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Association between nicotine replacement therapy use in pregnancy and smoking cessation

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ABSTRACT

Background: There is an urgent need to find better ways of helping pregnant smokers to stop. Randomized controlled trials (RCTs) have not detected an effect of nicotine replacement therapy (NRT) for smoking cessation in pregnancy. This may be because of inadequate dosing because of faster nicotine metabolism in this group. In England, many pregnant smokers use single form and combination NRT (patch plus a faster acting form). This correlational study examined whether the latter is associated with higher quit rates.

Methods: Routinely collected data from 3880 pregnant smokers attempting to stop in one of 44 Stop Smoking Services in England. The outcome measure was 4-week quit rates, verified by expired-air carbon monoxide level < 10 ppm. Outcome was compared between those not using medication versus using single form NRT (patch or one of the faster acting forms), or combination NRT. Potential confounders were intervention setting (specialist clinic, home visit, primary care, other), intervention type (one-to-one, group, drop-in, other), months pregnant, age, ethnicity and occupational group in multi-level logistic regressions.

Results: After adjustment, combination NRT was associated with higher odds of quitting compared with no medication (OR = 1.93, 95% CI = 1.13–3.29, $p = 0.016$), whereas single NRT showed no benefit (OR = 1.06, 95% CI = 0.60–1.86, $p = 0.84$).

Conclusions: Use of a combination of nicotine patch and a faster acting form may confer a benefit in terms of promoting smoking cessation during pregnancy. While this conclusion is based on correlational data, it lends support to continuing this treatment option pending confirmation by an RCT.

1. Introduction

Maternal smoking during pregnancy is associated with a range of negative health consequences for the offspring. It is known to be associated with low birth-weight, increased perinatal mortality and sudden infant death syndrome (Agrawal et al., 2010; Office of the Surgeon General: Office on Smoking and Health, 2004; US Department of Health and Human Services, 2001). It is an independent risk factor for obesity (Oken et al., 2008), early onset adult diabetes (Montgomery and Ekbom, 2002) and high blood pressure (Lawlor et al., 2004). Intrauterine exposure to maternal smoking is also associated with asthma and there is evidence that this is the case even in offspring of non-smoking mothers but who themselves were exposed in utero to maternal smoking, suggesting that smoking may induce genotoxicity (Li et al., 2005). Maternal smoking during pregnancy is associated with an increased risk of psychiatric morbidity and all cause mortality in childhood, adolescence and young adulthood (Ekblad et al., 2010).

In the United Kingdom, 26% of pregnant women smoke immediately before or during pregnancy, with 12% smoking throughout and at time of delivery (The NHS Information Centre, 2011); a similar proportion (13%) has been reported for the US (Tong et al., 2009). Due to social pressure and stigma, underreporting of smoking in pregnancy is likely (Shipton et al., 2009), so true smoking rates may be higher.

In the general population, pharmacological support has been found to be effective for smoking cessation and pharmacotherapy includes varenicline, bupropion and nicotine replacement therapy (NRT). NRT is either used as a single NRT product or a combination of NRT products (combination NRT), usually a transdermal patch

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and a faster-acting product such as gum, lozenge or inhalator (Stead et al., 2012). In the general population, randomized controlled trials have shown such a combination of NRT products to be more efficacious than single NRT (RR = 1.34, 95% CI = 1.18–1.51 (Stead et al., 2012) and a similar advantage has been found in clinical practice (OR = 1.42, 95% CI = 1.06–1.91; Brose et al., 2011).

In pregnancy, the evidence for the effectiveness of pharmacotherapy for smoking cessation is less conclusive. Varenicline and bupropion have not been evaluated in pregnancy (Tobacco Use and Dependence Guideline Panel, 2008) and are not licensed for use with this population of smokers. A systematic review of randomized controlled trials (RCTs) has found insufficient evidence to determine whether NRT in pregnancy is safe (Coleman et al., 2012), and guidelines for its use are cautious. In the UK, NRT can be used in pregnancy if it is judged to be necessary (Department of Health, 2011) (i.e., if the advantages and disadvantages of NRT use have been discussed and if it is deemed that cessation without NRT is unlikely), while the US Department of Health and Human Services does not recommend its use (Tobacco Use and Dependence Guideline Panel, 2008). A systematic review of RCTs (Coleman et al., 2012) has also found no clear evidence for effectiveness of NRT in pregnancy, while another meta-analysis that included a quasi-randomized controlled trial but excluded one of the RCTs in the systematic review suggested that it may have a benefit (Myung et al., 2012). Most trials evaluated the nicotine patch and none used combination NRT. Nicotine is more rapidly metabolized in pregnancy (Dempsey et al., 2002), theoretically making the same amount of NRT less effective than in non-pregnant smokers. Therefore, it could be that combination NRT would be needed to confer a significant benefit.

