

Quetiapine versus haloperidol in the treatment of delirium: a double-blind, randomized, controlled trial

BACKGROUND

- Haloperidol is the treatment of choice for delirium due to its short half-life, low anticholinergic side effects, and little sedation but is limited in use due to its extrapyramidal side effects.
- Quetiapine is an atypical antipsychotic effective for schizophrenia, bipolar disorder, and major depressive disorder, but there are only limited studies of safety and efficacy when used for delirium.

OBJECTIVE

- To compare the efficacy and tolerability of quetiapine and haloperidol in controlling delirious behavior

METHODS

- **Design:** Single center, prospective, double-blind, flexible dose, randomized controlled trial
- **Duration:** 7 days
- **Inclusion criteria**
 - Patients presumed to have delirium requiring consultation-liaison services from the psychiatric department
 - Male or female 18-75 years old
 - Met the definition of delirium as defined by the *Diagnostic and Statistical Manual of Mental Disorders*
- **Exclusion criteria**
 - Substance-induced delirium (i.e., alcohol withdrawal delirium)
 - Known allergy or intolerance to quetiapine or haloperidol
 - Pregnancy or breast-feeding
 - Taking an antipsychotic medication
 - Hepatic or renal failure
 - Consent withdrawal
 - Safety/efficacy reasons decided by the primary physician
 - Transferring to other hospitals/hospital discharge
 - Not being able or allowed to take oral medications
 - Receiving other antipsychotic medications
- **Patients enrolled:** 52 patients (24 – quetiapine, 28 – haloperidol)
- **Drug regimen:** Flexible dose quetiapine (25-100 mg/d) or haloperidol (0.5-2.0 mg/d) before bedtime & as needed
- **Primary outcome:** DRS-R-98 severity score difference between the two treatment groups
- **Secondary outcomes:** Differences between the two treatment groups, including DRS-R-98 noncognitive and cognitive subscale scores, response rate, remission rate, total time of sleep, and CGI-I scores
- **Power:** For a power of 95% and a 0.05 CI, a sample of 34 per treatment group was needed to detect a mean difference of 5 points assessed by the DRS-R-98
- **Data handling method:** Intent-to-treat

RESULTS

- **Primary outcome measure:** The mean (SD) of the decrease in DSR-R-98 severity scores over the 7-day trial period was -22.9 (6.9) for the quetiapine group and -21.7 (6.7) for the haloperidol group (P = 0.59).
- **Secondary outcome measures:** No secondary outcomes were determined to be statistically significant.

- **Author's conclusion:** Low doses of both quetiapine and haloperidol are equally effective and safe for the management of behavioral disturbance in delirious patients, given together with environmental manipulation.

STRENGTHS

- Potential conflicts of interest does not appear to be an issue in the study.
- The study design was appropriate and optimal for determining the outcomes.
- The cognitive assessment scores were an appropriate way to measure the outcomes.
- Only the study medications were allowed to be used in the treatment of the patients.

LIMITATIONS

- Due to the small sample size, power was not met and no outcomes were statistically significant.
- The study medications used were given at lower doses than normally used in practice.
- Patient adherence to medication was not addressed.
- The ages of patients included in the study were not a good representation of the true population as many elderly patients experience delirium, and it would be difficult to extrapolate the results to these patients.
- Patients with cognitive disorders (including dementia) and acute CNS pathology were not excluded from the study which may have caused some inaccuracy of delirium measurement.
- The mean time between delirium first being identified and patient randomization to a treatment group may have allowed for the delirium to resolve on its own, which could have skewed the results.
- There was no placebo used, and even though haloperidol is the treatment of choice, it still affects patients differently and is associated with a variety of side effects.

CONCLUSION

- Quetiapine appeared to be similar in efficacy to haloperidol in treating delirium.
- The results would be hard to extrapolate in practice to patients outside the inclusion criteria.
- **Future research:** Further studies should be done using a larger sample size and clinically recommended doses of study medication, excluding patients with delirium of CNS pathology or cognitive disorders, and including older patients.

Reference: Maneeton B, Maneeton N, Srisurapanont M, Chittawatanarat K. Quetiapine versus haloperidol in the treatment of delirium: a double-blind, randomized, controlled trial. *Drug Design, Development, and Therapy* 2013; 7:657-667.

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