Secondary Prevention of Chronic PTSD by Early and Short-Term Administration of Escitalopram:

A Prospective Randomized, Placebo-Controlled, Double-Blind Trial

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ABSTRACT

Objective: Prospective studies have not identified a viable pharmacologic strategy for secondary prevention of posttraumatic stress disorder (PTSD). The authors examined whether preventive intervention via early and short-term administration of a selective serotonin reuptake inhibitor (SSRI), within 1 month of exposure to a traumatic event (before diagnosis of PTSD could be made), may reduce the severity of PTSD symptoms according to *DSM-IV* at 13 months' follow-up.

Methods: Over 25,000 screening calls to patients referred to an emergency department for a traumatic event performed between June 2006 and December 2008 yielded 353 participants who were recruited within the month following a traumatic event . Participants were randomly assigned in a double-blind design to escitalopram (n = 176) or placebo (n = 177). The per-protocol analysis comprised 198 participants (escitalopram, n = 102; placebo, n = 96) who received treatment for 12 to 24 weeks and were available for follow-up at week 56.

Results: The primary outcome measure, the Clinician Administered PTSD Scale (CAPS), revealed no prevention effect. However, a secondary outcome, the Pittsburgh Sleep Quality Inventory (PSQI), showed better results for the SSRI group than for the placebo group. For a subset of participants who experienced intentional trauma (missile attacks, rape, or physical assault; n = 50), the prevention effect was found on both primary and secondary measures (CAPS, PSQI and measures of depression and global illness severity).

Conclusions: Early and short-term administration of escitalopram was not shown to prevent PTSD, although it did improve sleep quality. In a subgroup of participants who experienced intentional trauma, however, this early-treatment approach may be effective as secondary prevention. This large study is the first to investigate the preventive effect of early administration of escitalopram on PTSD. It highlights the relevance of the type of trauma (intentional vs unintentional) to the outcome.

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Posttraumatic stress disorder (PTSD) is a debilitating condition that affects 10%–20% of those who are exposed to a traumatic event.[1] Due to its chronic and disabling course, PTSD is highly detrimental to the quality of life and productivity of those afflicted and their families.[2] Unlike most psychiatric disorders, PTSD is typically triggered by a remarkable event. This affords a window of opportunity for secondary prevention, comparable to that available in the "golden hours" for conditions such as ischemic stroke and myocardial infarction.[3]

Researchers have studied treatment of PTSD using psychological approaches such as debriefing, modified prolonged exposure,[4,5] and cognitive therapy.[4] Debriefing may be beneficial for some patients,[6] yet may actually increase the likelihood of developing PTSD for others, such as for individuals with high anxiety levels.[7] More focus and support are currently assigned to prolonged exposure and cognitive therapy.[4,5] Pharmacologic treatment protocols to prevent PTSD have generally not been successful. In some cases, the use of a benzodiazepine has been found to be associated with an increased prevalence of PTSD, both in humans[8] and in an animal model.[9] While an earlier pilot study[10] supported the beneficial role of early propranolol administration in preventing PTSD, a later placebo-controlled trial[11] failed to demonstrate a significant treatment effect. Some evidence based on a retrospective case review study[12] suggests that morphine during early resuscitation and trauma care of US soldiers was significantly associated with a lower risk of PTSD after injury. In a small retrospective study, [13] the dose of morphine was found to positively correlate with the amount of change in PTSD symptoms from admission to 6-month follow-up among children with burns. Naturalistic studies[14–16] and a small pilot study[17] suggest preventive effects of hydrocortisone.

PTSD has been linked to the hippocampus.[18] Selective serotonin reuptake inhibitors (SSRIs) stimulate hippocampal neurogenesis.[19] Indeed, early administration (1 day after exposure) of the SSRI sertraline was associated with a significant decrease in PTSD-like behavior (extreme behavioral response) in rats.[20] Based on this finding, a pilot retrospective study[21] examined whether early administration of sertraline (1 to 3 months after an earthquake) would change the trajectory of PTSD in a group of 56 survivors. In that study, those who received sertraline exhibited fewer signs and symptoms of PTSD at 6 to 9 months' follow-up than did those who were not treated. However, 2 small studies that compared patients who received escitalopram versus placebo (n = 19 and 17, respectively, in 1 study[5] and n = 12 and 17, respectively, in the second,[22]) showed no benefit of escitalopram at the 9-month or 13-month follow-up.

