The ment with IPX066 compared with IR CD-LD, regardless of disease severity subgroup. The improvements in “off” time were significantly greater for IPX066 subgroups (P < 0.001) and lower severity subgroups (P < 0.02). Numerical improvements from baseline in “off” time were seen with IPX066 vs. IR CD-LD in each disease severity subgroup. The improvements in “off” time were significantly greater for IPX066 vs. IR CD-LD in the higher severity “off” (P < 0.001) and in both the higher (P < 0.02) and lower severity (P < 0.001) UDPS subgroups. The improvement by IPX066 compared to IR CD-LD in the lower severity “off” subgroup did not reach significance (P = 11), possibly due to a smaller sample size in this subgroup. IPX066 did not show significant global improvement in troublesome dyskinesia after treatment with IPX066 compared with IR CD-LD, regardless of disease severity subgroup.

REVIEW AND META-ANALYSIS

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OBJECTIVES: We performed a systematic review of randomized controlled trials (RCTs) to estimate the efficacy of melatonin versus placebo or other hypnotic agents on the improvement of sleep latency and quality in patients with primary insomnia. METHODS: We searched the published literatures in eight electronic databases, including Ovid-Medline, EMBASE, the Cochrane Library, and five Korean databases through October 2014. We included articles comparing efficacy for sleep between placebo or hypnotic agent and melatonin for at least 2 weeks. The quality of studies was evaluated by using the Cochrane’s risk of bias. The mean difference (MD) or standardized mean difference (SMD) was calculated using the random-effects method for each study. To assess heterogeneity of inter-trial, we used the I2-statistic. Subgroup-analyses were performed by assessment tools, study designs, ages and dosage of melatonin. Funnel plots were used to assess publication bias. RESULTS: Eighteen RCTs were identified and the comparison included treated with melatonin and placebo. Compared with placebo, melatonin significantly reduced sleep onset latency (MD: -5.68 min [95% CI: 4.70 to 36.41], p = 0.001), and increased total sleep time (MD: 20.56 min [95% CI: 4.70 to 36.41], p = 0.01) and sleep efficiency (MD: 3.47% [95% CI: 0.37 to 6.58], p = 0.03). Sleep quality was also improved (SMD: 0.22 [95% CI: 0.03 to 0.40], p = 0.02) in melatonin group but this result was concluded based on a small number of studies in subgroup-analyses for each outcome, there was no clinically remarkable finding. We did not find any evidence of statistical heterogeneity and publication bias. CONCLUSIONS: Melatonin showed to be effective for sleep in comparison with placebo, thus can be an effective option for the treatment of insomnia. Further studies are needed to conclude safety profiles, economic usefulness and tolerance of melatonin.

COMPARISON OF CLINICAL EFFECTIVENESS OF TREATMENTS FOR PSEUDOBULBAR AFFECT (PBA) A-15 RESULTS FROM A SYSTEMATIC REVIEW

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OBJECTIVES: PBA is a neurologic disorder characterized by involuntary, uncontrollable laughing and/or crying episodes that are often incongruent with the patient’s internal emotional state. PBA has also been called pathological laughing/crying, emotionalism, emotionalism, etc. Although FDA approval of dextromethorphan/quinidine (DMQ) in 2010, multiple agents including antidepressants, antipsychotics, dopamine agonists and sedatives were used off-label for the management of PBA symptoms. We conducted a systematic review of therapies (licensed and unlicensed) for PBA symptoms to evaluate their relative clinical effectiveness. METHODS: PubMed, Medline, in process, Embase, and the Cochrane central register of controlled trials were used. Several electronic databases were searched: Medline, Embase, Study type RCTs and non-RCTs in adult patients with PBA/PBA-like symptoms (pathological laughing/crying, emotionalism, etc.). Interventions: DMQ, antidepressants, antipsychotics, dextromethorphan/quinidine alone. Outcomes: measures: change from baseline in various measures of PBA/emootionalism symptoms or symptom burden (NPI, SF-36, PRS scores and the caregiver strain index (CSI)). RESULTS: Nine RCTs and three observational studies were included. Among off-label drugs, six RCTs of 3 SMQs (Dextromethorphan/quinidine with or without doxepin) showed significantly improved PGI scores compared with placebo (P < 0.001). However, the meta-analysis showed that DMQ significantly reduced both ARD and disability progression vs placebo. Teriflunomide 7 mg significantly reduced ARD but not disability progression. Teriflunomide 14 mg significantly reduced rates of severe relapses compared with placebo. In the first 3 years of the study, 52.6% (P = 0.001) of patients with BSMS treated with teriflunomide had a progression of EDSS compared to 65.4% (P = 0.001) in the placebo group. CONCLUSIONS: These studies showed that DMQ was more effective in reducing ARD compared with placebo while significantly reducing the progression of disability in patients with PBA.

