

Nathan Smith
Conferences Manager
Diabetes UK
Email: nathan.smith@diabetes.org.uk

319

J Nizza*, AJ Nelson, I Petropoulos, D Cuthbertson, JP Wilding, R Malik, U Alam

Aims: In diabetic neuropathy, nerve conduction velocities are thought to decline by 0.5m/s/yr. We evaluated the electrophysiological changes in trials of pathogenetic treatments for diabetic peripheral neuropathy (DPN).

Methods: A literature search identified double-blind RCTs of ≥ 1 year duration from 1971 to 2017. Change in peroneal MNCV (PMNCV) and sural SNCV (SSNCV) and amplitude (SSNAmp) were extracted from placebo and treatment arms.

Results: 19 trials were identified (placebo:n=2483, treatment:n=3260) with a duration of 68.7 ± 37.3 weeks. One trial (placebo:n=10) in the decade 1980-1989, eleven trials (placebo:n=811) in 1990-1999 (DC1) and seven trials (placebo:n=1662) in 2000-2009 (DC2). In DC1 (placebo arm), PMNCV (0.33 ± 0.9 m/s/yr) and SSNCV (0.15 ± 1.50 m/s/yr) increased, while SSNAmp (-0.09 ± 0.63 mV/yr) declined. In DC2 (placebo arm), PMNCV (-0.09 ± 0.34 m/s/yr), SSNCV (-0.03 ± 0.96 m/s/yr) and SSNAmp (-0.13 ± 0.15 mV/yr) marginally declined. There was no difference between DC1 and DC2 in the placebo and treatment arms for PMNCV, SSNCV and SSNAmp ($p=NS$ for all). When evaluating all trials (n=19), both PMNCV and SSNCV increased in the placebo arm (0.17 ± 0.6 m/s/yr and 0.09 ± 1.09 m/s/yr respectively), while SSNAmp showed a small reduction (-0.11 ± 0.24 mV/yr) ($p=NS$ for all). There was only a marginal improvement in electrophysiology in the treatment arm compared to placebo (PMNCV 0.6 ± 1.29 m/s/yr, SSNCV 0.52 ± 1.05 m/s/yr, SSNAmp 0.79 ± 0.98 mV/yr, $p=NS$ for all).

Conclusions: The failure of clinical trials in diabetic neuropathy may be related to the improvement in electrophysiology in the placebo arm over time. A detailed analysis of the study demographics is merited to clarify factors that lead to a lack of placebo worsening. The use of electrophysiology as a surrogate end point for DPN a predominately small fibre pathology warrants candid discussion.