The current randomized, double-blind, placebo-controlled trial was designed to examine, in a sufficiently powered study, whether early SSRI administration (within the first month after a traumatic event) would result, at 13 months' follow-up, in reduced severity of PTSD symptoms. Since this is a secondary prevention study, the effect sizes that are expected are different from (ie, smaller than) treatment studies.[23]

METHODS

Study Design and Participants

Over 25,000 recruiting phone calls were made between June 2006 and December 2008 to individuals who were either self-referred or referred by medical personnel to a hospital emergency department for a traumatic event in 1 of 5 medical centers in Israel or 1 medical center in Cape Town, South Africa (Figure 1). A total of 353 participants from 5 medical centers distributed across Israel and 1 center in South Africa were recruited (333 from Israel and 20 from South Africa). Enrolled participants were randomly assigned to treatment and placebo arms.

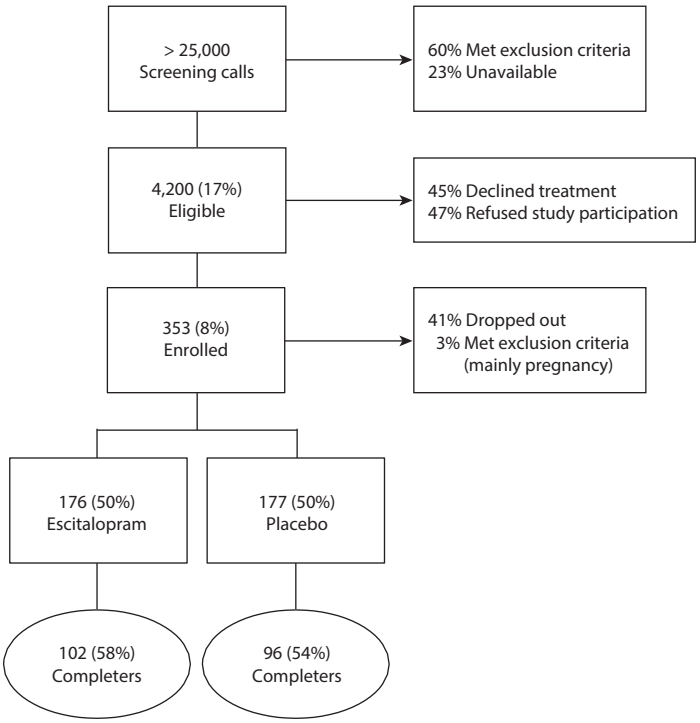
The local institutional review board of each participating medical center approved the study. Telephone screening for study eligibility was conducted after individuals gave verbal consent to answer a few questions regarding their state following admission to the emergency department. During the screening visit, all persons who were recruited to the study provided written informed consent. The study was registered at ClinicalTrials.gov (identifier: NCT00300313).

Inclusion criteria required that participants had undergone a traumatic event within the month prior to enrollment (before diagnosis of PTSD could be made), were between the ages of 18 and 65 years, and met at least 2 *DSM-IV* criteria for acute stress disorder, namely, re-experiencing and hyperarousal. Study exclusion criteria were serious injury (Abbreviated Injury Scale score ≥ 3)[24]; a diagnosis of *DSM-IV* bipolar disorder, schizophrenia, or personality disorder; a history of alcohol or drug abuse, mental retardation, or dementia; having significant suicide risk or a past serious suicide attempt, as evaluated by the Mini-International Neuropsychiatric Interview (MINI)[25]; the intake of psychiatric medications, such as medications for depression, psychosis, or relapse prevention (mood stabilizers); participation in psychotherapy; electroconvulsive treatment within the previous year; sensitivity to citalopram or escitalopram; any major physical illness; being pregnant or lactating; and being of childbearing age and not using contraceptives.

Clinical Points

- Posttraumatic stress disorder (PTSD) is unique among other psychiatric disorders since, in most cases, the timing of the onset is clear in coinciding with the trauma.
- Learning from other medical conditions (eg, cerebrovascular accident, myocardial infarction), it is clear that what is done in the first few hours and the first days (the "golden hours" or window of opportunity) is critical to the trajectory of the disorder in both directions—either significant and even dramatic improvement or else further deterioration and exacerbation.
- Early and brief administration of a selective serotonin reuptake inhibitor in the first month before the diagnosis of PTSD could be made, and continuing for 2 to 4 months is safe and may favorably alter the trajectory of PTSD (as measured a year after exposure), especially in those who were exposed to intentional trauma.

