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| **CATEGORY** | **DATA/ANALYSIS** |
| Does the RCT state a clear primary hypothesis? | **Not as explicit as possible.** Goal was to assess the efficacy and safety of haloperidol for the treatment of delirium and its associated symptoms and outcomes in critically ill patients. Primary outcome was number of delirium- and coma-free days up to 14 days. |
| Does the hypothesis seem implausible? If so, discount any support the RCT creates for the hypothesis. | **Maybe implausible.** Delirium is a hyperdopaminergic state and haloperidol blocks dopamine transmission, **but prior trials have been negative.** |
| Equivalence to my patients | 18 or older, in ICUExclude: admission secondary to acute neuro condition, pregnancy, breast-feeding, allergy to haloperidol, hx of ventricular dysrhythmia, QTC > 500, NMS, parkinsonism, schizophrenia, other psychotic disorder, dementia, IQCODE score > 4, expected admit < 24 hours, deafness, blindness, in alcohol or drug withdrawal.Average age 64, 68% male, APACHE-IV (Acute Physiology and Chronic Health Evaluation) score 73**75% of screened patients were ineligible, so external validity may be poor.** |
| Blinding | Yes, only on-site pharmacist and statistician not blinded |
| Ratings scales (validated) | Richmond Agitation Sedation ScaleIntensive Care Delirium Screening ChecklistConfusion Assessment Method for ICU |
| Randomization | Computer generated |
| Similarity at baseline | Yes, except median mSOFA (Sequential Organ Failure Assessment) score was lower in the haloperidol group (5 for haloperidol, 6 for placebo) |
| Equal treatment post-randomization | Yes |
| Follow-up duration  | 14 days |
| Sample size | 142 randomized, 132 analyzed, 65 haloperidol, 67 placebo **(fairly small sample size)** |
| Intent-to-treat?*Drop-out rate.* *Imputation method(s)?* | During the 14-day primary intervention period, 5 of the 132 dropped out, 1 haloperidol, 4 placebo. **Not clear how the study handled the 5 dropouts.** Patients who died were considered to have had zero DCFDs during the intervention period.  |
| Statistical significance: p value set at what level? One- or two-sided? (Don’t overvalue statistical significance.) | Two-sided p = 0.05 |
| Bonferroni or other correction for multiple statistical comparisons | **Do not see, although they had at least 10 secondary outcomes and 10 post-hoc exploratory outcomes. Investigators calculated statistical significance for these outcomes even though they were not independent events.** |
| Effect sizes and how they were measured*Absolute change in a biological parameter or rating scale**Percent change in a biological parameter or rating scale**Percentage of subjects reaching a prospectively defined outcome, e.g., absolute or percentage change in a biological parameter or rating scale or a particular benchmark with respect to a biological parameter or rating scale (might then be converted into a number needed to treat, risk ratio or odds ratio)**Standardized mean difference**Number needed to treat**Risk ratio**Odds ratio**Hazard ratio**How heterogeneous are the effect sizes? For the primary outcome, did the study report a prediction interval? The 95% PI = M ± 1.96SD with M being the mean effect size and SD being the standard deviation of the effect size. If so, what does the PI suggest about whether the effect is clinically meaningful and whether I should offer the treatment to a given patient?* | DCFDs adjusted risk ratio (haloperidol/placebo) was 0.98, 95% confidence interval 0.73-1.31, p = 0.87.Patients who received haloperidol were less likely to fall or step out of bed, 9% versus 27%.Patients who received haloperidol were less likely to self-extubate, adjusted odds ratio 0.70 or receive a benzodiazepine, 57% versus 73%.**No prediction interval provided.** |
| Bottom line*After considering costs and benefits, should I offer the treatment to a given patient?* | Not for routine use. Perhaps prescribe for delirious patients who are disruptive such that behavior interferes with care or endangers others. |