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Efficacy of sertraline in post-traumatic brain injury (post-TBI) depression and quality of life: A systematic review and meta-analysis of randomized controlled trials

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A B S T R A C T

The relative paucity of robust studies on pharmacological treatments for depression following traumatic brain injury precludes establishment of firm recommendations for its routine use in this population. The purpose of this study is to determine the efficacy and tolerability of sertraline in the treatment of post-TBI depression and improvement in quality of life. Randomized controlled trials (RCT) were identified by electronic search through PubMed, Scopus, CINAHL (Cumulative Index to Nursing and Allied Health Literature), LILACS (Literatura Latino-Americana e do Caribe em Ciencas da Saude), Cochrane Library, Clinicaltrials.gov, and HERDIN (Health Research and Development Information Network database). Random effects meta-analysis of data for depression scale scores, treatment response, and quality of life scale scores was conducted. Four RCTs were included with a total of 224 patients. There were no significant mean differences in the Hamilton Depression Rating Scale (HAM-D17) scores (MD = 2.63, 95% CI [−1.32,6.57], p = 0.19), Maier subscale scores (MD = 0.88, 95% CI [−2.26, 4.01], p = 0.58), odds ratio of treatment response (OR = 1.04, 95% CI [0.13, 8.43], p = 0.97) and quality of life scale scores (SMD = −1.52, 95% CI [−5.65, 2.61], p = 0.47) between sertraline and placebo. The pooled evidence from four RCTs shows that sertraline is not superior to placebo in terms of improving depression and quality of life of patients with post-TBI depression. There is also insufficient evidence regarding its safety in this subset of patients.

1. Introduction

Traumatic Brain Injury (TBI) remains to be one of the most pressing public health concerns, and one of the most common causes of mortality and morbidity worldwide, occurring in 10 million persons annually [1,2]. TBIs result in a multitude of neurobehavioral changes that lead to long-term disability, difficulties in fulfilling social roles, and decreased quality of life [3–5]. Depression remains to be the most widely recognized post-TBI mood disorder [4,6]. The reported prevalence of depression post-TBI ranges from 6 to 77% [7]. In one study including 559 adults, 53.1% were reported to develop major depression in the year following TBI [5]. The estimated lifetime prevalence of major depression following TBI is reported to be 26.7% [8].

The development of depression following TBI results from the complex interaction of neuroanatomical, psychological, and social factors [4]. Neuroanatomic circuits implicated include the (1) the orbitofrontal cortex (OFC), (2) the dorsolateral prefrontal cortex (DLPFC), (3) the anterior cingulate circuit, (4) the temporal lobes, and (5) the basal ganglia. These neuroanatomic circuits function in behavioral control, processing of memory, and mood regulation [9]. The shearing and straining forces brought about by TBI can disrupt these circuitries and induce neurochemical changes in the serotonergic and cholinergic projections that innervate them [9–11].

Taken altogether, the high rate of depression after TBI and its effects on immediate and long-term outcomes justify the exploration of approaches to reduce the burden of post-TBI depression.

Selective serotonin reuptake inhibitors (SSRIs) are medications that increase the levels of serotonin that bind to serotonergic postsynaptic receptors rendering them capable of modulating several neuropsychiatric conditions such as depression, obsessive-compulsive disorder, and panic disorder [12]. The 2006 Neurobehavioral Guidelines Working Group included SSRIs, particularly sertraline (25–200 mg/day), as a therapeutic option in treating TBI-related depression. However, due to the paucity of robust studies and randomized clinical trials, guidelines for routine use could not be established [13,14]. Since then, several studies investigating the efficacy of sertraline in post-TBI depression have been conducted, albeit with conflicting results [15–20].

This study aims to determine the efficacy, safety, and tolerability of sertraline in the treatment of post-TBI depression using the best available evidence.

2. Methods

The authors searched for existing literature and relevant studies published after 1980. The specific search terms used were “sertraline”, “Zoloft”, “sertraline hydrochloride”, “depression”, “major depressive

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disorder", "major depression", "traumatic brain injury", "brain injury", "brain trauma" and "head injury". Databases searched included PubMed, Scopus, CINAHL (Cumulative Index to Nursing and Allied Health Literature), LILACS (Literatura Latino-Americana e do Caribe em Ciencas da Saude) and CDSR (Cochrane Database of Reviews). The authors handsearched relevant reference lists of existing review articles and primary studies to ensure a wider coverage of the literature. The authors also searched through ClinicalTrials.gov to identify any completed or ongoing trials.