Figure 1. CONSORT Diagram of the Recruitment Process



Randomization and Masking

Participants who met study criteria were assigned to either escitalopram or placebo in a randomized, double-blind procedure. The randomization was conducted by Trialog Clinical Trials, Ltd, an independent company that was not involved in the study except for the randomization procedure. Each center received the medications (escitalopram and placebo) directly from Trialog with participant numbers marked on them.

Procedure

The study was divided into 2 phases: a short treatment phase (12 to 24 weeks, starting within the first 30 days following the traumatic event) and a long no-treatment follow-up phase, which ended 13 months after the event (at week 56). Week 56 (13 months) was chosen to avoid effects stemming from the first anniversary of the traumatic event. Participants received their first medication within the first 30 days following the traumatic event. During the first 4 weeks of treatment, participants were instructed to take 1 daily capsule of 10-mg escitalopram or placebo and were titrated gradually up to 20 mg. After 4 weeks of drug adjustment, all participants received the maximal dosage (20 mg) for up to 24 weeks (but not less than 12 weeks). Medication intake and psychiatric status were monitored every 2 to 4 weeks by trained psychiatrists. No-treatment follow-up continued from completion of medication until week 56, about 13 months after the traumatic event. No additional trauma (that would fit PTSD criterion A in *DSM-IV-TR*) was recorded for any of the participants during the study follow-up.

Outcome Measures

The primary measure assessing PTSD prevention was the difference, from baseline to follow-up, in each participant's score on the Clinician Administered PTSD Scale (CAPS).[26] The CAPS includes 17 interviewer-rated items that cover the core symptoms of PTSD according to the *DSM-IV* criteria and rates the frequency and the intensity of the symptoms on a 5-point scale (0–4).

Secondary measures included the following: (*a*) the 17-item self-report PTSD Symptoms Scale (PSS-SR) that measures *DSM-IV* diagnostic criteria rated by frequency of occurrence[27]; (*b*) the Pittsburgh Sleep Quality Index (PSQI),[28] which records sleep disturbances, sleep quality, and sleep duration and habits; (*c*) the 10-item Montgomery-Asberg Depression Rating Scale (MADRS),[29] rated by clinicians; (*d*) the Clinical Global Impressions Severity of Illness scale (CGI-S) and Improvement scale (CGI-I),[30] rated by clinicians; and (*e*) the self-report visual analog scale (VAS) for depression and anxiety.[31]

The raters in the study were psychiatrists who were trained in attaining research measurements. Interrater reliability for the different scales was between 0.6 and 0.7. The data were monitored by a contract research organization (PFC Pharma Focus Israel) to ensure that none of the information on the questionnaires was missing.

Statistical Analysis

As per the protocol, the study was designed to examine secondary prevention; specifically, to test the hypothesis that participants treated with escitalopram for 12 to 24 weeks would exhibit significantly less severe PTSD symptomatology at 56 weeks. A power analysis that was conducted prior to the study's initiation, assuming a mean reduction of approximately 15 points in CAPS (SD = 25 points), indicated that 100 participants would be needed to complete each study arm. The hypothesis was tested using analysis of covariance to compare change from baseline to week 56 among those treated for 12 to 24 weeks with placebo or active treatment, while controlling for baseline scores on primary and secondary outcome measures, age, sex, socioeconomic status (SES), and medical center. Effect size (Cohen *d*) was derived from eta squared:

$$(d = 2\sqrt{\frac{\eta^2}{1-\eta^2}}).$$

Analysis was first conducted on all types of trauma together (n = 198). The course and outcome of PTSD among people who experience intentional trauma (such as a terror attack or physical or sexual assault) have been shown to differ from the course and outcome for persons who experience traumatic events that were unintended (such as car accidents and natural disasters).[32,33] A separate analysis included only individuals who experienced intentional trauma (n = 50).

Safety data were collected for all persons who were randomly assigned to one of the study arms, irrespective of the length of treatment or availability for follow-up.

RESULTS

Participants who completed the study (ie, the per-protocol sample, n = 198) differed from those who did not (n = 155) in sex distribution: 62.3% of the men were completers compared to only 50.8% of the women (odds ratio = 1.60, $P = .029$). No statistically significant differences ($P < .16$) were observed between the study arms regarding age, SES, marital status, CAPS score at baseline, or type of trauma (intentional or unintentional).