The English Stop Smoking Services provide a unique opportunity to evaluate the effectiveness of NRT in pregnancy. The services have been set up to offer support to all smokers in England and are free at the point of access. Each year, about 800,000 attempts to stop smoking are made with the support of the services; among those are approximately 20,000 pregnant women (Department of Health, 2011). The services offer an evidence-based combination of medication and behavioral support. Pregnant smokers can choose to use no medication, a single NRT product or combination NRT. Support can be provided in different settings such as specialist clinics, where it is provided by practitioners specifically employed to deliver stop smoking support or in other settings such as primary care or pharmacies, where it is often delivered by health care professionals alongside their main role, e.g. as nurse of pharmacist. Overall, specialist clinic settings have been found to be more effective than interventions set in primary care (Brose et al., 2011). The type of behavioral support also varies; most smokers are seen in one-to-one situations, while some are seen in groups or in drop-ins (without appointment). Overall, groups have been found to be more effective than one-to-one interventions, while drop-ins appear to be less effective (Bauld et al., 2010; Brose et al., 2011).

This study aimed to assess the association of single and combination NRT with success of quit attempts of pregnant smokers in clinical practice while adjusting for smoker and treatment characteristics. If an apparent benefit is observed for combination NRT, which has not yet been evaluated in RCTs, it would lend support to the current practice in England pending confirmation by an RCT.

2. Methods

2.1. Study design

Anonymised routinely recorded data were used on pregnant smokers trying to stop with the support of the English Stop Smoking Services from April 2009 to June 2011. As defined by the Department of Health (Department of Health, 2011), a supported quit attempt is completed with a follow-up four weeks after the quit date. Although the standard follow-up period of four weeks is short, in pregnancy even this would be expected to confer a benefit to the fetus, and other evidence suggests that the relative quit rates tend to be sustained longer term (Ferguson et al., 2005; Stapleton, 1998). Anonymised data were obtained from QuitManager (North 51, Nottingham, UK), an online database system for recording information on client demographics, intervention characteristics and outcomes in accordance with the standard monitoring requirements of the Department of Health in England (Department of Health, 2011). Forty-nine of the 58 services using it at the time agreed to share anonymised data for the current study, representing 32% of all English stop smoking services. Ethical approval was not required for this audit of routinely collected and anonymised NHS clinical data.

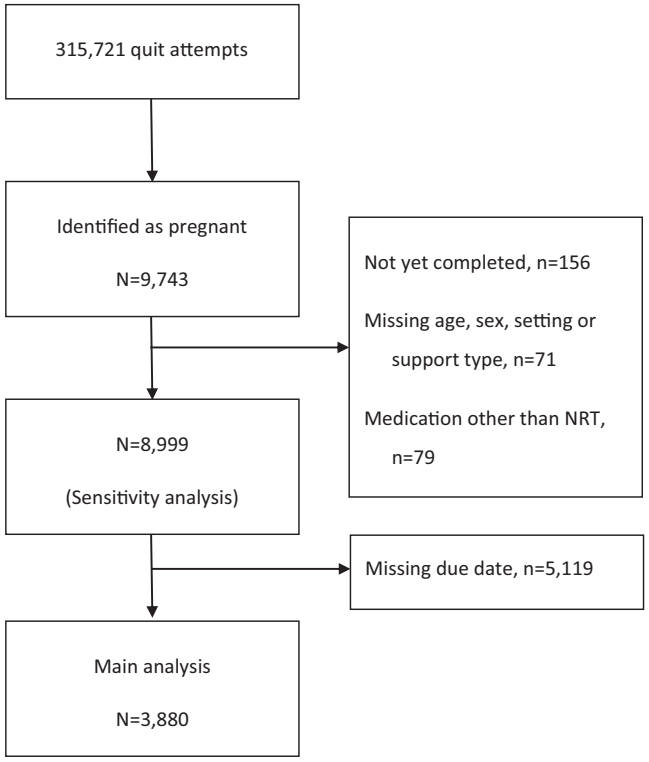

Fig. 1. Sample selection.

2.2. Participants

Data from pregnant smokers (n = 9743) were identified in a data base of 315,721 cases. Cases for which 4-week follow-up data had not yet been entered were excluded (n = 156). All cases with missing age (n = 49), intervention setting (n = 7) or intervention type (n = 11), or gender recorded as male, indicating data entry errors (n = 4) were excluded, as were 73 cases that recorded that clients had received varenicline and six that had received bupropion. Cases receiving telephone support (n = 438) were excluded as, due to the nature of the intervention, biochemical validation of abstinence is rarely attempted. Cases that did not have information on due date recorded (n = 5119) were excluded from the main analyses but included in a sensitivity analysis. Thus, 3880 cases supported by one of 44 regional stop smoking services were included in the main analysis (Fig. 1). Client and intervention characteristics are described in Table 1. It is not recorded if a pregnant smoker made more than one quit attempt with the support of the stop smoking services during their pregnancy, so occasionally, multiple attempts during the same pregnancy may have been included.

2.3. Measures

The main outcome measure was biochemically validated successful quitting as defined by the Russell Standard (Clinical) and as stipulated by the Department of Health in England: i.e. quitters who reported four weeks after the designated quit date that they have not smoked for at least 2 weeks and their expired-air carbon monoxide (CO) concentration is below 10 parts per million (Department of Health, 2011). As is standard practice, those who did not report their smoking status or did not attend for CO validation at 4-week follow-up were regarded as continuing to smoke (Department of Health, 2011; West et al., 2005).

Predictors included were medication (none, single NRT, combination NRT), intervention setting (specialist clinic, home visit, primary care, other), intervention type (one-to-one, group, drop-in, other), age at the time of the quit attempt, occupational grade (in employment, not in employment, full-time student, unable to code), ethnicity (white, other or unknown) and months pregnant. For 1127 clients, data