Two-year efficacy of varenicline tartrate and counselling for inpatient smoking cessation (STOP study): A randomized controlled clinical trial

Background:

- Disease burden related to smoking is projected to increase to 8 million deaths by 2030.
- Varenicline works on nicotinic receptors and eases cravings and lowers smoking associated reward pathway stimulation.
- Previous studies have not measured varenicline's efficacy after 52 weeks.

Objective:

- To determine the long-term efficacy (104 weeks) of varenicline and counseling compared to counseling alone. Secondary objectives included adverse event occurrence and mortality rates.

Methods

- **Design:** Open-label, randomized, multicenter controlled clinical trial.
- **Inclusion Criteria:** Ages between 18-75, smoked at least 10 cigarettes on average a day over the past 12 months, and who had presented to the hospital with a serious tobacco related illness (Cardiac, Vascular, or respiratory).
- **Exclusion Criteria:** Had cancer within the past seven years, a creatinine clearance of less than 30ml/min, acute or preexisting psychological illness, pregnant and breastfeeding patients, or patients who were using nicotine replacement product or who had used varenicline in the past 12 months.
- **Primary outcome measure:** Difference in 104 week self-reported abstinence between varenicline plus counseling and counseling alone.
- **Secondary outcomes measured:** Adverse effect rates during the 12 weeks of varenicline treatment and mortality rates at 104 weeks between varenicline plus counseling and counseling alone groups.
- 392 patients (196 per group) received either
    - Varenicline (dosing below) plus counseling for 12 weeks (VT+C)
    - Counseling only for 12 weeks (CO)

      *Varenicline: 0.5 mg qd for three days, then 0.5mg bid for 4 days, then 1 mg twice a day for remainder of 12 weeks.
- The power of the study was 80% with an alpha level of 0.05 to detect a 15% difference between treatment and control groups. This was calculated to be sufficient with a sample size of 196 patients per group.
- The study used the intent to treat method for data handling.

Results

- 117 patients (59.7%) in the VT+C group and 101 patients (51.3%) in the CO group (218 total) completed the 104 week study.
- **Primary Outcome measure:** The self-reported abstinence rates at the 104 week endpoint was 29.2% (n=56) in the VT+C group and 18.8% (n=36) in the CO group; odds ratio 1.78; 95%CI 1.10 to 2.86; p = 0.02.
- **Secondary Outcome measure:** There was a decrease in cigarettes smoked among non-abstinent subjects observed in both groups at 104 weeks. VT+C showed a decrease

from 24.9 SD2.67 to 17.1 SD11.72 and CO showed a decrease from 24.7 SD2.89 to 15.4 SD8.82 respectively. The study reported the most common adverse effect for varenicline was nausea (16.3%). Other adverse events included Abnormal Dreams (6.12%), Headache (6.12%), Insomnia (5.1%), Vomiting (4.08%), and Dizziness (2.04%). There were 10 deaths in the VT+C group during the 2 year period and 12 deaths in the CO group.

Strengths

- Patients were randomized between groups.
- Evaluated patients at 104 weeks duration which was longer than previous studies.

Limitations

- Study was open labeled.
- Included patients motivated to quit after serious smoking related hospitalization.
- Study population was mostly Caucasian (96%) from southern Australia, which could limit generalizability of results.
- Power was only calculated for 52 weeks not 104 weeks.
- Excluded patients with current or preexisting psychiatric conditions (including depression).
- Active control was not used.
- No main conflicts of interest reported, but there seemed to be bias statements in the text.
- Abstinence was self-reported which could overestimate abstinence rates especially in an open-label study. Stated that abstinence was verified using exhaled carbon monoxide test in a subset of participants only, but that data was not reported. Additionally, exhaled carbon monoxide would only verify abstinence for a limited time prior to the test even if reported.
- Large % of patients did not complete the 104 weeks.

Conclusion

- Despite the abstinence difference between Varenicline plus counseling and counseling alone being statistically significant, due to other factors and limitations described previously, the results may not be clinically significant.
- Future studies are needed to confirm the results of this study. The Studies should be blinded, adequately powered for the 104 week duration, and include a more diverse patient population. Ideally, the self-reported abstinence would be verified by an adequate laboratory test. It would also be beneficial to compare varenicline to another active therapy like nicotine replacement therapy since the efficacy between these two treatment options is highly debated.

Reference: Carson-Chahhoud KV, Smith BJ, Peters MJ, Brinn MP, Ameer F, Singh K, et al. Two-year efficacy of varenicline tartrate and counselling for inpatient smoking cessation (STOP study): A randomized controlled clinical trial. PLoS ONE. (2020) 15(4): e0231095. https://doi.org/10.1371/journal.pone.0231095

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