

SUMMARY, PTF3

Introduction and aim: There is a lack of evidence for evaluating which types of treatment approaches are the most efficient for trauma-affected refugees, especially when it comes to pharmacological treatment. Additionally, only a very few studies have been published on predictors of treatment outcomes for this patient group. This omission in evidence constitutes a problem for patients and clinicians as well as for society. Accordingly, this PhD thesis aims to generate new knowledge on pharmacological treatment and predictors of treatment outcome for trauma-affected refugees in order to optimise treatment outcome for this patient group.

Methods: This thesis includes four papers based on two studies – a literature review and a randomised trial called PTF3: The aim of the literature review was to provide an overview of the existing literature on the pharmacological treatment of refugees with PTSD and/or depression. Searches were performed in PubMed, psycINFO, EMBASE and the Cochrane library using MeSH/Thesaurus terms as well as free text words. Abstracts (and if necessary full papers) were reviewed and all types of studies (except reviews) describing specified pharmacological interventions were included. The aim of PTF3 was to examine differences in the effects of venlafaxine and sertraline on Post-traumatic Stress Disorder (PTSD), depression and functional impairments in trauma-affected refugees as well as research predictors for treatment outcome. The patients included were 207 adult refugees diagnosed with PTSD and/or depression who had their first appointment at Competence Centre for Transcultural Psychiatry (CTP) between April 1st 2012 and September 16th 2013. Patients were randomised into one of the two treatment groups: a sertraline group (n=109) or a venlafaxine group (n=98). Patients in both groups received the same manual-based Cognitive Behavioural Therapy (CBT) as well as social counselling. The mean length of the treatment course was 6.3 months. The primary outcome measure was self-reported PTSD symptoms assessed on the Harvard Trauma Questionnaire (HTQ). Other outcome measures were self-reported depression and anxiety symptoms measured on Hopkins Symptom Check List-25 (HSCL-25), self-reported social functioning measured on the Social Adjustment Scale Self Report, short version (SAS-SR), and observer-rated depression and anxiety symptoms assessed on the Hamilton Depression and Anxiety Ratings Scales (HAM D+A). Social support was assessed on the Crisis Support Scale (CSS), level of functioning assessed on the Sheehan Disability Scale (SDS),

quality of life was assessed on the WHO-5, the somatisation items of the Symptom Checklist-90 (SCL-90), pain in four different body areas measured on Visual Analogue Scales (VAS) and levels of symptoms and functioning assessed on the Global Assessment of Functioning (GAF). These measures are all self-report ratings except the GAF-scores which were completed by the medical doctor in charge of the treatment and the HAM D+A, which were performed by blinded assessors. Furthermore a rating index consisting of 15 potential psychosocial predictors was specifically developed for this study. Five of the items were rated by the medical doctor, five by the psychologist and five by the social counsellor. The items rated by the medical doctor concerned the patient's upbringing, previous and current psychiatric condition and treatment as well as chronic pain. The items rated by the psychologist all related to the patient's prerequisites for engaging in psychotherapy, while the items rated by social counsellor related to the patient's social situation such as job situation and dwelling.

Results: *The literature review:* Fifteen studies were included, of which the majority were primarily focused on antidepressants. The included studies differed widely in method and quality. Most of the available studies were observational/case studies. Few studies reported effect sizes, confidence intervals and statistical significance of findings.

PTF3: In the intention-to-treat sample, we found small but significant improvements in both the sertraline and the venlafaxine group on the primary outcome measure HTQ, as well as on a number of other ratings: We found no statistically significant group differences between the venlafaxine and sertraline groups on the primary outcome measure, the HTQ, but found a small but statistically significant group difference on the SDS and a borderline significant group difference on WHO-5 and VAS-leg, all in favour of sertraline.

For the CTP predictor index we found a statistically significant correlation to the change in score between baseline and follow-up on most of the ratings, with the exception of two of the VAS scales for pain and the GAF-functioning score. For the primary outcome measure HTQ the correlation was borderline significant ($P=0.06$). The only item from the rating scale that was significantly correlated to outcome on HTQ was job status, while a number of other items were significantly related to changes in depression and anxiety symptoms. The size of correlation coefficients was, however, modest. In addition, we found that the following baseline variables

were significantly associated with improvements on HTQ in univariate analyses: female gender, younger age, being family reunified (versus being a refugee), shorter duration of stay in Denmark and a lower level of depression and anxiety at baseline. In adjusted analyses only gender was significantly correlated to outcome on HTQ, while the correlation was borderline significant for duration of stay in Denmark.

Conclusion: Existing evidence for pharmacological treatment of trauma-affected refugees was generally scarce. In our trial, PTF3, we aimed to overcome some of the methodological shortcomings found in other studies by conducting a relatively large randomised trial. We found small differences in the effects of two antidepressants on a number of secondary outcome measures, all in favour of sertraline. We therefore continue to recommend SSRIs as the first line of pharmacological treatment for trauma-affected refugees. Moreover, we found that the CTP predictor index total score correlates significantly with treatment outcome on most of the rating scales used, but that the sizes of the correlation coefficients were not large. There is a need for further studies on other pharmacological agents as well as studies focusing on identifying predictors of treatment outcome for trauma-affected refugees.