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Healing Begins with Knowledge

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A Clinical Review Article on Current Therapeutic

Modalities to Aid Smoking Cessation

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Dedication

I would like to thank my family, who I love so very much, for their unconditional support. Matt, thank you so much for all of the encouragement and for believing in me. I could not have made it through without you. A special thank you as well to Professor Parish for his unfaltering patience and gentle guidance.

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Introduction and Background

In 2001 it was estimated that 46.2 million adults in the United States smoke cigarettes (Centers for Disease Control and Prevention *Cigarette Smoking Among Adults—United States, 2001*, 2003). Of these adults 70% want to quit smoking and 46% try to quit smoking each year with only 2.5% able to quit permanently (Fiore, 2000; Sweeney, Fant, Fagerstrom, McGovern, & Henningfield, 2001).

Smoking cigarettes poses an extraordinary hazard not only to those that smoke cigarettes but also to persons who are exposed to second hand smoke. Smoking cigarettes is known to cause chronic lung disease, heart disease, stroke, and cancer of the lung, larynx, esophagus, mouth, and bladder. It also contributes to the development of cancer of the cervix, pancreas and kidney. In addition, second hand smoke poses a significant health risk with an estimated 3,000 non-smokers dying of lung cancer each year and greater than 35,000 dying of heart disease. Up to 300,000 children experience respiratory tract infections due to exposure to second hand smoke. Babies born to women who smoked during pregnancy are at higher risk for low birth weight, SIDS, and respiratory distress. Smoking related illnesses cost the nation greater than $150 billion each year and currently cigarette smoking is responsible for 1 in 5 deaths (Centers for Disease Control and Prevention *Targeting Tobacco Use: The Nation's Leading Cause of Death*, 2003).

The main substance responsible for tobacco dependence is nicotine. As such, nicotine replacement therapy (NRT) has been developed and has proved to be a means to control withdrawal symptoms related to tobacco dependence and to aid persons in smoking cessation (Houezec, 2003). Patients using NRT improve the likelihood of

remaining abstinent at one year, at a rate 1.5 to 2.7 times higher than those using placebo (Sims & Fiore, 2002). Common symptoms of nicotine/tobacco withdrawal include craving, weight gain, insomnia, irritability, depressed mood, frustration, anger, anxiety, difficulty in concentrating, and restlessness. These symptoms can be unrelenting and make it quite difficult for cigarette smokers to abstain from repeated tobacco use even after the utilization of pharmacotherapy (Sweeney et al., 2001). These same withdrawal symptoms also in part explain a very high relapse rate, with some studies reporting relapse rates up to 80% in the first year following cessation (Sims & Fiore, 2002). Currently, there are six first line therapies indicated to aid patients in smoking cessation, five that are nicotine containing and one that is not. The five nicotine containing FDA approved methods of nicotine replacement therapy are nicotine gum, inhaler, patch, nasal spray and lozenge. The non-nicotine containing therapy is bupropion SR (Zyban) (Centers for Disease Control and Prevention *Coverage For Tobacco Use Cessation Treatments,* 2004). Bupropion SR is hypothesized to be effective for smoking cessation by enhancing dopaminergic activity, as it is a selective reuptake inhibitor of both dopamine and norepinephrine (Sutherland, 2002).

The physiological basis for nicotine replacement is two-fold. Consumers who regularly use tobacco products maintain high daily levels of nicotine and experience transient bursts of elevated nicotine levels throughout the day (Sweeney et al., 2001). None of the aforementioned therapies, when used singly, has the capability to duplicate the dual effects of nicotine tobacco users achieve with chronic use of tobacco products. Recent studies have shown that combination NRT is more effective for smoking cessation than monotherapy ("New Tools to help you quit smoking," 1999).

