriptyline v placebo	43% v 90%	52% (29 to 71)	2 (2 to 4)
Nortriptyline v IPT	43% v 64%	33% (-12 to 61)	Not significant
IPT v placebo	64% v 90%	29% (4.6 to 51)	4 (2 to 30)

*Abbreviations defined in glossary; RRR, NNT, and CI calculated from data in article.

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Commentary

Most studies looking at the outcome of depression in old age have reported similar results: 20–30% of patients recover completely and 70–80% relapse or remain depressed at follow up. The study by Reynolds *et al* shows that treatment with nortriptyline or IPT is superior to placebo in preventing relapse. It also suggests that the combination of these 2 treatments offers patients the best possible 3 year outcome.

Common sense suggests that psychotherapy should improve the outcome of patients by increasing compliance and addressing the psychosocial issues that are often associated with depression in old age. Cognitive behavioural and interpersonal therapies were designed to address clearly defined problems and may therefore be particularly suitable for use in older adults. Reynolds *et al* showed that long term IPT is associated with fewer relapses. It would be

interesting to see if these results can be replicated with the use of larger samples of patients and if other forms of psychological treatment are also effective.

The most relevant clinical question arising from this study is whether the long term combined use of IPT and nortriptyline is the most effective strategy in the elderly. The answer to this question is uncertain for several reasons. Firstly, it is unclear if the positive effects of psychotherapy are dependent on its indefinite continuation. Secondly, the use of a more flexible drug regimen could have produced a more favourable outcome. A simple change of medication may effectively treat the relapse of depressive symptoms in the elderly.¹ In addition, newer antidepressants produce less troublesome side effects than tricyclics—their use may improve compliance to treatment and, as a consequence, reduce the risk of relapse. Thirdly, the sam-

ple of patients selected for this study is unlikely to adequately represent the population of older people with depression. They all had a recurrent depressive disorder (median number of previous episodes = 4) with >1 episode during the previous 3 years. Less severe forms of illness may not require combination of treatments to avoid relapse.

Reynolds *et al* remind us that the maintenance treatment of older adults with recurrent depression should not always be limited to the use of antidepressants. Future studies need to clarify which are the most cost effective options to avoid relapse of depressive symptoms in older adults.

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¹ Flint AJ, Rifat SL. *Br J Psychiatry* 1997;170:268–72.