Background Characteristics

Background characteristics at baseline for the escitalopram and placebo groups are presented in Table 1. No statistically significant differences were found between the groups in mean age, education, CAPS total score at baseline, and type of trauma. Regarding the latter, 74.7% of the entire cohort was in a car accident, while the rest were victims of intentional trauma such as terror attacks (Israel, n = 5), missile attacks (Israel, n = 26), and physical assault, including rape (Israel, n = 8; South Africa, n = 11). In the escitalopram group, there were significantly more men and slightly more individuals of lower SES, with near statistical significance (see Table 1). The intentional trauma group was marginally younger than the car accident group (mean [SD] age = 36.6 [12.43] vs 40.2

[12.7] years, $P = .08$) and had a slightly lower proportion of women than men (40%, [20/50] vs 52%, [77/148], $P = .14$). Notably, no differences were found in mean values for education, baseline CAPS score, and SES between those who experienced intentional or unintentional trauma.

Treatment Effect

Ninety-one percent of the participants (180/198) who completed the study underwent the full 24 weeks of treatment. The remaining 18 completers underwent at least 12 weeks of treatment. At the end of the treatment phase (12 to 24 weeks), no significant effect was observed of escitalopram compared to placebo on the outcome measures investigated (CAPS, PSS-SR, MADRS, PSQI, VAS anxiety and depression, CGI-I, and CGI-S) in an analysis that included the entire sample and in a subanalysis of participants who experienced intentional trauma (Table 2).

Table 1. Baseline Characteristics of the Escitalopram and Placebo Treatment Arms[a]

Variable	Escitalopram (n = 102)	Placebo (n = 96)	Statistics
Age, mean (SD), y	39.6 (13.2)	39.1 (12.2)	$t_{196} = 0.22$, $P = .82$
Sex			$\chi^2_1 = 5.14$, $P = .023$
Male	60 (58.8)	41 (42.7)	
Female	42 (41.2)	55 (57.3)	
Education			$\chi^2_3 = 1.99$, $P = .37$
Less than 12 years	23 (22.5)	27 (28.1)	
12 years	46 (45.1)	34 (35.4)	
More than 12 years	33 (32.4)	35 (36.5)	
Socioeconomic status			$\chi^2_2 = 5.11$, $P = .08$
Low	60 (58.8)	45 (46.9)	
Medium	31 (30.4)	30 (31.3)	
High	11 (10.8)	21 (21.9)	
Marital status			$\chi^2_2 = 0.69$, $P = .71$
Single	26 (25.5)	21 (21.9)	
Married	60 (58.8)	62 (64.6)	
Separated/divorced/ widowed	16 (15.7)	13 (13.5)	
Religiosity			$\chi^2_2 = 1.23$, $P = .54$
Observant	18 (18.8)	19 (21.8)	
Partially observant	26 (27.1)	28 (32.2)	
Nonobservant	52 (54.2)	40 (46.0)	
Event type			$\chi^2_1 = 0.33$, $P = .56$
Intentional	78 (76.5)	70 (72.9)	
Unintentional	24 (23.5)	26 (27.1)	
CAPS total score, mean (SD)	71.9 (22.1)	72.8 (21.8)	$t_{195} = 0.30$, $P = .77$

[a]Values shown as n (%) unless otherwise noted.
Abbreviation: CAPS = Clinician Administered PTSD Scale.

Secondary Prevention Effect

Table 2 presents the mean differences of outcomes for the escitalopram and placebo groups at the end of the treatment phase and at the end of follow-up. Of the 198 participants who completed follow-up, 102 (52%) were in the escitalopram and 96 (48%) in the placebo group. A significant prevention effect was observed on the PSQI ($P = .009$, effect size [ES] = 0.39, Figure 2A). Although there were no statistically significant effects for CAPS, PSS-SR, MADRS, VAS anxiety and depression, CGI-I, and CGI-S scores, modest effect sizes were found for scores on the CAPS, PSS-SR, CGI-I, and CGI-S (between 0.20 and 0.28) (Table 2). An 11% difference favoring escitalopram over placebo emerged for a mean CAPS score change from baseline to the end of follow-up (Figure 2B, Table 2). A separate analysis on sleep-related items revealed significant lower scores for the escitalopram than the placebo group at the end of the follow-up phase. These results were obtained in items related to sleep from the CAPS (item 13, $F = 3.367$, $P = .046$) and PSS (item 13, $F = 3.351$, $P = .042$), but not at the MADRS (item 4, $F = 1.553$, $P = .107$), and not in items related specifically to dreams (CAPS, item 2, $F = 1.414$, $P = .118$; PSS-SR, item 2, $F = 1.369$, $P = .121$; PSQI, item 5.8, $F = 0.389$, $P = .733$)

