No Evidence Standard NRT Helps Pregnant Women Quit Smoking
Deborah Brauser

February 29, 2012 — Nicotine replacement therapy (NRT) appears to be ineffective for smoking cessation during pregnancy, new research suggests.

In a randomized controlled trial of more than 1000 pregnant women, overall smoking abstinence rates were not significantly different between those who received NRT patches in addition to behavioral cessation support and those who received placebo patches plus behavioral support.

"Smoking in pregnancy is a massive public health problem that needs attention," lead author Tim Coleman, MD, professor of primary care at the United Kingdom Center for Tobacco Control Studies at the University of Nottingham and general practitioner/family physician at Unity Surgery in Mapperley, told Medscape Medical News.

"NRT works outside of pregnancy, but women metabolize nicotine and cotinine a lot faster when they are pregnant. So this raised questions as to whether or not [it would work] for smoking cessation in pregnancy at current standard doses," explained Dr. Coleman.

Unfortunately, the results from this study showed that there was "no evidence that standard-dose NRT helps pregnant women who smoke to stop or that it either improves or worsens birth or pregnancy outcomes," he added.

However, medication compliance rates were extremely low for all of the participating women.

Dr. Coleman noted that 2 possible explanations for this could be that pregnant women are very reluctant to use any medication or that the standard dose of NRT used might not have generated high enough nicotine levels to effectively substitute for the nicotine received from smoking, resulting in withdrawal symptoms and a desire to stop using the patches.

Overall, the results "suggest that guidelines for smoking cessation in pregnancy should be revised to encourage the use of only those interventions that have a secure evidence base — specifically, behavioral support," write the investigators.

The study is published in the March 1 issue of the New England Journal of Medicine.

Inconclusive Data

According to the researchers, in high-income countries, the prevalence rate of smoking during pregnancy is between 13% and 25%.

Although behavioral support therapies have been shown to be effective in helping pregnant women to stop smoking, there has been "considerable uncertainty" about the effectiveness of smoking cessation medications in this population.

In addition, although NRT "is widely recommended during pregnancy," data on both its effectiveness and safety have been inconclusive.

For example, as reported by Medscape Medical News, a recent study by Danish researchers found that exposure to nicotine in either tobacco smoke or NRT in utero significantly increased risk for colic in infants.

For this study, 1050 women in England who were aged 16 to 50 years and who were with pregnancies of 12 to 24 weeks' gestation were enrolled at 7 centers between May 2007 and February 2010. All participants reported smoking at least 5 cigarettes a day at baseline.
The women were randomly assigned to receive either 8 weeks of active NRT patches at doses of 15 mg/16 hr plus behavioral cessation support from midwives (n = 521; 96.5% white; mean age, 26.4 years) or matching placebo patches and behavioral support (n = 529; 97.4% white; mean age, 26.2 years).

"The primary outcome was abstinence from the date of smoking cessation until delivery, as validated by measurement of exhaled carbon monoxide or salivary cotinine," report the investigators.

"Safety was assessed by monitoring for adverse pregnancy and birth outcomes."

Possible Explanation

Results showed that overall validated abstinence rates for the group receiving NRT was 9.4% compared with 7.6% in the group receiving placebo (unadjusted odds ratio [OR], 1.26; 95% confidence interval [CI], 0.82 - 1.96).

However, there was a significant between-group difference at the 1-month time point, with abstinence rates of 21.3% and 11.7% for the NRT group and placebo group, respectively (OR, 2.05; 95% CI, 1.46 - 2.88).

Compliance rates for longer than 1 month of use for the groups were only 7.2% and 2.8%, respectively. "Adverse events" were reported by only 8.8% of the women as the reason for treatment discontinuance.

Dr. Coleman noted that the fact that the participants did not use complete courses of the patches is something that has been found in several other studies of NRT in pregnancy.

"We know that metabolism is increased by the middle of the second trimester, but we don't know [exactly] when the increase begins," he said.

"My theory...is that in our trial, increases in metabolism became substantial at some point for most women at least 1 month after they joined the study — at roughly 20 weeks' gestation. This increase in metabolism would render NRT less effective at controlling their withdrawal symptoms, making them more likely to return to smoking."

There were no significant between-group differences in rates of adverse pregnancies and/or adverse birth outcomes — except for one. The women receiving NRT had significantly more cesarean deliveries than did the placebo group (20.7% vs 15.3%).

This finding "was not expected and...seems likely to be a chance occurrence," write the researchers.

"However, caution is warranted in interpreting the absence of apparent harm with [NRT] as an indication of its safety, given the low adherence rates."

Nevertheless, Dr. Coleman reported that the investigators hope to conduct a new trial that evaluates the safety and effectiveness of a higher dose of NRT in this patient population.

Clinical Uncertainty Remains

"In the current study, the higher abstinence rate at 1 month...indicates the efficacy of the medication; however, the majority of women who quit smoking for a short time did not use the patch for more than 4 weeks," writes Cheryl Oncken, MD, from the Departments of Medicine and Obstetrics and Gynecology at the University of Connecticut Health Center in Farmington, in an accompanying editorial.

Dr. Oncken notes that a "central question" is whether these women stopped NRT before or after they had a smoking relapse.

"[T]he former would suggest that future trials should focus on adherence to therapy, whereas the latter would suggest
that the medication is not efficacious for smoking cessation," she writes, adding that "[e]lucidating reasons for the low adherence" would also be helpful for future pharmacotherapy studies.

Overall, until more safety and efficacy data concerning NRT during pregnancy are released, "this therapy cannot be recommended with any clinical certainty," concludes Dr. Oncken.

The study was supported by a grant from the National Institute for Health Research Health Technology Assessment Program. The study authors have disclosed no relevant financial relationships. Dr. Oncken reports having received travel/accommodations and grants/pending grants for smoking cessation studies from Pfizer and Nabi Biopharmaceuticals. In addition, she reports a current contract with Pfizer to provide study medication and placebo inhalers for a newly funded National Institutes of Health study.


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No Evidence that Standard NRT Helps Pregnant Women Quit Smoking: 
Article Review by Dr. L. Zawertailo

This is a very well-controlled randomized, double-blind placebo-controlled clinical trial comparing nicotine patch treatment to placebo patch in pregnant smokers. There were 1,050 participants (521 randomized to nicotine patch (15 mg over 16 h) and 529 randomized to placebo patch). Everyone received manualized behavioural support through their midwives and were told they could access additional support through the National Health Service (study took place in the UK). Patch treatment was started on the target quit date – subjects were given 4 weeks worth of patches. Those who were abstinent at the end of the 4-week treatment period (CO validated) were issued another 4-week supply of patches. When subjects were admitted to hospital in labor, smoking status was ascertained and expired CO and salivary cotinine was measured.

The primary outcome was continuous abstinence from the quit date to child birth. Secondary outcomes were abstinence from quit date to one-month follow-up.

RESULTS

Compliance rates were very low in both groups. Only 7.2% in the nicotine patch group and 2.8% in the placebo group reported using the trial meds for more than one month. There was no difference between groups in the primary outcome. However, at one-month abstinence rates were significantly higher in the nicotine patch group compared to the placebo group. There were no between group differences in birth outcomes, except that there were more c-sections in the nicotine patch group compared to the placebo group.

CONCLUSIONS

The authors attribute that lack of difference in sustained abstinence rates to the low adherence to patch treatment. I agree with this conclusion.

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