The authors included all randomized controlled trials with parallel group designs that examined the effects of sertraline in the treatment of post-TBI depression. The criteria used to select studies for inclusion in this review were: (1) trials utilizing sertraline as a treatment intervention; (2) depression as a primary or secondary outcome measure; (3) studies that utilized validated diagnostic scales to quantitatively assess depression; (4) studies conducted in adults; (5) studies published after 1980; and (6) studies available in English. The fifth criterion specifying 1980 as starting point was selected to reflect consistency with the most robust review of the literature conducted by the World Health Organization (WHO) collaborating centre task force on mild TBI in 2004 [14].

This review excluded open-label or single-blind trials, descriptive studies, case-control studies or case reports, and ongoing studies or trials with incomplete data at the time of its writing.

As for the types of participants, the present review and meta-analysis included patients 18 years or older with a history of TBI (i.e., those with documented loss of consciousness or radiologic evidence of traumatically induced brain abnormality). All the participants included in the trials were diagnosed with major depressive disorder using standardized diagnostic criteria. Patients who met the criteria for bipolar disorder, psychotic disorder, substance abuse disorder, bereavement, or those identified to have suicidal ideations or intent were excluded from this study. Patients were also excluded if they (1) were treated or are currently taking other antidepressants, (2) are only undergoing psychotherapy, (3) have serious or unstable medical illnesses, (4) have a history of allergy or serious adverse reaction to the drug, and (5) were pregnant or breastfeeding.

Two study authors independently evaluated the abstracts to screen for eligible articles. Thereafter, the authors independently reviewed the full texts of selected studies and decided which trials met the criteria for inclusion in this study. Any disagreement was resolved through discussion with a third party.

3. Data abstraction and quality assessment

Two data abstractors assessed and extracted data regarding study design, methods, participants and demographic characteristics, intervention, and summary statistics using a data extraction form. Each abstractor was blinded to the results of the other, and data extraction was done independently. Any disagreement was resolved by discussion and consultation with a third party.

Quality and risk of bias assessment was also done of in congruence with the methods set out in the Cochrane Handbook for Systematic Reviews of Interventions [16]. The following specific domains were considered:

- Selection bias
- Performance and detection bias
- Attrition bias
- Reporting bias
- Other potential sources of bias

Two reviewers independently rated the overall risk score of each included study. The overall risk was labeled high if one or more domains was assessed to have a high risk of bias. The overall risk was labeled low if an adequate protocol was described in all the domains. All other combinations were rated as unclear overall risk of bias.

4. Data synthesis

For studies included in the meta-analysis, measures of treatment effect were reported as (1) mean difference in Hamilton Depression Rating Scale 17 (HAM-D17) scores, and (2) odds ratio of treatment response. The mean values and standard deviations of HAM-D17 scores before and after intervention were recorded for both sertraline and placebo groups. The mean difference in HAM-D17 score was calculated using the formula, m_{pre}-m_{post}, where m_{pre} is the mean score at baseline and m_{post} is the mean score after intervention. Pooled standard deviations of the standard mean difference were calculated using the formula:

$$\sqrt{\frac{[(n-1)x\ SD_{pre}] + [(n-1)x\ SD_{post}]}{(2_n + 2)}}$$

where SD_{pre} and SD_{post} are the standard deviation at baseline and at the end of treatment [12]. The odds ratio of treatment response was derived by pooling the actual number of patients who had a 50% drop in HAM-D17 scores at the end of treatment in studies that reported the said outcome [15,19]. In assessing quality of life as an outcome measure, weighted standardized mean difference (SMD) was used to establish the magnitude of effect size between the treatment and control groups. The mean differences, SMD, pooled standard deviations, and odds ratio were analyzed using Review Manager version 5.3. All *p*-values were two-tailed, and *p*-values < 0.05 were considered as statistically significant. The degree of heterogeneity was assessed using the I^2 statistic.

5. Results

A total of 91 references were identified after searching through electronic databases, and one additional record after screening through reference lists of review articles. After removal of duplicates, 71 records were screened, 54 of which were excluded after reading the titles and abstracts. A total of 17 full-text articles were evaluated for eligibility for inclusion. Fig. 1 shows the study flow diagram.

Four studies were considered eligible for this review. Table 1 shows the characteristics of included studies. Three of the studies compared sertraline with placebo [19–21]. The study by Ansari et al. randomized patients to a treatment arm which received sertraline and a control arm which did not receive any treatment [18].

The studies included participants 18 years and above with a history of TBI and were diagnosed with depression. Three studies used the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria in establishing the diagnosis of depression [19–21], while one study used the Patient Health Questionnaire-9 (PHQ-9) [18].

The duration of injury varied across all the trials included. Three studies reported duration as mean ± SD. In Lee et al, the duration of injury for participants randomized to sertraline and placebo groups was 31.9 ± 5.8 days and 30.0 ± 6.5 days respectively. The mean duration of injury in Ashman et al was 17.7 ± 13.7 years, while that in Fann et al was 4.6 ± 2.8 months. In Ansari et al., majority of the participants had the injury for more than 6 months (46.3%)

Only three studies provided information on the severity of TBI. Majority of participants in Ashman et al were classified to have moderate TBI (38.7%), while those in Fann et al and Ansari et al. were classified to have mild TBI (46.7% and 53.4% respectively). Lee et al mentioned mild to moderate TBI in their inclusion criteria, but did not provide any information regarding the number or percentages of patients under each severity classification.

