OVERTREATMENT IN PHARMACORESISTANT EPILEPSY: A PROSPECTIVE RANDOMIZED STUDY OF AN INTERVENTION AIMED AT REDUCING ADVERSE EFFECTS

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Pharmacoresistant epilepsy is associated with impaired quality of life (QOL) as a consequence of seizures, associated comorbidities and adverse effects of antiepileptic drugs. Observational studies demonstrated that reducing seizure frequency without achieving complete seizure freedom has little impact on quality of life (Vickrey et al., 1994; Gilliam et al., 2002). A randomized study in North America suggested that use of the Adverse Event Profile (AEP) questionnaire, a self-administered instrument for the assessment of adverse AED effects, minimizes overtreatment and the associated burden of adverse drug effects compared with conventional clinical management Gilliam et al., 2004), but the general applicability of these findings is uncertain. SOPHIE (Study of Outcome of PHarmacoresistance In Epilepsy) was a prospective, mainly observational study aimed at assessing adverse effects, quality of life, mood status, seizure outcome and AED treatment characteristics in patients with pharmacoresistant epilepsy consecutively recruited at 11 tertiary referral epilepsy centres in Italy over an 18 month follow-up period (Alexandre et al., 2010; Canevini et al., 2010). A subgroup of patients participated in a randomized prospective intervention study (discussed in this presentation) to determine whether systematic screening with the AEP questionnaire improves quality of life and reduces the burden of toxicity. The AEP and the Quality of Life in Epilepsy-31 (QOLIE-31) questionnaires were administered at 0 (baseline), 6, 12 and 18 months. Co-primary outcome variables were changes in AEP and QOLIE-31 scores. Patients with a high burden of toxicity (AEP score ≥45) at baseline were randomized to the intervention group (AEP scores made available to the physician) or control group (AEP scores not made available to the physician). A total of consecutive 222 patients aged ≥16 years with an AEP score ≥45 were enrolled. AEP scores tended to decrease between the baseline and the final visit in both groups, with a significant improvement (reduced toxicity burden) compared with baseline (intervention group: 57.3±6.8 vs 48.9±9.9; control group: 56.7±6.1 vs 49.4±11.2 respectively, $p<0.0001$ for both groups). QOLIE-31 scores improved gradually over time in both groups with a

significant increase compared with the baseline score (intervention group: 43.7±13.5 vs 50.3±16.2; control group: 44.7±13.2 vs 51.7±16.2, $p<0.0001$ for both groups). However no differences in degree of improvement emerged between the two groups on the two co-primary variables. Changes in secondary outcome variables, including Beck Depression Inventory scores, Clinical Global Impression scores, AED loads and seizure related outcome also showed no statistically significant differences between the intervention group and the control group. These data indicate that systematic screening for adverse AED effects in patients with pharmacoresistant epilepsy may be useful in identifying the burden of toxicity but it is per se insufficient to guide medication changes aimed at reducing adverse effects. Interventions to address overtreatment in refractory epilepsy should include educational programmes and other measures aimed at ensuring effective utilization of all clinically available information to patient's benefit.

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