Among participants who had experienced intentional trauma (escitalopram, n = 24; placebo, n = 26), prevention effects with noteworthy effect size were found for scores on the CAPS (ES = 0.58, $P = .09$, Figure 2B), PSS-SR (ES = 0.78, $P = .10$), PSQI (ES = 0.59, $P = .08$, Figure 2A), MADRS (ES = 0.73, $P = .03$), and CGI-S (ES = 1.12, $P = .02$) (Table 2).

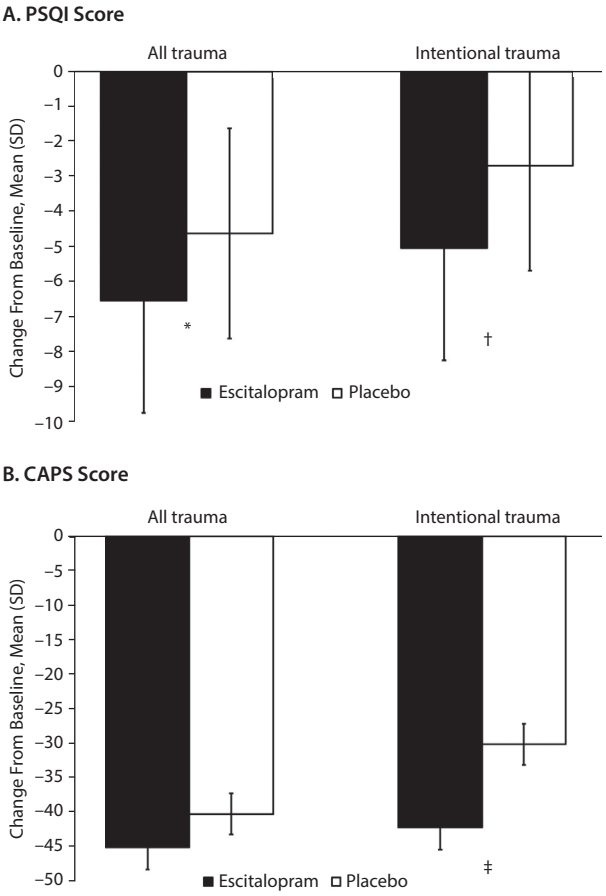
Table 3 presents adverse event data for all participants who were randomly assigned to a study arm. The 20-mg

Table 2. Mean (SE) Differences in Outcome Measures Between the Medication and Placebo Groups (ANCOVA) for Treatment and Prevention Effects[a]

	Treatment Effect[b]		Prevention Effect[c]	
Outcome Measure	Any Trauma[d]	Intentional Trauma[e]	Any Trauma[d]	Intentional Trauma[e]
CAPS	2.21 (4.02), $P = .58$; ES = 0.09	9.51 (7.03), $P = .19$; ES = 0.50	4.87 (3.71), $P = .19$; ES = 0.20	12.14 (6.99), $P = .09$; ES = 0.58
PSS-SR	0.71 (1.94), $P = .71$; ES = 0.06	4.62 (4.22), $P = .40$; ES = 0.42	2.78 (2.07), $P = .18$; ES = 0.24	8.44 (4.86), $P = .10$; ES = 0.78
PSQI	0.81 (0.76), $P = .29$; ES = 0.18	0.28 (1.38), $P = .84$; ES = 0.06	0.91 (1.91), $P = .009$; ES = 0.39	2.44 (1.35), $P = .08$; ES = 0.59
MADRS	0.64 (1.52), $P = .67$; ES = 0.06	3.41 (2.35), $P = .16$; ES = 0.53	0.66 (1.44), $P = .65$; ES = 0.06	5.63 (2.50), $P = .03$; ES = 0.73
VAS depression[f]	0.10 (0.46), $P = .82$; ES = 0.00	0.55 (0.83), $P = .51$; ES = 0.25	0.24 (0.44), $P = .59$; ES = 0.09	0.88 (0.81), $P = .29$; ES = 0.36
VAS anxiety[f]	0.22 (0.47), $P = .64$; ES = 0.09	0.84 (0.92), $P = .37$; ES = 0.34	0.52 (0.46), $P = .26$; ES = 0.18	1.18 (0.81), $P = .15$; ES = 0.48
CGI-I[g]	0.17 (0.19), $P = .37$; ES = 0.14	0.52 (0.46), $P = .27$; ES = 0.41	0.33 (0.20), $P = .10$; ES = 0.28	0.66 (0.41), $P = .12$; ES = 0.33
CGI-S[f]	–0.02 (0.21), $P = .91$; ES = 0.01	0.68 (0.34), $P = .06$; ES = 0.76	0.10 (0.22), $P = .14$; ES = 0.21	0.94 (0.36), $P = .02$; ES = 1.12