Three of the four trials used a starting dose of sertraline 25 mg/day with protocols for dose titration [19–21]. Fann et al and Ashman et al titrated the sertraline dose after one week, then every two weeks based on clinical response and tolerability until a maximum dose of 200 mg/

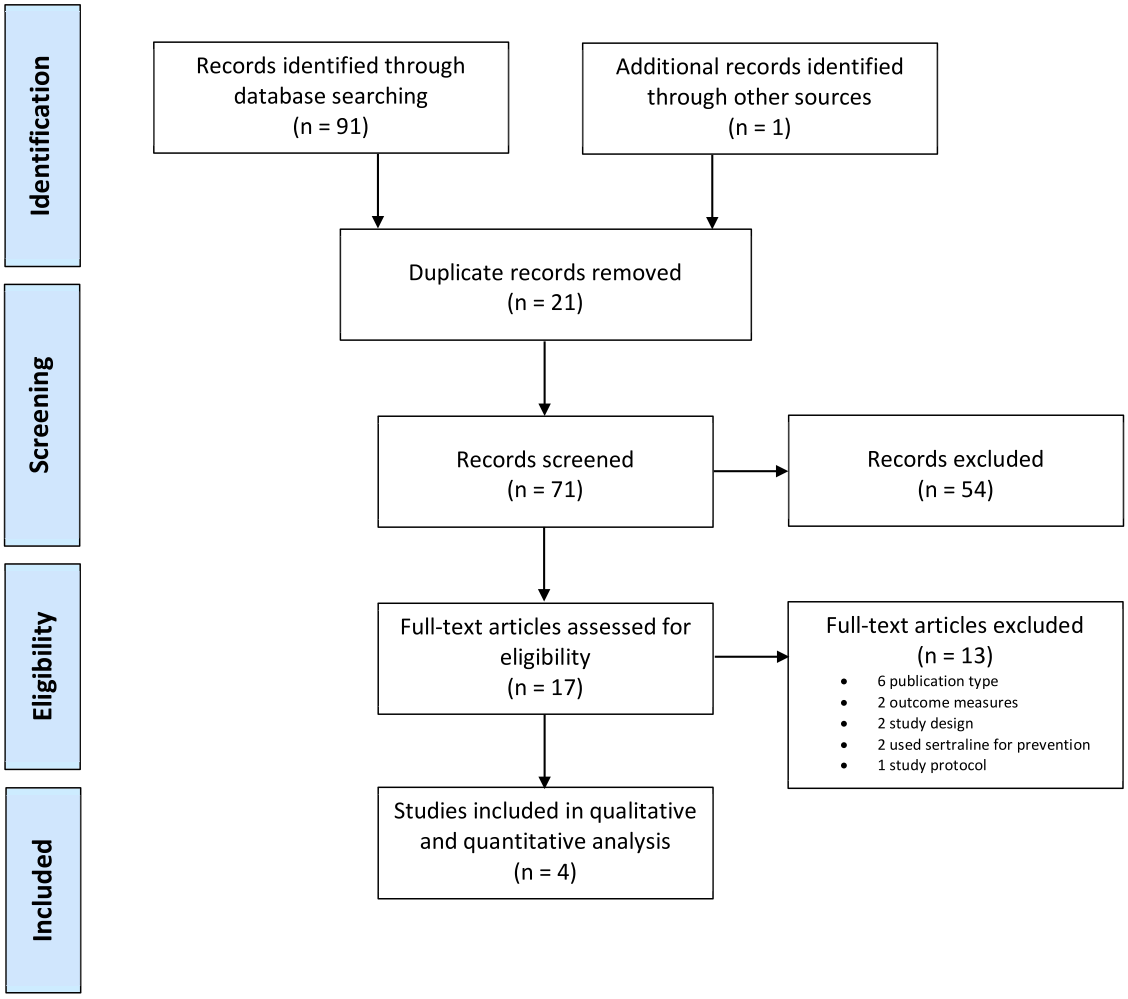

Fig. 1. PRISMA Study Flow Diagram.

day was reached. Lee et al increased the sertraline dose by 25 mg every two days until a maximum of 100 mg/day was reached. The trial by Ansari et al. used a sertraline dose of 50 mg/day for the whole duration of the study.

