Тема: Применение трициклических антидепрессантов (Амитриптиллин) и психотерапии у пациентов с постинсультной депрессии

Выполнила: Мусаева И.М
Проверила: Кошмаганбетова Г.К

АКТУАЛЬНОСТЬ

Депрессия - развивается примерно у каждого 3-го больного, перенесшего инсульт, и может негативно влиять на процесс реабилитации. Рассматривается роль психологических факторов, генетической предрасположенности, локализации поражения головного мозга, недостаточности моноаминов в патогенезе депрессии. Постинсультная депрессия часто не диагностируется, хотя ее выявлению помогают простые исследования (шкалы Бека, Гамильтона). При развитии депрессии отмечается положительный результат лечения антидепрессантами; сочетание психотерапии и антидепрессантов дает еще более выраженный эффект. Отмечается положительное действие длительного приема (6 мес и более) трициклических антидепрессантов и селективных ингибиторов обратного захвата серотонина, представлены данные о высокой эффективности и хорошей переносимости эсциталопрама при постинсультной депрессии. Подчеркивается, что предупреждение и лечение депрессии может существенно улучшить процесс реабилитации и качество жизни больного.

Депрессия ухудшает качество жизни как самих пациентов, так и членов их семьи и ухаживающих за ними лиц . Постинсультная депрессия затрудняет восстановление и реабилитацию, снижает социальную активность и усугубляет инвалидность. В одном из последних исследований раннее возникновение постинсультной депрессии (в первые 7–10 дней с момента развития инсульта) ассоциировалось с нарастанием инвалидности (оцениваемой по индексу Бартел) в ближайшие 1 и 2 года, однако при этом не наблюдалось существенного увеличения смертности

ЦЕЛЬ ИССЛЕДОВАНИЯ

- Сравнить эффективность трициклических антидепрессантов (Амитриптиллина) и психотерапии при постинсультной депрессии

ГИПОТЕЗА

- Нулевая - лечение постинсультной депрессии с Амитриптиллином и психотерапии не отмечает эффекта.
- Альтернативная- лечение постинсультной депрессии с Амитриптиллином и психотерапии приводит к снижению постинсультной депрессии.

ЗАДАЧИ

- Произвести литературный обзор .
- Определение групп пациентов генеральной совокупности для формирования выборки.
- Путем рандомизации распределить пациентов на 2 группы :
- 1 группа: получающие трициклический антидепрессант (Амитриптиллин)
- 2 группа: получающие психотерапию.
- Проанализировать результаты анализов и сделать заключение

ДИЗАЙН ИССЛЕДОВАНИЯ

Открытое рандомизированное контралируемое исследование

ВЫБОРКА

Исследование проводилось в городской поликлинике №3 в г. Актобе. В исследование были взяты те пациенты в возрасте от 30-70 лет, независимо от пола у которых по шкале Гамильтона 14—18 баллов, что соответствует депрессии средней степени тяжести .

Выборка-систематическая

КРИТЕРИИ ВКЛЮЧЕНИЯ

- Пациенты после инсульта в возрасте 30-70 лет, независимо от пола которые по шкале Гамильтона набирают 14-18 баллов
- Пациенты которые по шкале Комы Глазго набирающие 15 баллов.

КРИТЕРИИ ИСКЛЮЧЕНИЯ

- Пациенты после инсульта у которых по шкале Гамильтона набирают 19-22 баллов.
- Пациенты которые по шкале Комы Глазго набирают 13-14 баллов
- Пациенты с когнитивными расстройствами
- Пациенты после инсульта до 30 лет и свыше 70 лет.
- Беременность и период лактации
- Гиперчувствительность к амитриптилину и вспомогательным веществам.
- Применение одновременно с лекарствами, подавляющими моноаминоксидазу.
- Пациенты которые в анамнезе имеется: Аритмия, ХСН, Атриовентрикулярная блокада 2 степени, Феохромоцитома.

ИССЛЕДОВАТЕЛЬСКИЙ ВОПРОС

Приведет ли к снижению тяжести депрессии у постинсультных больных с депрессии средней степени тяжести?

