New drug treatment and mechanism of the central anticholinergic drug trihexylphenidyl in reducing posttraumatic nightmares in patients with PTSD

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Objective: The central anticholinergic drug trihexylphenidyl (TP) was previously reported to show remarkable effectiveness against posttraumatic stress disorder (PTSD) flashbacks (FB) as well as the associated onset mechanism at WFSBP, 2015, Athens) and (CINP. 2016, Seoul). The objective of the current study was to assess the efficacy of TP in reducing the nightmares associated with PTSD and elucidate the underlying mechanism.

Methods: An open-label trial was conducted between 2009 and 2017 in outpatients who received a diagnosis of PTSD in accordance with DSM-5. TP (2 mg 1T-3T) was administered to 29 outpatients with PTSD depending on their condition. This study targeted refractory patients who had experienced no therapeutic benefit from any psychotropic drug over a number of years. The primary outcome variable was the change from baseline to endpoint in global Clinician-Administered PTSD Scale (CAPS-5) score and memory-related items B2 (nightmares) and B3 (flashbacks) for PTSD memory-related assessment. Secondary efficacy measures were the impact of event scale-revised (IES-R), which presents the overall clinical profile. Informed consent was obtained from all patients. This study was approved by the Ethical Committee of Warakukai. UMIN trial ID: UMIN000028461.

Result: The therapeutic outcome in 29 patients demonstrated an extremely high efficacy rate. with 70.3% achieving complete remission (CR), indicating CR+ partial remission (PR: 29.7%=100% (flashbacks CR was 66.5%).

Conclusion: This study is the first pharmacological report on the novel use of TP against nightmares in PTSD. TP was markedly effective in the treatment of both nightmares and flashbacks. The nightmares onset mechanism is more closely linked to ACh transmission,and the nightmares is different to regular dream caused by Ch5 (PPN) and Ch6 (LDT) in the brain stem. Posttraumatic nightmares are flashbacks in dreams. The state in which neurotransmission of ACh-memory-rerated-Ccircuit (comprised by Ch4/Meynert-Amygdala, Ch1/medial septal nucleus, Ch2/Broca's diagonal band-hippocampus) generating PTSD-flashbacks is added to regular REM is considered posttraumatic nightmare (author's hypothesis).

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