5.1. Outcome measures

Three RCTs used HAM-D17 as primary efficacy outcome measure [19–21]. HAM-D17 is a 17-item, multidimensional, clinician-rated scale designed to measure the severity of symptoms in patients diagnosed with depression. The scale has been reported to have a high validity and reliability [22]. A higher score in HAM-D17 signifies a greater degree of disease severity. Fann et al and Ashman et al reported Maier and Philipp Severity Subscale score to examine the core symptoms of depression. The Maier subscale specifically measures the following HAM-D17 items: 1 (depressed mood), 2 (feelings of guilt), 7 (work and activities), 9 (agitation), 10 (anxiety/psychic), 11 (anxiety – somatic), 14 (genital symptoms). Fann et al and Ashman et al also reported the percentage of patients who were able to achieve treatment response.

Ansari et al. used a validated Hindi version of PHQ-9 as a depression scale for diagnosis, and measuring treatment efficacy. The PHQ-9 is a brief, self-administered questionnaire that assesses the presence of major depressive disorder using a modified DSM-IV criteria [23].

The trials included in this review used varied tools in assessing the quality of life among patients suffering from post-TBI depression. Fann et al used the Medical Outcome Study Short-Form 36 (SF-36) to assess quality of life as a secondary outcome measure. It consists of eight specific domains and is considered to be the most widely used measure of quality of life in patients with TBI [24]. Ansari et al. made use of the Hindi version of WHO Quality of Life scale (WHOQOL-BREF) to measure quality of life. WHOQOL-BREF is a 26-item self-report questionnaire with 24 items representing four domains namely, (1) physical health, (2) psychological health, (3) social relationships, and (4) environment [25]. Ashman et al used the single-item, Likert-type Life-3 QOL scale where a higher score correlated with a better subjective quality of life [26]. Lee et al used the Korean version of the SmithKline Beecham 'Quality of Life' Scale (SBQoL), a 23-item, self-reported scale with scores that are positively correlated with the patient's subjective quality of life. The scales utilized by the included studies have been used in patients with TBI, and have been reported to exhibit reasonable validity, reliability, and responsiveness [27].

5.2. Excluded studies

A total of 13 studies were excluded after reading the full text. Six references were review articles, two were excluded due to study design (open-label, prospective), two were excluded due to different outcome measure (cognition), and two were excluded due to methodology (sertraline used as a preventive intervention rather than treatment). One reference was excluded from this review because it was trial protocol.

Table 1
Characteristics of Included Studies.

Study Name	Total no.	Study Duration (weeks)	Age (years)	Sex	Duration of TBI[a]	TBI severity	Depression Criteria	Baseline depression score	Outcome Measure of Depression	Outcome Measure of Quality of Life
Ansari 2017	80	24	18-24 years: 35% 25-34 years: 27.5% 35-44 years: 16.25% 45-65 years: 15% 55-64 years: 5% > 65% years: 1.25%	M: 80 F: 0	< 3 months: 30% 3-6 months: 23.8% > 6 months: 46.3%	Mild: 53.4% Moderate: 46.3%	PHQ-9[b]	PHQ-9 Sertraline: 36.9 ± 12.9 Control: 36.9 ± 12.9	Post-treatment PHQ-9 score	Pre- and post-treatment WHOQOL-BREF[f] score
Ashman 2009	52	10	49.1 ± 10.9	M: 30 F: 22	17.7 ± 13.7 years	Mild: 35.5% Moderate: 38.7% Severe: 25.8%	DSM-IV[c] HAM-D17[d] score of at least 18	HAM-D17 Sertraline: 27.5 ± 7.1 Placebo: 25.2 ± 8.0	Post-treatment HAM-D17, Maier subscale, treatment response	Pre- and post-treatment Life-3 score
Fann 2017	62	12	Sertraline: 38.0 ± 12.3 Placebo: 36.9 ± 12.9	M: 47 F: 15	4.6 ± 2.8 months	Mild: 46.7% Moderate: 21% Severe:32.2%	DSM-IV HAM-D17 score of at least 15	HAM-D17 Sertraline: 23.1 ± 5.3 Placebo:22.7 ± 4.8	Post-treatment HAM-D17, Maier subscale	Pre- and post-treatment SF-36[g] score
Lee 2005	30	4	Sertraline: 33.6 ± 12.3 Placebo: 35.5 ± 7.2	M: 24 F: 6	Sertraline: 31.9 ± 5.8 days Placebo: 30.0 ± 6.5 days	Not available	DSM-IV BDI[e] score > 18	Not available	Post-treatment HAM-D17	Pre- and post-treatment SBQoL[h] score

[a] Traumatic Brain Injury.
[b] Patient Health Questionnaire-9.
[c] Diagnostic & Statistic Manual of Mental Disorders-IV.
[d] Hamilton Depression Rating Scale-17.
[e] Beck Depression Inventory.
[f] World Health Organization Quality of Life – BREF Scale.
[g] Medical Outcome Study Short Form – 36.
[h] SmithKline Beecham Quality of Life Scale.

