Highlights

- Stroke is associated with increased risk of depression and of suicidal ideation and acts.
- It is unclear if the routine use of antidepressants after a stroke decrease the cumulative prevalence of suicidal ideation.
- The results of this RCT showed that the cumulative prevalence of recurrent wish to die or self-harm affected 2.5% and 3.7% of participants treated with placebo and fluoxetine after 52 weeks of follow up.
- Routine daily treatment with fluoxetine for 26 weeks neither increases nor decreases the cumulative prevalence of suicidal/death ideation after 26 and 52 weeks.

Wishing to Die or Self-Harm after Stroke:

A Planned Secondary Analysis of the AFFINITY Randomised Controlled Trial

Running title: Post-stroke suicide ideation

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ABSTRACT

We investigated the cumulative prevalence of self-harm ideation among stroke survivors of the AFFINITY trial. We assessed these thoughts with the last item of the PHQ-9, and functional impairment with the modified Rankin Scale (mRS). Of 1221 participants (age 63.9±12.3 years, 775 men), 11 reported wishing to die or self-harm at baseline. By week 52, 36 of 1159 surviving participants had reported wishing to die or self-harm. Treatment with fluoxetine for 26 weeks did not change the prevalence of these thoughts compared with placebo. Clinically significant symptoms of depression were present in 95% of participants with recurrent self-harm thoughts.

1. Introduction

Stroke is associated with adverse health outcomes, including self-harm [1]. Strokes double the risk of suicide attempts and increase the risk of death by suicide, although the quality of available evidence is low [2]. Suicide acts are commonly preceded by suicidal thoughts, although available studies have often relied on the use of administrative data, chart reviews, or one-off assessments of suicide ideation [2]. There is also uncertainty about whether the use of antidepressants after a stroke reduces the prevalence of post-stroke suicidal thoughts.

The Assessment of Fluoxetine in Stroke Recovery (AFFINITY) trial recruited 1280 stroke survivors and followed them for 52 weeks [3]. Assessments included the collection of mental health data over a period of 52 weeks. We used these data to examine the cumulative prevalence of the expressed wish to die or self-harm, as well as the incidence of suicide attempts and completion. We also sought to clarify if, compared with placebo, the routine daily treatment with fluoxetine affected the prevalence of thoughts about death and self-harm.

2. Methods

AFFINITY was a randomised, double-blind, parallel (1:1), placebo-controlled trial of daily treatment with 20 mg of fluoxetine for 26 weeks following an acute ischaemic or haemorrhagic stroke (< 2 weeks), with an additional period of 26 weeks of follow up. Study details and neurological outcomes have been published [3]. Briefly, we randomised consenting participants to treatment with fluoxetine or placebo 2 to 15 days after an acute stroke. Inclusion required a modified Rankin Scale (mRS) score of ≥ 1. We excluded 59 of 1280 participants who did not complete the Patient Health Questionnaire (PHQ-9) at baseline. Participants were recruited between 11 January 2013 and 30 June 2019. The trial was approved by the Royal Perth Hospital Ethics Committee and registered with the Australian and New Zealand Clinical Trials Registry, ACTRN12611000774921.

We used the last item of the PHQ-9 to assess the 'wish to die or self-harm'. We considered this to be present when thoughts occurred most days during the preceding 2 weeks. Assessments took place at baseline, 4, 12, 26 and 52 weeks. Clinically significant symptoms of depression were defined by a PHQ-9 total score of ≥ 9. Treating clinicians recorded adverse events during the trial, including suicide attempts and deaths by suicide. At baseline we also collected information about participants' age (years) and sex (male/female).

3. Results

The mean age of the 1221 participants was 63.9±12.3 years and 775 (63.5%) were men. Of these, 607 were randomly assigned treatment with placebo and 614 with fluoxetine. Treatment groups were balanced for socio-demographic and clinical measures [4]. At baseline, 11 (0.9%) participants reported wishing to die or self-harm thoughts – 8 had clinically significant symptoms of depression. By week 26, 14 (2.3%) of 607 participants treated with placebo and 17 (2.8%) of 614 of those treated with fluoxetine reported wishing to die or self-harm. By the week 52 assessment, 15 (2.5%) of 607 treated with placebo and 23 (3.7%) of 614 treated with fluoxetine had acknowledged such thoughts (Figure 1, left panel) (two-sample test of proportions z=-1.28, p=0.200). The number of participants treated with placebo (n=607) and fluoxetine (n=614) who reported wishing to die or self-harm at least once (i.e., not necessarily most days of the week) during the two weeks preceding the assessment was 41 (6.7%) and 38 (6.2%) at baseline, 58 (9.6%) and 56 (9.1%) at week 4, 65 (10.7%) and 68 (11.1%) at week 12. 79 (13.0%) and 79 (12.9%) at week 26, and 85 (14.0%) and 90 (14.7%) at week 52 (Figure 1, right panel). Two-sample test of proportions showed no effect of treatment by 52 weeks (z=-0.33, p=0.744). There was one death by suicide during the trial: a man in his mid-50s died 16 weeks after randomisation. This person had denied wishing to die or self-harm at baseline and again at week 4, and had a total PHQ-9 score of 4 and 8 at the respective assessments. By week 12, this person had been lost to follow up. This participant had been assigned treatment with placebo. No other suicide attempts were recorded during the trial.

