

Safety and Efficacy of Nicotine Replacement Therapy in the Perioperative Period: A Narrative Review

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Abstract

Patients who smoke cigarettes are at increased risk for development of complications both during and after surgical procedures, including respiratory, cardiac, and healing-related complications. Abstinence from smoking can considerably reduce these risks. Pharmacotherapy, including nicotine replacement therapy (NRT), is an important component of efficacious tobacco use interventions. However, the use of NRT in the perioperative period is controversial. In this narrative review, we discuss the current evidence for the efficacy and safety of NRT in patients scheduled for surgical procedures, with emphasis on evidence from human studies. We performed a literature search for articles published from January 1, 1990, through May 1, 2015, in the PubMed online database using various permutations of the Medical Subject Headings terms *surgery*; *surgical procedures*, *operative*; *nicotine*; and *smoking cessation*. Studies were selected for inclusion according to their relevance to the preclinical and clinical evidence pertaining to how NRT affects surgical outcome and long-term rates of abstinence from tobacco. There is strong evidence that NRT enhances the efficacy of tobacco use interventions. Some preclinical studies suggest that nicotine in high doses that exceed those produced by NRT decreases the viability of skin flaps. Although the available data are limited, there is no evidence from human studies that NRT increases the risk of healing-related or cardiovascular complications. Individual clinical trials of tobacco use interventions that include NRT have revealed either no effect or a reduction in complication rates. Therefore, given the benefits of smoking abstinence to both perioperative outcomes and long-term health and the efficacy of NRT in achieving and maintaining abstinence, any policies that prohibit the use of NRT in surgical patients should be reexamined.

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Patients who smoke cigarettes are at increased risk for development of complications both during and after surgical procedures, including respiratory, cardiac, and healing-related complications.^{1,2} Abstinence from smoking can considerably reduce these risks.³⁻⁵ In addition, surgical treatment itself has been reported to increase the likelihood of quitting smoking, even if the need for surgical intervention is not directly related to a patient's smoking status.^{6,7} Thus, the scheduling of elective surgical procedures presents a key opportunity to provide tobacco use interventions at this "teachable moment" for smoking cessation.⁶ Nonetheless, many patients still find it difficult to abstain from cigarettes during the perioperative period, with a substantial proportion of patients reporting smoking even on the morning of their surgical procedure.⁸

Pharmacotherapy, including nicotine replacement therapy (NRT), is an important

component of efficacious tobacco use interventions.⁹ However, the use of NRT in the time around surgery (the perioperative period) is controversial. Nicotine has widespread pharmacological actions on multiple organ systems, and concerns have been raised that NRT may increase the risk of wound-related and cardiovascular complications. These concerns have led some surgeons in the United States to prohibit the use of NRT in the perioperative period, including in some cases the requirement of several nicotine-free weeks before operation. A recent survey of general surgeons found that only 34% agreed that NRT was safe for patients to use during surgical treatment, although 61% agreed that it was safe after the operation.¹⁰ Such perceptions can remove a valuable tool that could help smokers facing surgical treatment quit.

The purpose of this narrative review is to discuss the current evidence for NRT's efficacy and safety in patients scheduled for surgical

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ARTICLE HIGHLIGHTS

- Patients who smoke cigarettes are at increased risk for perioperative complications, including healing-related and cardiovascular complications.
- Meta-analysis of existing studies, including studies that utilized nicotine replacement therapy (NRT) as a component of tobacco use interventions, reveals that abstinence from smoking reduces these risks.
- Nicotine replacement therapy increases the efficacy of tobacco use interventions, increasing the likelihood that patients can maintain abstinence from smoking.
- Although the available data are limited, there is no evidence from human studies that NRT increases the risk of healing-related or cardiovascular complications.
- Given the benefits of smoking abstinence to both perioperative outcomes and long-term health and the efficacy of NRT in achieving and maintaining abstinence, any policies that prohibit the use of NRT in surgical patients should be reexamined.

treatment and other invasive procedures. We performed a literature search for articles published from January 1, 1990, through May 1, 2015, in the PubMed online database using various permutations of the Medical Subject Headings terms *surgery*; *surgical procedures*; *operative*; *nicotine*; and *smoking cessation*. Randomized controlled trials, prospective cohort studies, laboratory-based investigations, systematic reviews, and meta-analyses were selected for inclusion according to their relevance to the various topic areas examined in this article, with particular attention to human studies.

EFFICACY OF NRT

Nicotine replacement therapy is currently available in the United States in 5 delivery methods—gum, lozenges, nasal spray, patches, and inhalers.¹¹ In this review, NRT refers to the nicotine patch (7, 14, or 21 mg of nicotine per patch, depending on baseline cigarette consumption) unless otherwise indicated. Other pharmacotherapy for nicotine dependence is available, including the partial nicotinic agonist varenicline and the antidepressant bupropion (Table), but NRT is the only one available without a prescription (in

gum and patch forms) and is supported by the deepest evidence base.⁹ The pharmacological rationale for its efficacy is that provision of nicotine will reduce nicotine withdrawal symptoms that could otherwise occur in smokers attempting abstinence.¹² Plasma nicotine levels provided by NRT vary according to dose and delivery method but in general are lower than those maintained during active smoking when conventional dosing is employed.^{11,12} The evidence for its efficacy to increase abstinence rates is robust, and national guidelines for tobacco treatment include provision of NRT as an A level, evidenced-based recommendation for all health care professionals.⁹ In a wide range of populations, addition of NRT in any form to any tobacco use intervention in efficacy trials increases abstinence rates by approximately 60%,^{11,13} although effectiveness trials and observational studies reveal that its population-level effectiveness to produce sustained abstinence is less.¹⁴

Nicotine replacement therapy is commonly incorporated as a component of tobacco use interventions specifically designed for surgical patients, which typically combine pharmacological and behavioral approaches. These interventions are efficacious in terms of both increasing abstinence rates and decreasing perioperative complications. The most recent systematic review of perioperative tobacco use interventions included 12 studies examining abstinence outcomes and concluded that such interventions are efficacious to promote both short- and longer-term abstinence, with efficacy increasing as intervention intensity increases.⁵ Of the 12 trials included in the review, with sample sizes ranging from 46 to 286 participants, 9 included NRT as a component of their interventions. None of these studies specifically examined the efficacy of adding NRT to behavioral interventions in terms of maintaining sustained perioperative abstinence, although there is no reason to believe that its efficacy would be less in the perioperative period compared with other settings.

The sole placebo-controlled trial of NRT in the perioperative period (N=121) was not intended or powered to examine its effects on postoperative abstinence.¹⁵ Indeed, a tobacco use intervention was not delivered; rather, the purpose of the study was to examine the effect of NRT on perioperative stress and nicotine withdrawal symptoms. Nonetheless, even without a

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