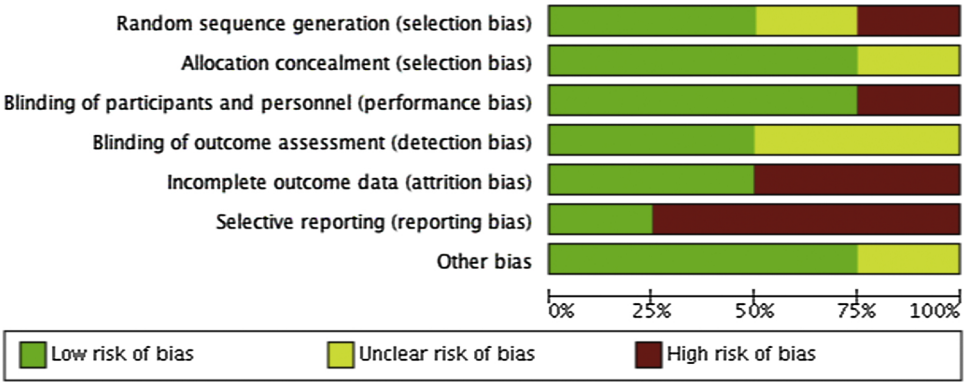

Fig. 2. Risk of Bias Graph.

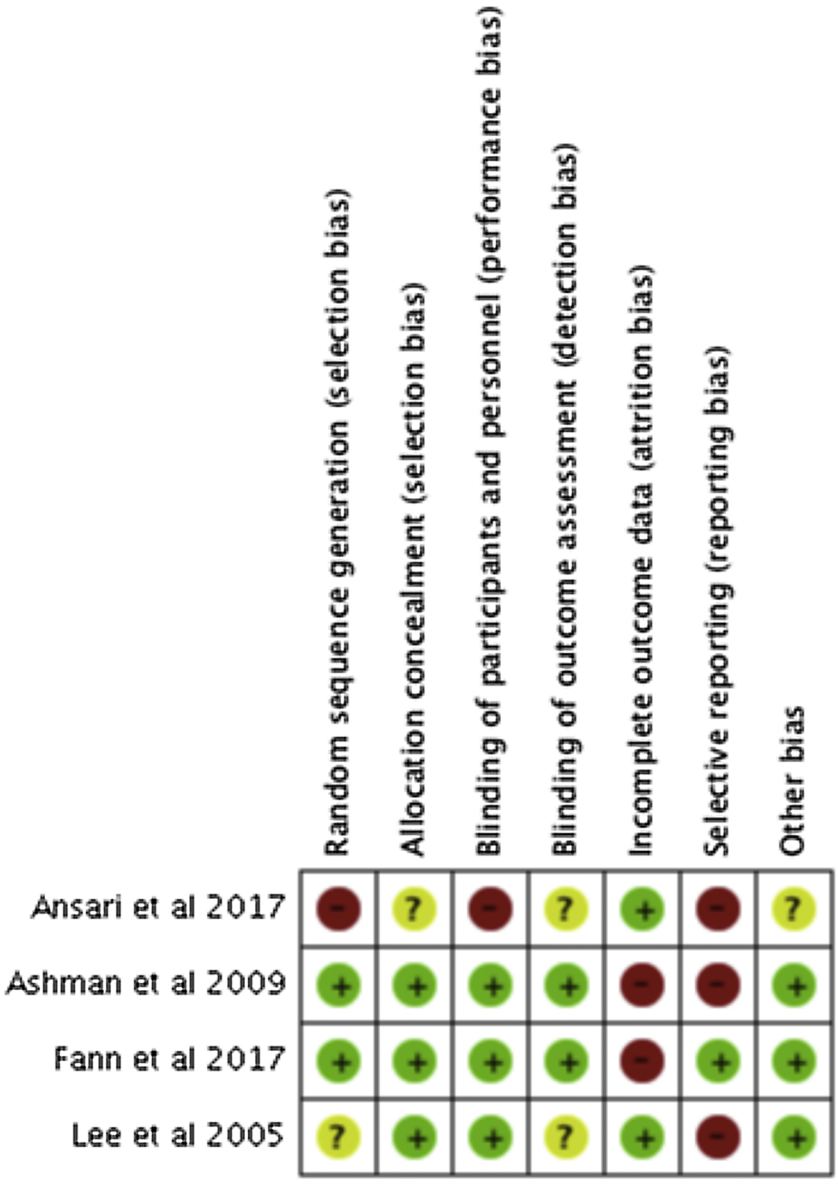

Fig. 3. Risk of Bias Summary.

6. Risk of bias in included studies

The result of risk of bias assessment for the studies included in this review are illustrated in Figs. 2 and 3.

