

## A Useful Adjunct for Promoting Smoking Cessation

Prochazka AV, Weaver MJ, Keller RT, Fryer GE, Licari PA, Lofaso D. A randomized trial of nortriptyline for smoking cessation. *Arch Intern Med* 1998;158:2035-9.

### Study Overview

**Objective.** To determine the value of adding nortriptyline hydrochloride to a smoking cessation program.

**Design.** Randomized, double-blind, placebo-controlled trial.

**Setting and participants.** 214 patients were enrolled in the study. Enrollees smoked 10 or more cigarettes per day, were between 18 and 70 years of age, were without current major depression, and were participating in a smoking cessation behavioral intervention program conducted at an affiliated Department of Veterans Affairs Medical Center and an Army Medical Center in Colorado.

**Methods.** Patients were begun on nortriptyline ( $n = 108$ ) or matched placebo ( $n = 106$ ) at 25 mg before bed 10 days prior to quit day and titrated to 75 mg/day or to the maximal tolerated dose. The behavioral intervention consisted of two group sessions and 12 individual follow-up visits, based on the American Cancer Society model. The study drug was continued for 8 weeks after the quit day.

**Main outcome measures.** Sustained smoking abstinence, defined as self-reported cessation within 1 week of the quit day, expired carbon monoxide of 9 ppm or less at each of the 12 follow-up visits, and a urine cotinine level of less than 50 ng/mL at the final visit (6 months after quit day). Withdrawal symptoms such as anxiety, difficulty concentrating, restlessness, and impatience were measured using a daily diary.

**Main results.** The cessation rate at 6 months was 14% in the nortriptyline group and 3% in the placebo group ( $P = 0.003$ ; absolute difference, -11%; 95% confidence interval [CI] = -18% to -4%). The nortriptyline cohort experienced a significant reduction in several withdrawal symptoms including anxiety, irritability, difficulty concentrating, restlessness, and impatience by day 8 after quit day. Use of nortriptyline also was associated with more frequent adverse effects, including dry mouth (64%) and dysgeusia (20%).

### Conclusion

Adding nortriptyline to a behavioral smoking cessation pro-

gram may significantly enhance the program's value in inducing cessation.

### Commentary

This study by Prochazka and colleagues suggests that the use of nortriptyline may assist in promoting smoking cessation among some smokers, particularly those self-motivated to stop. The higher cessation rates associated with nortriptyline may be related to the decrease in withdrawal symptoms, such as anxiety and stress; the drug's anticholinergic actions (especially dry mouth and taste changes that made cigarettes "not taste good" when subjects were receiving nortriptyline); or a combination of the two effects [1,2]. Despite the encouraging findings, the authors acknowledge that the most appropriate dosage and duration of therapy to optimize the positive effect of nortriptyline has not been determined. In fact, the relapse rate in the nortriptyline group after patients stopped taking the drug suggests that a longer period of drug therapy may be required. Also, this study has a relatively small sample size and low enrollment of subjects with symptoms of depression (or other conditions), so the value of nortriptyline in patients with depression and other comorbidities has yet to be determined.

### Applications for Clinical Practice

As is commonly appreciated, smoking is the leading preventable cause of mortality, and cessation can reduce morbidity and mortality associated with smoking. At the same time, smoking cessation rates resulting from current therapeutic alternatives are suboptimal [3,4]. One class of drugs that may improve cessation is the tricyclics. For smokers motivated to quit, use of nortriptyline under a physician's care or other drug therapies demonstrated to have a positive effect may enhance cessation rates.

### References

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