[a]ANCOVA tested for escitalopram versus placebo, controlling for baseline scores on primary and secondary outcome measures, sex, medical center, sociodemographic status, and age.
[b]24 Weeks for 91% of participants (n = 180), 12–23 weeks for the others (n = 18).
[c]Week 56.
[d]Data analyzed for participants who experienced any trauma.
[e]Data analyzed for the subgroup of participants that experienced intentional trauma.
[f]VAS and CGI-S values increase from least to most severe.
[g]CGI-I rescored to 7 (very much improved) to 1 (very much worse).
Abbreviations: ANCOVA = analysis of covariance, CAPS = Clinician Administered PTSD Scale, CGI-I = Clinical Global Impressions Improvement scale, CGI-S = Clinical Global Impressions Severity of Illness scale, ES = effect size, MADRS = Montgomery-Asberg Depression Rating Scale, PSQI = Pittsburgh Sleep Quality Index, PSS-SR = PTSD Symptom Scale–Self-Report Version, VAS = visual analog scale.

Figure 2. Mean Change From Baseline in Scores on (A) the PSQI and (B) the CAPS (analysis of covariance) for the Escitalopram and Placebo Groups at the End of Follow-Up (prevention effect) for Participants Who Experienced Any Type of Trauma (n = 198) or Intentional Trauma (n = 50)



*P = .009, ES = 0.39.
†P = .08, ES = 0.59.
‡P = .09, ES = 0.58.
Abbreviations: CAPS = Clinician Administered PTSD Scale, ES = effect size, PSQI = Pittsburgh Sleep Quality Index, PTSD = posttraumatic stress disorder.

Table 3. Number of Participants With Serious Adverse Events[a]

Event	Active (n = 176)	Placebo (n = 178)
Abdominal bleeding	0	1
Chest pain	0	1
Crohn's disease	0	1
Fracture of hand and finger (amputation of fingertip)	1	0
Diarrhea	1	0
Inflammatory pelvic disease	1	0
Menometrorrhagia	1	0
Myocardial infarction	2	0
Nephrolithiasis bilateral	0	1
Perianal abscess superficial invasion	1	0
Pneumonia	1	0
Pregnancy	1	3
Thyroidectomy	0	1
Rash	0	1
Total	**9**	**9**

[a]No patient had more than 1 serious event.

dose of escitalopram for up to 24 weeks was well tolerated. In fact, there was no difference in the total number of serious adverse events between the escitalopram and the placebo arms (9 in each).

DISCUSSION

This double-blind, placebo-controlled, random-assignment study showed that early, short-term administration of an SSRI (1) did not prevent PTSD in a general sample of individuals who experienced different types of trauma; (2) may be effective as secondary prevention for quality of sleep; and (3) led to a decrease with noteworthy effect size in PTSD severity in a subgroup of participants, namely, those who experienced intentional trauma.

This study is the first to test the secondary prevention effect of an SSRI in a large sample. In smaller studies, an effect of an SSRI vs placebo in preventing PTSD was not found.[5,22] Interestingly, the difference in CAPS score between the treatment and placebo groups found in the present study is the same as that shown in a previous study[5]: an 11% difference between escitalopram and placebo groups at 6 to 9 months' follow-up.

During the study period (2006 to 2008), the catchment area of 2 of the participating Israeli centers was exposed to missile attacks (the Second Lebanon War and Operation Cast Lead). This afforded the opportunity to analyze separately the effects of missile attacks together with other intentional traumas such as physical assault and rape. Previous studies suggested that the course and outcome of PTSD among individuals who experienced intentional trauma is different and more severe than among people who experienced any type of trauma.[32,33] In the current study, individuals who experienced intentional trauma exhibited greater benefit from the intervention than did those who experienced any trauma. Lange and colleagues[34] also reported different responses to an intervention based on the type of trauma (intentional vs non-intentional). Hence, the type of trauma should be considered when establishing protocols for early intervention.