NUMBER NEEDED TO TREAT ANALYSIS TO ASSESS THE COMPARATIVE EFFICACY OF THERAPIES FROM TERIFLUNOMIDE AND DIMETHYL FUMARATE STUDIES IN RELAPSING MULTIPLE SCLEROSIS

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OBJECTIVES: Teriflunomide is a once-daily oral immunomodulator approved for relapsing-remitting MS. Here we report the key efficacy, safety, and post hoc analyses from the randomized, placebo-controlled phase 3 trials TEMSO and TOWER (NCT00134563 and NCT00718801). METHODS: In TEMSO/TOWER, a total of 1088/169 patients with relapsing MS were randomized (1:1) to once-daily teriflunomide 14 mg, teriflunomide 7 mg, or placebo. Treatment duration was 108 weeks (TEMSO) or variable, based on time of enrolment (TOWER, 48–152 weeks, ending 48 weeks after last patient randomized). Primary and key secondary endpoints were analyzed relative to placebo, and progression confidence intervals adjusted for multiplicity endpoints included safety and tolerability. Post hoc analyses examined the effect of teriflunomide on 5 severe relapse outcomes: (A) relapses with sequelae defined by Panitch, (B) Expanded Disability Status Scale (EDSS) score worsening ≥ 1, (C) ≥ 3.0, (D) ≥ 2.0, or (E) ≥ 1.0. Exploratory subanalyses were performed for each endpoint. RESULTS: Teriflunomide 14 mg, 7 mg, and placebo were well tolerated and showed statistically significant reductions in the key secondary endpoints. Conclusions: Teriflunomide 14 mg was shown to delay conversion to relapsing-remitting MS (RRMS) EDSS 7.0, or SPMS (any EDSS state) from EDSS 4.0 or 5.0 was estimated from transition probability matrices using algebraic techniques from Mandel 2007: the time to EDSS ≥ 7.0 or EDSS was derived for each matrix (DMF, untreated) by using matrix multiplication to estimate the proportion of patients who had reached these states over time. The transition matrix for untreated patients was derived using placebo arm data from clinical trials 3,4(Mformerly known as gastro-resistant DMF), or no DMT treatment. The transition matrix for untreated patients was derived using placebo arm data from clinical trials 3,4(Mformerly known as gastro-resistant DMF) for RRMS population) and London Ontario dataset (for transitions from RRMS to SPMS). The transition matrix for DMF was estimated by applying treatment effect on disability progression sourced from a mixed treatment comparison), to the probability of progressing in the untreated matrix. Probabilistic sensitivity analysis was conducted to estimate 95% confidence intervals (CIs). RESULTS: The time for progression from EDSS 4.0 to ≥ 7.0 or SPMS was estimated at 5.9 years (95% CI: 0.05 to 10.25) for patients treated with DMF and 5.0 years (95% CI: 5.59 to 6.24) for untreated patients. The time from EDSS 5.0 to ≥ 7.0 or SPMS was 2.78 years (95% CI: 4.32 to 6.37) for patients treated with DMF and 3.64 years (95% CI: 3.34 to 3.96) for untreated patients. CONCLUSIONS: Our analysis showed that DMF therapy was associated with a longer time interval between EDSS 4.0 or 5.0 and progression to EDSS ≥ 7.0 or SPMS relative to no DMT treatment.


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