6.1. Selection bias

Ashman et al and Fann et al were considered to have a low risk of bias because the two studies provided adequate protocols for random sequence generation and allocation concealment. Lee et al reported methods on allocation concealment but did not mention any information regarding randomization, thus the risk of bias was considered unclear. Ansari et al. did not provide any information on the said parameters, and was therefore judged to have a high risk of bias.

6.2. Performance and detection bias

Ashman et al and Fann et al reported adequate methods for blinding participants, personnel, and outcome assessors. Lee et al reported sufficient data on participant blinding but did not provide enough information regarding blinding of outcome assessors. The said study was considered to have an unclear risk of bias. In the study by Ansari et al., there was not enough information regarding blinding of outcome assessors. However, since the design utilized a control arm where subjects did not receive any treatment, the overall risk was considered high.

6.3. Attrition bias

In Lee et al, all participants randomized to treatment groups completed the study, thus it was judged to have a low risk of attrition bias. In Ashman et al, only 41/52 eligible participants completed the study (20.9% attrition) and was deemed high risk. In this study, three participants did not complete the trial due to clinical reasons while eight participants did not comply with the trial protocol. In the study by Ansari et al., 80/89 participants completed the study (10.1% attrition) and was adjudicated as low risk. The study did not provide any information regarding reasons for non-completion of the nine patients who dropped out from the trial. In Fann et al, only 21/31 participants in the sertraline group and 28/31 participants in the placebo group completed the study (20.9% attrition), thus classifying it as high risk.

6.4. Reporting bias

Lee et al used a case report form to record all adverse events that occurred during the study. However, in the published article, only the 'autonomic' aspects of adverse events were reported. The study did not provide information on adverse events that did not reach statistical significance, thus it was adjudicated as high risk. Ashman et al and Ansari et al. were also classified as high risk for reporting bias because the two studies did not present the adverse events. The study by Fann et al provided detailed descriptions of all outcome measures and adverse events, and was thus judged to have a low risk of reporting bias.

7. Effects of interventions

7.1. Post-TBI depression

Of the included trials, three studies qualified for the quantitative analysis of the effects of sertraline versus placebo in treating post-TBI depression with HAM-D17 score as the common outcome measure. One RCT reported the scores after four weeks of treatment [21], another RCT reported scores after 10 weeks [19], and one RCT reported scores at weeks 1,3,6,8,10, and 12 [20]. Using random effects model, the analysis showed that there is no statistically significant mean difference in the change in HAM-D17 scores of patients treated with sertraline compared to those treated with placebo (MD = 2.63, 95% CI [-1.32,6.57], p = 0.19). There was significant heterogeneity in the included studies with an I^2 of 95% (p < 0.00001). (see Fig. 4)

A subgroup analysis comparing studies with evaluation of depressive symptoms after 10 weeks of treatment was conducted. The analysis showed that there is no statistically significant mean difference in the change in HAM-D17 scores at ten weeks in patients treated with sertraline compared to those treated with placebo (MD = 1.27, 95% CI [-5.59, 8.13], p = 0.72). Of note, the degree of heterogeneity remained significantly high even after removing the four-week trial of Lee et al from the analysis (I^2 = 98%, p < 0.00001). (see Fig. 4)

A pooled analysis of the mean difference in Maier subscale scores was also conducted. As shown in Fig. 3, there is no statistically significant mean difference in the change in Maier subscale score between sertraline and placebo among patients with post-TBI depression (MD = 0.88, 95% CI [-2.26, 4.01], p = 0.58). A significant degree of heterogeneity was found in the two studies analyzed (I^2 = 95%, p < 0.00001).

Two placebo-controlled trials reported the number and percentage of patients who were considered as treatment responders. Random effects meta-analysis showed that there is no significant difference in the odds of treatment response between sertraline and placebo among patients with post-TBI depression (OR = 1.04, 95% CI [0.13, 8.43], p = 0.97). The two studies showed a high degree of heterogeneity with an I^2 of 84%. (see Fig. 5)

The study by Ansari et al., which included 80 patients who completed a 24-week treatment protocol, measured the efficacy of sertraline in treating post-TBI depression by comparing the pre- and post-treatment PHQ-9 scores. This study reported a statistically significant improvement in depressive symptoms among patients treated with sertraline compared to those who did not receive any treatment (pre-treatment PHQ-9 score 14.88 ± 3.603 vs. post-treatment PHQ-9 score 5.33 ± 2.987, p = 0.04) [18].