P – Пациенты на амбулаторном лечении с постинсультной депрессии средней степени тяжести (по шкале Гамильтона)

I – Прием трициклических антидепрессантов (Амитриптиллин)

C- Применение психотерапии

O- Благоприяиный- снижение степени тяжести депрессии. Неблагоприятный-суицид.

T- 12 недель

ЭТИЧЕСКИЕ АСПЕКТЫ

- Одобрено КЭ
- Информированное согласие с полным раскрытием всей необходимой информацией на понятном языке (на 2-х языках), крупный шрифт в 2-х экземплярах
- Имеют право отказаться на любой стадии исследования
- Действие в интересах пациента
- Польза для пациента и общества

ИССЛЕДОВАТЕЛЬСКИЙ ВОПРОС ПО СТАТЬЕ

- Оценить эффективность антидепрессантов у больных с постинсультной депрессии (по шкале Монсгомери)
- P - пациенты с постинсультной депресии
- I – применение антидепрессантов
- C – плацебо
- O – снижение депрессии
- T- 24 недель

ДИЗАЙН ИССЛЕДОВАНИЯ ПО СТАТЬЕ

- Окрытое рандомизированное контролируемое многоцентровое исследование.

ВЫБОРКА ПО СТАТЬЕ

- Систематическая

Efficacy, acceptability, and tolerability of antidepressant treatments for patients with post-stroke depression: a network meta-analysis

B. Qin[1] *H. Chen[1] *W. Gao[1] *L.B. Zhao[2] *M.J. Zhao[3 4] H.X. Qin[1] W. Chen[1] L. Chen[1] M.X. Yang[1]

ABSTRACT

The aim of this study was to investigate the efficacy, acceptability, and tolerability of antidepressants in treating post-stroke depression (PSD) by performing a network meta-analysis of randomized controlled trials of the current literature. Eligible studies were retrieved from online databases, and relevant data were extracted. The primary outcome was efficacy as measured by the mean change in overall depressive symptoms. Secondary outcomes included discontinued treatment for any reason and specifically due to adverse events. Fourteen trials were eligible, which included 949 participants and 9 antidepressant treatments. Few significant differences were found for all outcomes. For the primary outcome, doxepin, paroxetine, and nortriptyline were significantly more effective than a placebo [standardized mean differences: −1.93 (95%CI=−3.56 to −0.29), −1.39 (95%CI=−2.59 to −0.21), and −1.25 (95%CI=−2.46 to −0.04), respectively]. Insufficient evidence exists to select a preferred antidepressant for treating patients with post-stroke depression, and our study provides little evidence that paroxetine may be the potential choice when starting treatment for PSD. Future studies with paroxetine and larger sample sizes, multiple medical centers, and sufficient intervention durations is needed for improving the current evidence.

MATERIAL AND METHODS

Data sources and search strategy

We conducted a systematic search of the PubMed, EMBASE, Cochrane Central Register of Controlled Trials, Web of Science, PsycINFO, World Health Organization International Trial Registry, and clinicaltrials.gov databases from their inception to March 2017 using search terms such as “post-stroke depression” (see Supplementary Tables S1–S5). Only studies published in English were included in this investigation. Moreover, we inspected the reference lists of the included studies and previous reviews of the use of antidepressants in treating PSD. Additionally, we reviewed all the references listed in the trials we found, and investigators were also contacted via telephone or email about unpublished trials.

Selection criteria

Studies were included if they involved a RCT assessing any antidepressant available worldwide, at any dose and administered in any form, that were compared with other antidepressants or a placebo for treating PSD, and if the antidepressants were used as a monotherapy. The study subjects met the following criteria: 1) no limitations on gender, age, race, region, or nationality of the patients; 2) patients were diagnosed as having had a stroke clinically and/or by computed tomography or nuclear magnetic resonance imaging, and 3) patients had a diagnosis of depression, as confirmed on the basis of DSM criteria or other validated rating scales for depression. Exclusion criteria were as follows: 1) combination therapy, such as an antidepressant combined with psychotherapy, and 2) relevant outcome indexes not reported. Two reviewers independently assessed all citations and discarded those that were irrelevant based on the title of the publication and its abstract. If the article was possibly relevant, we retrieved the full-length article for further assessment. Two reviewers independently

