Clonazepam for the Treatment of Panic Disorder

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Abstract: Clonazepam was initially licensed as an anti-epileptic agent, but its use in a wide variety of psychiatric conditions, including panic disorder (PD) has now been well established. This overview evaluates the current role of clonazepam alone or in combination with antidepressants and/or behavioral therapy in the treatment of PD. We review the data establishing the use of clonazepam in the treatment of PD as well as new information, particularly confirmation of long-term efficacy and safety. We also discuss a regimen for safely tapered withdrawal of clonazepam, the characteristics of the respiratory subtype of PD, and CO2-induced panic attacks as a diagnostic measure and predictor for therapeutic success. It has been shown that panic attacks can more readily be induced by CO2 in PD patients with the respiratory subtype than those with the non-respiratory subtype. More than 25 years after the first report of efficacy in PD in 1984, clonazepam, alone or combined with selective serotonin reuptake inhibitors (SSRIs) and/or behavioral therapy, remains an important therapeutic modality for the management of PD.

Keywords: Behavioral therapy, carbon dioxide test, clinical studies, clonazepam, panic disorder, selective serotonin reuptake inhibitors, tapering.

INTRODUCTION

Clonazepam is a potent, long-acting nitrobenzodiazepine derivative with anticonvulsant, muscle-relaxant, and anxiolytic properties that has been used for years in the treatment of PD [1-3]. In line with other benzodiazepines, clonazepam increases the effects of γ-aminobutyric acid (GABA) via modulation of the GABA receptor, however, it acts only in GABAa receptor [4, 5]. Actually, clonazepam potentiates the inhibitory effect of gamma-aminobutyric acid (GABA) and reduces the use of serotonin, regulating 5HT1 5HT2 receptors and frontal cortex, distinguishing it from other benzodiazepines [6], playing a relevant role in the antipanic effect [7]. Some years ago, clonazepam was used as an alternative for PD patients resistant to antidepressants. Open clinical controlled studies and the control of panic attacks provocation in CO2 inhalation test justify the inclusion of clonazepam in the pharmacotherapeutic modalities to PD [2]. The compound was originally developed for the treatment of epilepsy but was subsequently shown to be effective in many psychiatric indications, especially Panic Disorder (PD) [3, 8-15]. Use of clonazepam in PD was approved by the American Food and Drug Administration (FDA) in 1996.

Today, a variety of drug treatments for PD are available. These are mainly antidepressants such as SSRIs and tricyclic antidepressants, as well as high-potency benzodiazepines such as clonazepam and alprazolam [16-19]. In the past, treatment recommendations differed considerably since they had to be based mainly on short- and intermediate-term results. The advantages of high-potency benzodiazepines shown in short-term studies (earlier onset of action and fewer side effects) had to be balanced against the concerns regarding discontinuation syndromes, recurrence, rebound, or withdrawal [13, 20]. In recent years, long-term results for treating PD with benzodiazepines have become available, allowing a more fact-based choice of drug treatment for PD [14, 15].