It is the responsibility of all health care professionals to offer repeated guidance, support, and advice in regard to the importance of smoking cessation and offer the best possible means by which patients may succeed in abstaining from smoking cigarettes. Health care professionals may not be utilizing the most effective methods available to help chronic tobacco users quit, for a number of reasons. 'Nicotine dependence' and 'Nicotine withdrawal' are now designated as medical conditions by the DSM-IV of the American Psychological Association (Sweeney et al., 2001). Nicotine dependence is just that, a dependence, and should be viewed in the same light as patients who suffer from opiate, amphetamine or cocaine dependence. It is a chronic condition in which remissions and relapses are to be expected. It is thought that clinicians do not think of tobacco dependence in this light and are therefore discouraged when patients relapse to tobacco use and perhaps do not revisit quitting with them again (Fiore, 2000). It is also thought that clinicians do not discuss NRT with patients who want to try to quit smoking, for a few reasons. First, NRT is available over-the-counter (OTC) and classically clinicians are more inclined and/or informed to discuss prescription options first. Second, they may lack knowledge of how to tailor OTC NRT to a patient's individual needs, including combination therapy. And lastly, they may be hesitant to prescribe NRT to patients with known heart disease.

The role that nicotine plays in smoking related illness is misunderstood. Nicotine is responsible for the addictive properties of tobacco use, however it is the tar, carbon monoxide, and other harmful gases taken in with the nicotine that cause chronic bronchitis, emphysema and lung cancer. Nicotine has been shown to exert cardiovascular effects and has been recognized as an agent that may precipitate a

cardiovascular event. The mechanism of action being, production of a hypercoagulable state, that may promote thrombosis. However, this phenomenon is associated with a bolus dose of nicotine achieved through cigarette smoke and is not associated with gradual delivery of nicotine via NRT (Houezec, 2003). Although recent studies have shown that combination NRT can increase abstinence rates up to 15% over monotherapeutic NRT, it currently is not FDA approved. Labels on various products do not promote combination NRT use and in fact warn consumers against it (Sweeney et al., 2001). Despite this current lack of FDA approval, combination therapy should be considered for all patients on an individualized basis, especially those who have a significant history of tobacco use and for those who have failed monotherapy.

The effects of smoking cigarettes and second hand cigarette smoke are harmful to all that are exposed to it. It is estimated that 442,398 deaths are attributable to cigarette smoking each year (Centers for Disease Control and Prevention *Targeting Tobacco Use: The Nation's Leading Cause of Death,* 2003). It is the responsibility of physician assistants and all health care personnel to encourage and support smokers in their efforts to quit, employing the most effective strategies available. 'Tobacco dependence is a complex mixture of pharmacological, psychological and social components (Houezec, 2003). The scope of this article will focus on the pharmacological aspects of nicotine dependence and will review currently available therapies for smoking cessation and how these aids may best be employed to improve smoking cessation rates.

Pharmacokinetics of Nicotine

Tobacco products are widely recognized as highly addictive agents. As noted previously, nicotine has been implicated as the primary addictive ingredient in tobacco products. It is important to note that the abuse potential of an agent is related to the time between administration and the resulting positive reinforcing effects. In this light, smoking in particular proves to be exceptionally addictive as it is rapidly absorbed via the pulmonary venous system and reaches the brain in 10-20 seconds. This is more rapid than the intravenous administration and systemic venous absorption of nicotine.

Nicotine is a weak base that rapidly crosses membranes at physiologic blood pH (7.4). It also readily crosses the basic oral and nasal mucous membranes. Absorption is further facilitated by the thin epithelium and rich blood supply of these mucous membranes. Because smoking behavior varies greatly from person to person, it is hard to predict nicotine exposure on an individual basis. However, it is estimated that on average, smokers absorb about 1mg of nicotine per cigarette. The liver is the primary site of nicotine metabolism and its elimination half-life is two hours. With an elimination half-life of two hours and regular smoking it is consistent that blood nicotine levels increase over 6-8 hours. Average afternoon blood nicotine levels range from 10-50 ng/mL. In addition, depending on how cigarettes are smoked, they allow incremental peaks in blood nicotine concentrations of 5-30 ng/mL. Blood nicotine concentrations then fall throughout the night leaving smokers with little nicotine in their systems come morning (Houezec, 2003).

