The predictive value of early treatment response in antipsychotic-naïve patients with first-episode psychosis: Haloperidol versus olanzapine

BACKGROUND:

- Early theories suggest that there is a delayed onset of action of several weeks for antipsychotic drugs. Recently, it has become increasingly apparent that the therapeutic action actually begins much earlier in the course of treatment, in as little as the first two weeks.
- Antipsychotic effectiveness could be assessed soon after treatment initiation, without the need for extended 6-week trials.

OBJECTIVE:

- To investigate the predictive value of early treatment response in a group of antipsychotic-naïve, first-episode psychosis patients.

METHODS

- **Design:** Single site, double-blind, randomized, controlled experimental, parallel trial.
- **Duration:** Varied, based on length of hospitalization of patient
- **Inclusion criteria:** Experiencing their first episode of psychosis and no prior antipsychotic exposure
- **Exclusion criteria:** None listed for participation in the study
- **Primary outcome measure:** Percent improvement on the BPRS (Brief Psychiatric Rating Scale) total score at hospital discharge
- **Secondary outcome measures:** Presence of Akathisia at hospital discharge, affective symptomatology, and ability of early non-response at week 2 and 3 to predict non-response at hospital discharge
- 112 patients enrolled to receive either olanzapine or haloperidol
- 58 patients received olanzapine, treatment began at 5 mg/day, dose adjusted by 2.5 mg as clinically indicated
- 54 patients received haloperidol, treatment began at 2 mg/day, adjusted by 1 mg as clinically indicated
- Power was not mentioned
- Data handling method was per protocol

RESULTS

- 75 patients completed the study, 32 in the olanzapine group and 43 in the haloperidol group.
- **Primary outcome measure:** There was a 79% improvement at discharge in patients BPRS total score when treated with olanzapine. With haloperidol, there was an 81% improvement in scores at discharge.
- **Secondary outcome measure:** A total of 8 patients were experiencing akathisia at the time of discharge. Akathisia emerged as a significant predictor of less HAM-A improvement at discharge. Early response threshold

of 20% improvement does not adequately identify patients who will experience a poor treatment response.
- **Author's conclusion:** Early response at week 2 predicted treatment outcomes at discharge for patients treated with haloperidol, while early response at week 3 predicted treatment outcomes for patients treated with haloperidol or olanzapine.

STRENGTHS
- No conflicts of interest from study authors
- Statistical tests were appropriate for study data

LIMITATIONS
- Short study duration
- One site
- No exclusion criteria
- No data provided to account for adherence
- Non-study medications taken by patients were not reported
- Not using intent to treat method
- Not reporting confidence intervals or mentioning power of the study

CONCLUSION
- Although the study showed that olanzapine response was predictable starting at week 3, and haloperidol at week 2, this may not be related to actual practice.
    - Haloperidol and olanzapine work differently. It would have been more appropriate to use two treatments with the same mechanism of action, and dose appropriately.
- Further studies are needed. A larger scale study, including multiple sites, would be appropriate. Also, including a follow-up to confirm the predictive value of the medication.

Reference: Rassmussen SA, Rosebush PI, Anglin RE, Mazurek MF. The predictive value of early treatment response in antipsychotic-naïve patients with first-episode psychosis: Haloperidol versus olanzapine. Elesiver: Psychiatry Research. 2016;241:72-7.

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06.01.2016