Outcome measures

The primary outcome was the mean change in overall depressive symptoms, which was assessed in the first instance by a change in depression rating scale scores (difference in scores from baseline to endpoint). When a trial reported multiple scores, the Hamilton Depression Scale (HAMD) was preferred. A negative value indicated greater relief from depressive symptoms. Intention-to-treat datasets were used whenever available. Secondary outcomes were the proportion of patients who discontinued treatment for any reason (acceptability) and the proportion of patients who discontinued treatment due to adverse effects (tolerability). Because an NMA requires reasonable homogeneity, we focused on acute treatments, which we defined as those lasting 8 weeks. If data over 8 weeks were not available, we used data from between weeks 4 and 12 (the data points closest to 8 weeks were given preference).

Data extraction and quality assessment

Data extraction was performed independently by two reviewers and any discrepancies were resolved via discussion. Extracted data included the study methodology, identification of outcome measures, results, and final conclusions. We also used the risk of bias assessment tool from the Cochrane Handbook to assess the methodological quality of the studies. Assessed quality criteria were randomization, concealed allocation, blinding, incomplete outcome data, selective outcome reporting, and ‘other issues’.

DISCUSSION

This study performed a comprehensive comparison of the efficacy, tolerability, and acceptability of antidepressants using an NMA. Interventions were grouped into placebo, SSRIs (citalopram, fluoxetine, paroxetine, sertraline), TCAs (doxepin, imipramine, nortriptyline), SNRIs (duloxetine), and trazodone. The efficacy outcome was measured as the mean change in overall depressive symptoms, which was assessed as the change in depression rating scale scores (difference in scores from baseline to endpoint). To assess acceptability and tolerability, we examined the proportions of patients who discontinued treatment for any reason and who discontinued treatment due to adverse effects; a high treatment discontinuation rate indicates low efficacy, concerns regarding safety or the risk to become tolerant to the treatment. To our knowledge, this is a pivotal study to thoroughly explore the efficacy, tolerability and acceptability rankings of antidepressants for treating PSD and include a wide range of outcomes. Doxepin, paroxetine, and nortriptyline were found to be more effective than a placebo. Paroxetine was found to be more acceptable than doxepin. Doxepin was not found to be more tolerable than paroxetine or a placebo. These results indicate that one of the most efficacious treatments (doxepin) might not be the best choice in terms of overall acceptability and tolerability. Moreover, the evidence for nortriptyline was only from trials with small sample sizes, which might result in an exaggerated treatment effect ([35]).

The most important clinical implication of the results presented here is that paroxetine might be the potential choice when starting treatment for PSD because it appears to have a good balance between efficacy, acceptability, and tolerability. Paroxetine's potential was originally demonstrated in a pivotal study in which it effectively improved the depressive symptoms of patients with PSD ([36]). In addition, it was also safe and well tolerated. Owing to methodological limitations, such as non-placebo-controlled and open-label designs, the results of this study are not definitive. Our findings are consistent with data from a previous study, and they strengthen the evidence that paroxetine might be the appropriate choice for treating PSD. However, the wide confidence interval of the effect sizes between paroxetine and placebo raises the question of whether this estimate is robust enough to inform clinical practice. Furthermore, in comparison with other antidepressants, paroxetine did not show a significant difference in efficacy outcomes, and in terms of acceptability and tolerability, paroxetine was not better tolerated than placebo. Finally, in the sensitivity analysis, excluding trials without a double-blind design, paroxetine was not significantly more effective than a placebo. The open-label designs might have introduced a bias because patients or investigators might have taken/prescribed concomitant treatments to enhance efficacy based on their knowledge and beliefs of treatment allocation. However, it has been suggested that potential benefits of an open-label design may be sometimes intentionally directed by the need to mimic a daily clinical routine where therapeutic flexibility is needed. Thus, our results should be interpreted and translated into clinical practice with caution due to the uncertain evidence in the present meta-analysis.

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