Previous prevention studies did not assess the effect of early administration of an SSRI on sleep quality, a prominent symptom of PTSD. In the current study examining sleep quality, another benefit emerged: the escitalopram-treated group scored significantly better than the placebo group on the PSQI. This effect probably reflects alteration in the development of the disorder rather than a direct effect of escitalopram on sleep quality, as it was measured 6–9 months after escitalopram had been stopped. This effect was specific to sleep quality, as was observed in the relevant items of the 2 PTSD questionnaires (CAPS and PSS). This finding lends further support to the secondary prevention effect on sleep of early administration of escitalopram. However, no specific change in nightmares was found in this subset of participants. The effect of early administration of escitalopram on sleep should be taken into consideration when assessing the effect of early intervention on PTSD.

The findings for the entire cohort raise the question of whether an 11% difference in CAPS score (ES = 0.20) is of clinical significance. The authors debated this issue. The effect sizes that are usually employed in secondary prevention are quite small; for example, vaccines are administered to millions to prevent infection in thousands and serious complications in hundreds. Along this line, the effect size observed in the current study (0.20) should be compared to the effect size of secondary prevention and not to the effect size of a treatment. Also, the design of the study, namely the assessment of the long-term effect of SSRI intake starting during the first month post-exposure and continuing for 3 to 6 months, raises issues regarding the administration of treatment for a disorder before it materializes. In such a situation, the therapeutic effect needs to be superior to spontaneous recovery (the time effect). Moreover, since the primary outcome measure—CAPS score at 13 months post-trauma—was assessed at 6 to 9 months after the intervention was stopped, the secondary prevention effect does not appear to be a carryover of the treatment.

Thus, the authors submit that the criteria for employing secondary prevention might be different from those used for treatment and should attempt to balance potential harm with potential benefit. Criteria to be considered in determining secondary treatment (in this case, short-term administration of an SSRI) include (*a*) the clinical effect, (*b*) risk and discomfort, and (*c*) the available options:

a. *The clinical effect*: A significant clinical effect on quality of sleep (which is a major complaint of PTSD patients) was found, together with some improvement in PTSD symptoms (a reduction of 11% in CAPS, ES = 0.2).
b. *Risk and discomfort*: The risk and discomfort of taking 20 mg of escitalopram for 3 to 6 months are fairly low. In terms of serious adverse events, they were minimal.
c. *Available options*: No known pharmacologic options have been found to be effective as secondary PTSD prevention. Psychological techniques were found to be effective[7,8]; however, differences in methodological research strategies (eg, defining the placebo group, blinding of the therapies) hamper comparison to the findings in the present study. Moreover, some of the treatments that are often given for PTSD (ie, debriefing and benzodiazepines) may interfere with the normal potent recovery process, while early intervention with escitalopram does not interfere and promotes sleep quality along with some PTSD symptom improvement.

The current study was not without limitations. Among those who were eligible for the study, 45% declined treatment. This number is in line with a previous study[8] that reported a 42.6% refusal rate to pharmacotherapy and is typical of recruiting from the general population. Fifty-six percent of the participants who enrolled in the study completed the protocol. Most of those who did not complete the study were lost to follow-up (49%). This high dropout rate might be expected for a population who did not have any diagnosed disorder for which they would sense improvement with time. Vaccination studies report on increase in dropout rates according to the number of follow-up sessions that are required by the study protocol (eg, 32.36%–89.12% for 4–6 sessions[35,36]). Therefore, the dropout rate in the current study (19 sessions) can be expected. In addition, when considering the present study results, one should bear in mind that the study was carried out on participants who were exposed to a single and discrete event. Therefore, the results are relevant for these types of events. Secondary prevention for other types of PTSD, including repetitive and continuous traumas, should be studied.

CONCLUSIONS

Early administration of escitalopram (before diagnosis of PTSD could be given, ie, in the first month following a traumatic event) has 3 important implications: (1) it does not prevent PTSD but slightly decreases its severity; (2) it is associated with better quality of sleep; and (3) it may be beneficial for a subgroup of PTSD patients (ie, individuals exposed to intentional trauma). The potential clinical utility of this approach needs to take into account the relatively few side effects of short-term administration of escitalopram and other frequently used options (eg, benzodiazepines and debriefing).

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