Nicotine Replacement Therapy

For more than twenty years, nicotine replacement therapy has been used to treat tobacco dependence (Haustein, Krause, Haustein, Rasmussen, & Cort, 2003). It remains the mainstay of treatment with proven pharmacological efficacy in randomized clinical trials doubling cessation rates in active versus placebo groups (Hurt, 1999). As noted earlier, there are five nicotine containing FDA approved methods of nicotine replacement therapy available on the market. Studies have shown that all forms of NRT are equally effective as part of a strategy for smoking cessation (Diefenbach, Smith, & Nahelsky, 2003). A randomized comparative trial of nicotine gum, nicotine nasal spray, nicotine transdermal patch, and nicotine inhaler concluded that perceived helpfulness, effects on craving, withdrawal symptoms and abstinence rates were similar among the four therapies (Hajek, West, Foulds, Nilsson, Burrows, & Meadow, 1999). In another study, West, Hajek, Nilsson, Foulds, May, & Meadows (2001) were interested in individual preferences and responses to nicotine gum, patch, nasal spray and inhaler and found that successful cessation was not related to a patient obtaining their first choice nicotine replacement product. Despite these findings, it is important to note that the rate of nicotine delivery, based on the pharmacokinetic properties of the different delivery systems available, proves to be a major difference between NRT products (Hurt et al., 1998). Patient needs, tolerability and cost should be considered when deciding which form of therapy is appropriate. These matters as well as method and onset of action, dosing, adverse reactions and cautions will be discussed for all the therapies reviewed in this article.

Nicotine Gum

Available since 1984, nicotine polacrilex gum is the oldest of the nicotine replacement product preparations (Hurt, 1999; Watts, Noble, Smith, & Disco, 2002). It became available over the counter in 1996 in two doses: 2-mg and 4-mg (Thompson & Hunter, 1998). The 2-mg dose is recommended for smokers smoking 1-24 cigarettes per day. The 4-mg dose is recommended for heavier smokers (>24 cigarettes per day) (Watts et al., 2002). Recommended duration of treatment is twelve weeks. The dosing schedule is as follows: chew one piece every 1-2 hours for the first six weeks of treatment, then one piece every 2-4 hours for the next three weeks, and finally one piece every 4-8 hours for the final three weeks. Maximum daily dosage should not exceed 24 pieces of gum (Sims & Fiore, 2002).

Pharmacologically, nicotine is absorbed slowly through the buccal mucosa with peak nicotine concentrations achieved 30 minutes after starting chewing. The gum provides replacement of approximately 30-64% of pre-cessation nicotine plasma concentrations. Adverse events associated with nicotine gum use include sore mouth or sore throat, dyspepsia, nausea, hiccups, flatulence, diarrhea and oral blisters. Under-dosing is a problem associated with nicotine gum use. Patients must also take special care to avoid acidic beverages while using the gum as they can impair the absorption of nicotine. Advantages of nicotine gum use include delayed weight gain, high patient tolerability, and patient control of nicotine intake. Approximate cost per day is $5.23 for 10, 2-mg pieces and $5.90 per day for 10, 4-mg pieces (Thompson & Hunter, 1998; Watts et al., 2002).

Nicotine Patch

The nicotine transdermal patch became available in the US as an aid to smoking cessation in 1991. It has been available over-the-counter since 1999 (Watts et al., 2002). There are four FDA approved patches available (Thompson & Hunter, 1998). The two patches available over-the-counter come in the following strengths: 5, 7, 10, 14, 15, and 21 mg. The recommended dosing schedule is 21mg/day for 6 weeks, then 14 mg/day for 2 weeks, followed by 7 mg/day for 2 weeks, then discontinue. A lower dose regimen for those smoking <10 cigarettes per day is 14mg/day for 6 weeks, then 7 mg/day for 2 weeks. The patches are worn for 16 hours or 24 hours a day, as directed for 8-10 weeks (Murphy, 2004).

The patches work by delivering a fixed dose of nicotine transdermally at a constant rate. Following patch application, plasma nicotine concentrations begin to rise, slowly peaking in 4-8 hours. It takes 2-3 days after initiation of therapy to reach steady state nicotine concentrations (Thompson & Hunter, 1998). In those who smoke a pack of cigarettes per day, standard dose patch therapy provides a median percent nicotine replacement of about 50% (Hurt, 1999). Advantages of the nicotine patch include ease of use and greater patient compliance attributed to once-a-day dosing. Local adverse effects associated with use of the patch include skin irritation at the application site to include erythema, burning, pruritis, edema, and less often vesicles. Insomnia, abnormal dreams, headache, nausea, and vertigo are associated systemic effects (Dale, Ebbert, Hays, & Hurt, 2000; Thompson & Hunter, 1998). An important disadvantage associated with use of the nicotine patch is that of its inability to respond to patient's urges to

smoke due to its steady method of nicotine delivery (Houezec, 2003). Approximate cost per day is $3.50-$3.89 (Watts et al., 2002).