7.2. Quality of life

The four studies assessed quality of life in the sertraline and control groups, and provided mean scores ± SD on different QoL scales. Overall, the random effects meta-analysis showed that there is no significant difference in the change in QoL scale scores between the sertraline and control groups (SMD = -1.52, 95% CI [-5.65, 2.61], p = 0.47). The four studies exhibited a high degree of heterogeneity with an I2 of 99% (p < 0.00001). (see Fig. 6)

7.3. Adverse events

Only two of the four studies reported adverse events. Of the 26 adverse effects noted in Fann 2017, three were found to be 10% more prevalent in the sertraline group compared to the placebo group (i.e., flatulence/gas, agitation/restlessness, and decreased libido or sexual interest). Of note, these reported adverse effects did not reach statistical significance between the two groups. In Lee et al, the only main adverse effect that was reported to have statistical significance was 'autonomic' aspects (7/10 participants, p = 0.45). This broad classification encompassed nausea/vomiting, diarrhea, constipation, palpitation and sweating. Ashman et al and Ansari et al. did not provide information regarding adverse events in any of their treatment arms.

8. Discussion

The high incidence of TBI and post-TBI depression underscores the need to investigate on effective strategies to decrease the disease burden. The presence of depression following TBI correlates not only with an unfavorable QOL but with longer length of stay in the intensive care unit (ICU) and more adverse discharge outcomes, further necessitating the need for its recognition and prompt management. [28,29] In contrast to previous reviews on pharmacologic treatment of

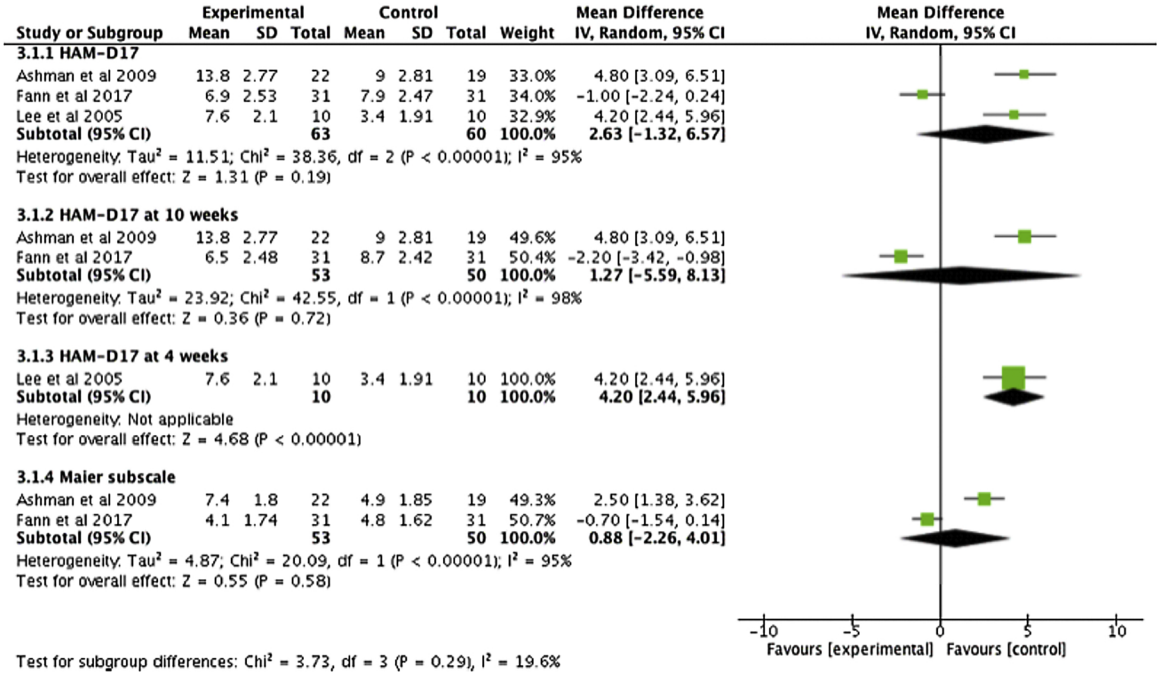

Fig. 4. Mean difference in the change in Hamilton Depression Rating (HAM-D17) and Maier subscale score between sertraline and placebo with subgroup analysis for mean difference in HAM-D17 scores at 10 weeks of treatment.

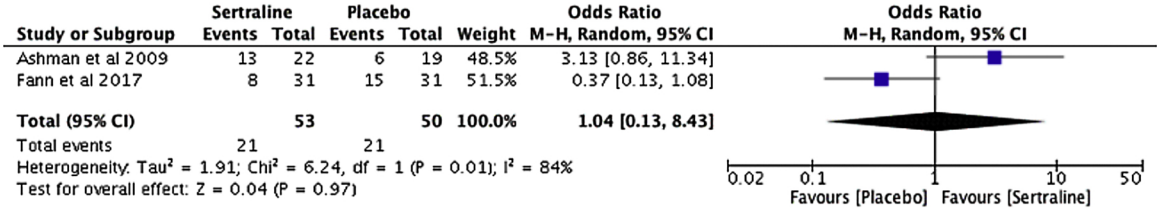

Fig. 5. Odds ratio of treatment response among patients with post-traumatic brain injury (post-TBI) depression treated with sertraline vs. placebo.

depression following traumatic brain injury, this study specifically looked into the possible effects of sertraline on the overall and core symptoms of depression, and its impact on the quality of life of patients with post-TBI depression [12,30,31].

