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**Prospective, Open, Randomized 3-years Long-term Treatment of Panic Disorder with Clonazepam, Paroxetine, or Their Combination and Follow-up During Additional 6 Years**

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Objective: To describe therapeutic features of 120 panic disorder (PD) patients treated with clonazepam, paroxetine, or clonazepam + paroxetine for 3 years and their follow-up for more 6 years. Method: A prospective open study randomized 120 PD patients to 2 mg/day clonazepam or 40 mg/day paroxetine. Poor responders were switched after 8 weeks to combined treatment with ~2 mg/day clonazepam + ~40 mg/day paroxetine. Tapered withdrawal of all treatments was performed after 3 years. Efficacy, safety, and cumulative relapse and remission were studied over the following 6 years, using panic attack (PA) count, clinical global impression-severity (CGI-S), and Hamilton anxiety scale (HAMA). Results: 94 patients completed 3 years treatment. All were free of panic attacks since at least one year before undergoing tapered drug withdrawal. After two months of tapering, 80% of clonazepam patients were drug-free, versus 55% on paroxetine. No serious or severe adverse event were observed but PA/month, CGI-S, and HAMA worsened slightly. In annually studied patients the relapse rates were similar after the 3 treatments with an advantage of clonazepam over the combination ( $p=0.0035$ ) and paroxetine ( $p=0.08$ , exact Fisher) at the first year after drug withdrawal. Cumulative relapses rate were 41%, 77%, and 94% at years 1, 4, and 6, but relapse therapy with either clonazepam or paroxetine was successful in nearly all cases. Conclusion: PD is a chronic disorder, with many patients relapsing after 3 years treatment. Response to retreatment was excellent. Paroxetine and clonazepam were associated with similar long-term prognoses but clonazepam was better tolerated.