

Critical Appraisal Topic (CAT)

St. John's Wart vs. varenicline (Chantix) for Smoking Cessation.

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Clinical Scenario:

A 56 year-old female patient presents to clinic with exacerbation of chronic cough and states "I really need to quit smoking." During the smoking cessation discussion the patient brings up St. John's Wart as an alternative treatment she has heard about from friends and questions its efficacy in smoking cessation versus "that new smoking pill" (indicating Chantix or varenicline).

Clinical Question:

Is St. John's Wart as effective as varenicline (Chantix) at producing successful smoking cessation in the adult population?

Articles:

Keating, G.M. & Siddiqui, M.A.A. (2006). Varenicline: A review of its use as an aid to smoking cessation therapy. *CNS Drugs*, 20(11), 945-960.

Sood, A., Ebbert, J., Prasad, K., Croghan, I., Bauer, B., & Schroeder, D. (2010). A randomized clinical trial of St. John's Wart for smoking cessation. *Journal of Alternative and Complementary Medicine*, 16(7), 761-767. doi: 10.1089/acm.2009.0445

Critical Review of Study/Appraisal of Key Evidence:

Study Design:

- Keating and Siddiqui, (2006), is a summary review of multiple trials including: two randomized, double-blinded, multicenter phase II studies and two randomized, double-blinded multicenter phase III trials evaluating the smoking abstinence rates in persons taking Varenicline providing level 2 evidence.
- Sood, et al., (2010), outlines a randomized, blinded, placebo-controlled, three-arm, dose-ranging clinical trial investigating the efficacy of St. John's Wart (SJW) for smoking cessation providing level 3 evidence.

Sample:

- Keating and Siddiqui, (2006), included review of two phase II dose-finding trials, one with 638 participants and one with 647 participants. Participants had the mean age of 40.5-43.7 years and had smoked for a mean of 23.4-26.0 years. It also included a review of two phase III trials including 1025 and 1027 participants comparing varenicline with bupropion sustained-release. The mean age of participants in these trials was 42.0-44.6 years who had smoked for a mean

duration of 24.1-27.1 years. The study also included 2 reviews of trials, with a total of 1210 and 1927 smokers respectively, assessing the effect of varenicline on smoking abstinence.

- Sood, et al., (2010), included a review of one trial, with 118 cigarette smokers enrolled. The mean age of study participants was 36.7 (\pm 12.4 years) who smoked an average of 20 (\pm 6.6) cigarettes per day for 20 (\pm 12.1 years). Of the 118 original participants, 51 (43%) withdrew from the study prior to the end of the medication phase.

Procedure:

- Keating and Siddiqui, (2006), was a literature review of several trials evaluating three different aspects of varenicline: (1) the varenicline dosing options for smoking cessation; (2) a comparison of varenicline and bupropion sustained-release medication's effects on smoking cessation; and (3) the effect of varenicline on smoking abstinence rates. In the first review of the dosing option trial, participants were given differing dosages of varenicline and evaluated for 4 week continuous quit rate and the primary defined endpoint. The comparison trial review included participants who were given varenicline or bupropion or placebo. The primary endpoint for these trials was the carbon monoxide (CO)-confirmed 4-week continuous abstinence rate. In the last review, participants were evaluated by CO-confirmed continuous abstinence rates and differing time intervals after an initial CO-confirmed 4-week continuous abstinence rate was established.
- Sood, et al., (2010), included 118 eligible participants who were randomly selected to receive SJW 300mg, 600mg or matching placebo 3 times per day combined with behavioral intervention for 12 weeks. Self-reported abstinence was biochemically confirmed with expired air CO testing.

Outcome(s) Measured:

- Outcomes measures in the Keating and Siddiqui, (2006), review include the effect varenicline dosing options on smoking cessation, the effectiveness of varenicline vs. bupropion sustained-release on smoking cessation and abstinence rates and the effect of varenicline on sustained smoking abstinence rates.
- Outcome measured in the Sood, et al., (2010), trial was the smoking abstinence rate of persons receiving 300mg SJW vs. persons receiving the 600mg SJW vs. persons receiving a matching placebo.

Results:

- The Keating and Siddiqui, (2006), review concluded that in phase III trials, 12 weeks' treatment with varenicline was associated with significantly higher 9-12 week continuous abstinence rates than placebo or bupropion-sustained release. A second conclusion identified long-term abstinence rates were 2.7-3.1 times higher with varenicline treatment and that an additional 12 weeks of varenicline therapy helped increase the likelihood of long-term abstinence. Overall, varenicline is an effective and generally well-tolerated treatment for use in smokers who want to quit.
- Sood, et al., (2010), concluded that SJW did not increase smoking abstinence rates, suggesting that it has little role in the treatment of tobacco dependence.

Clinical Bottom Line:

- St. John's Wart is not effective as a smoking cessation agent. In the randomized blinded study, SJW did not significantly increase tobacco abstinence rates or decrease nicotine withdrawal compared to placebo. The study dropout rate was high, but no differences in abstinence rates were observed among subjects reporting use of $\geq 75\%$ of their assigned doses. Some previously-conducted studies have reported conflicting results with respect to the efficacy of SJW for increasing smoking abstinence. In one blinded, placebo-controlled study using SJW at 900mg/day, 6/71 or 8.5% of participants on SJW and 9/72 or 12.5% on placebo achieved prolonged smoking abstinence at 4 weeks. In another study among 28 smokers who received SJW either 300mg daily or 300mg BID, the prevalence and continuous smoking abstinence rates were both 18% at 3 months.
- Varenicline is an effective and generally well-tolerated treatment for use in smokers who want to quit. In two, well-designed phase III trials, 12 weeks' treatment with varenicline was associated with significantly higher continuous abstinence rates at 9-12 weeks than bupropion sustained-release or placebo with abstinence rates being 44% and 43.9%, 29% and 29.8%, & 17 and 17.6% respectively. In the longer-term, continuous abstinence rates for weeks 9-52 demonstrated that the odds of remaining abstinent were 2.7-3.1 times higher with 12 weeks of varenicline treatment than with placebo; as well as with bupropion sustained-release. In addition, varenicline ameliorated the urge to smoke and the reinforcing effects of smoking to a significantly greater extent than placebo. Its effect on withdrawal symptoms was less consistent. Among those achieving abstinence, an additional 12 weeks of varenicline therapy helped increase the likelihood of long-term abstinence. In weeks 13-24, 12 additional weeks of varenicline therapy was associated with a 70.5% smoking abstinence rate compared to placebo at 49.6%. In weeks 13-52, abstinence rates were calculated at 43.6% with varenicline compared to 36.9% with placebo.

Relevance to clinical practice:

As healthcare providers, we strive to provide the most accurate, successful and cost-effective treatment options for the consumers of healthcare, our patients. In our ever-expanding world of global communication today, healthcare consumers are more educated and informed about new and innovative mainstream treatments. They are also more conscious and curious about non-pharmaceutical and complementary and alternative medicine options. The bottom line is that consumers of healthcare expect us, as healthcare providers, to be competent and knowledgeable regarding disease prevention, diagnosis and treatment and to utilize the most up-to-date, evidence-based information available. In reviewing the two studies mentioned above, it is shown that varenicline is an effective treatment option for achieving and maintaining smoking cessation in adults that are ready to quit, whereas, St. John's Wart had no significant effect on smoking cessation.

REFERENCES:

Keating, G.M. & Siddiqui, M.A.A. (2006). Varenicline: A review of its use as an aid to smoking cessation

therapy. *CNS Drugs*, 20(11), 945-960.

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