The pooled analysis revealed that treatment with sertraline does not significantly reduce the multidimensional and core symptoms of depression. This finding did not change even after doing a subgroup analysis to control for treatment duration. This study also showed that the likelihood of treatment response with sertraline does not significantly differ with that of placebo. This finding bears consistency with the more recent reviews on the role of pharmacologic treatment, particularly SSRI in the treatment of post-TBI depression. [30,31]

There are several factors that need to be considered in interpreting the presented data. The paucity of controlled studies limits the robustness of the meta-analysis. In addition, the small sample sizes of included RCTs and the high number of dropouts in two of the included studies poses limitations in interpreting the pooled treatment effects of sertraline.

The clinical effects of sertraline varied across the studies included in this review. The high degree of heterogeneity of the studies included may be attributed to differences in the diagnostic criteria used to diagnose depression, and the scales used to assess treatment outcomes. There is considerable variability in the reported prevalence and levels of depression with the use of clinician-administered questionnaires compared to self-report scales [5]. This emphasizes the need to establish uniform criteria for depression and the use of universally accepted scales to assess its severity. The studies also displayed variability in terms of time since injury, severity of injury, and time points for assessment of treatment response, which altogether hampers the ability of the pooled analysis to determine the definitive efficacy of sertraline in treating post-TBI depression.

Depression is a multidimensional disease that can be affected by both biomedical and psychosocial factors. In addition, other neuropsychiatric sequelae of TBI such as impairments in cognition, other

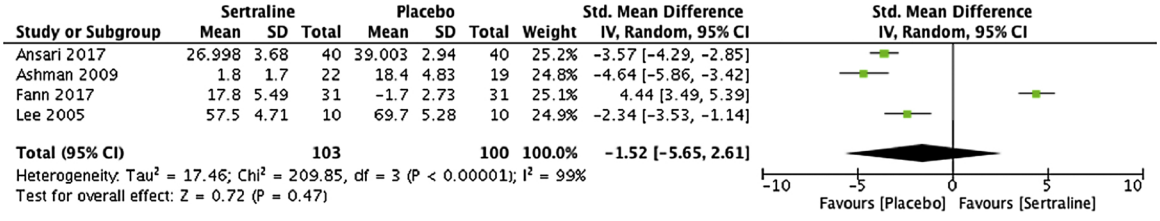

Fig. 6. Pooled effect size difference in quality of life among patients with post-TBI depression treated with sertraline vs. placebo.

mood disorders, and functional decline may have a bidirectional association with depression [4,5,7,32,33]. With these in mind, it is important to investigate the treatment effects of sertraline in these neuropsychiatric domains in order to fully determine the extent of sertraline's therapeutic potential in post-TBI depression. Furthermore, the treatment of depression in the real world setting necessitates a multidisciplinary approach that often combines pharmacologic and non-pharmacologic interventions (i.e., psychotherapy). As such, determination of the therapeutic effects of sertraline should also include its clinical efficacy in conjunction with other modes of treatment. At present, there are no identified studies that utilize combined drug and psychotherapeutic interventions in managing post-TBI depression.

The overall effect size for the pooled analysis also indicated that treatment with sertraline does not significantly affect quality of life in patients with post-TBI depression when quantitatively measured using validated scales. For reasons stated earlier, the heterogeneity of studies and the variability in QoL scales used pose limitations in the interpretation of the pooled effect size. Additionally, some of the scales only assessed overall quality of life but not its specific domains and/or determinants. As for the treatment safety in the post-TBI population, it is not possible to draw firm conclusions due to incomplete data on adverse events from the studies included.

9. Conclusions

The pooled evidence from four randomized controlled trials showed that sertraline at a dose of 25–200 mg/day does not significantly improve the multidimensional, as well as core depressive symptoms in patients with existing post-TBI depression when quantitatively assessed using validated rating scales. The limited evidence also showed that sertraline is no more beneficial than placebo in terms of likelihood of treatment response, and in the improvement in the overall quality of life of patients with post-TBI depression. There is also insufficient evidence regarding its safety and tolerability in this subset of patients. Further research utilizing standardized diagnostic criteria for depression, widely accepted scales, and similar treatment duration should be undertaken to determine the definitive efficacy of sertraline in treating post-TBI depression. The role of sertraline in other neuropsychological sequelae of TBI, as well as in the multidisciplinary approach to the treatment of depression warrants further investigation.

Disclosure

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