FIGURE 1

Thirty-six (94.7%) of the 38 participants who reported wishing to die or self-harm displayed clinically significant symptoms of depression during the study ($z=7.51$, $p<0.001$). Among the 175 participants for whom these ideas were not recurrent, 123 (70.3%) had clinically significant symptoms of depression ($z=9.90$, $p<0.001$).

4. Discussion

These results show that about 3% of stroke survivors acknowledge wishing to die or self-harm during the year following a stroke. As many as 14% of participants reported such thoughts at least once, albeit not persistently. Clinically significant symptoms of depression were associated with the wish to die or self-harm, and routine daily treatment with fluoxetine for 26 weeks had no effect on the cumulative prevalence of suicidal ideation.

Participants who completed the PHQ-9 had less severe and disabling neurological deficits than those who had not [4], so our results apply predominantly to stroke survivors with mild to moderate disability. This, alongside the exclusion of people with history of past suicide attempts, may have led to the recruitment of a sample less prone to developing self-harm ideation. We also acknowledge that our approach to the assessment of 'suicidal thoughts' relied on a single PHQ-9 item that covers only the two weeks before each assessment. Available evidence indicates that self-rating for suicide thoughts yields similar responses when compared to clinical interviews [5].

5. Conclusion

The wish to die or self-harm affects a progressively increasing number of post-stroke survivors over a period of 1 year. Clinically significant symptoms of depression are closely associated with self-

harm ideation and their presence should trigger the assessment of suicidal thoughts. Routine daily treatment with fluoxetine neither increases nor decreases the risk of post-stroke recurring suicidal thoughts. Management should rely on the appropriate education of patients and carers, effective treatment of depression, and restriction of access to means of self-harm for those deemed high risk.

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FIGURE LEGEND

Figure 1. The bars indicate the cumulative proportion of stroke survivors affected by death wishes or self-harm ideation according to their treatment assignment. The whiskers depict the standard error of the proportion. The left panel shows the results for participants who reported these thoughts most days during the two week preceding the assessment, and the right panel the results for participants who reported those thoughts at least once during the two weeks preceding the assessment.

Figure 1

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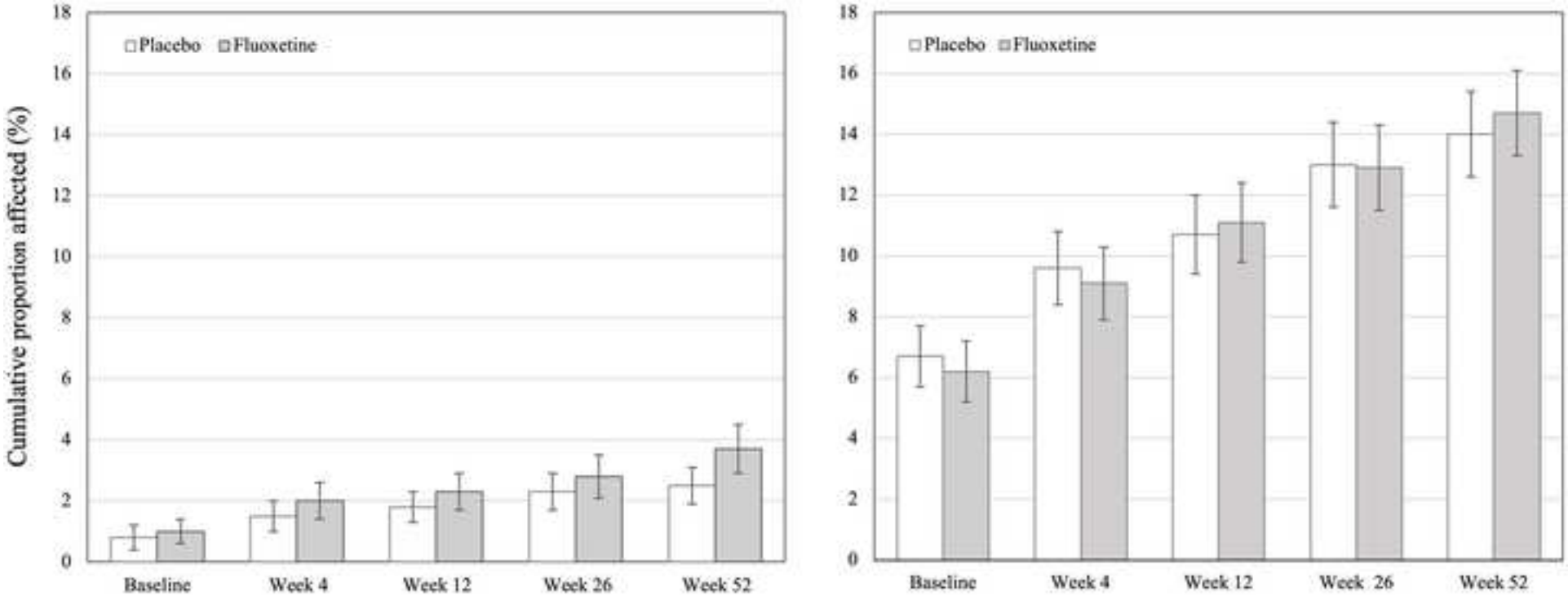

Conflict of Interest Statement:

The authors have no conflicts of interest to declare.

Ethics: The study was approved by the Royal Perth Hospital Ethics Committee, and all participating sites received ethics committee and institutional approval from their respective boards. All participants provided written informed consent.