Nicotine Nasal Spray

Nicotine nasal spray was approved as a treatment for nicotine dependence in the United States in 1996 and became available by prescription in 1997 (Thompson & Hunter, 1998; Watts et al., 2002). Today its accessibility remains by prescription only. The nasal spray is the only smoking cessation medication available whose pharmacological profile most closely mimics that of smoking a cigarette. It is available in a 10ml spray bottle that contains a water-based buffered solution, which contains 100mg of nicotine (Sims & Fiore, 2002; Thompson & Hunter, 1998). One spray is designed to deliver 0.5mg of nicotine; one dose is considered one spray in each nostril, which therefore delivers 1mg of nicotine. Recommended treatment is 1-2 doses per hour with a maximum of 5 doses/hr and 40 doses/day for 3 months (Murphy, 2004).

Nicotine is rapidly absorbed via the nasal mucosa with peak concentrations reached in 5-10 minutes. This rapid absorption is especially useful for treatment of the highly dependent smoker. Advantages of the nasal spray include on demand self-administration of nicotine to satisfy patient's urges to smoke and venous plasma concentrations of nicotine similar to that of 2mg nicotine gum (Thompson & Hunter; Houezec, 2003). A single 1mg dose of the nasal spray produces peak venous nicotine concentrations of 2-12 ng/ml and has been reported to provide more immediate relief of craving for a cigarette versus a single dose of 4mg nicotine gum (Hurt et al., 1998). Although adverse affects associated with use of the nasal spray usually subside in the

first week of use, most users report nasal and throat irritation, runny nose, sneezing, watery eyes, and cough. Patients with nasal or sinus problems, allergies, or asthma should consider alternative treatments as the nasal spray could exacerbate these conditions. Underadministration remains a problem associated with the nasal spray. Average cost per day, with an estimated 8 to 40 doses administered per day is $3.27 to $16.33 (Watts et al., 2002).

Nicotine Inhaler

In 1998, the nicotine inhaler became available by prescription in the United States to treat tobacco dependence (Watts et al., 2002). It remains a prescription only medication today. The inhaler, which resembles a cigarette, consists of a plastic mouthpiece and a cartridge. The cartridge contains 10mg of nicotine and 1mg of menthol. Though the cartridge contains 10mg of nicotine, it delivers only 4mg. The nicotine inhaler differs from cigarette smoking and traditional inhalers in that the device is meant to deliver vaporized nicotine to the buccal mucosa, not inhaled into the lungs (Okuyemi, Ahluwalia, & Wadland, 2001; Dale et al., 2000). Absorption is slow with rates similar to that of nicotine gum (Dale et al., 2000). The recommended dosage is 6 to 16 cartridges per day for 12 weeks duration. If needed, treatment can then be tapered over another 12-week period with a maximum of 6 months of therapy (Murphy, 2004). Compared with customary cigarette smoking, the ad lib use of the inhaler provides about 33% nicotine replacement (Rennard & Daughton, 2003).

An advantage of the nicotine inhaler is that its use mimics some of the behavior routines associated with cigarette smoking (Dale et al., 2000). As with other NRT's,

underuse of the inhaler remains a problem. Reported adverse events include mouth and

throat irritation, and cough (Watts et al., 1998). Use of the inhaler should be avoided in

persons with reactive airway disease as any inhaled nicotine can cause bronchospasm

(Rennard & Daughton, 2003). Cost per day with average use of the nicotine cartridges

(6-16 cartridges/day) ranges from $5.82 to $15.52 (Watts et al., 1998).

Nicotine Lozenge

In 2002, nicotine polacrilex lozenges received FDA approval for over-the-counter

marketing of the product for smoking cessation. It is available in 2mg and 4mg doses

and has demonstrated efficacy similar to that of nicotine gum (Rennard & Daughton,

2003; Murphy, 2004). Dosing is determined by the patient's smoking history. For

persons who smoke within 30 minutes of waking, the recommended dose is 4mg and

likewise for persons smoking beyond 30 minutes from waking, the recommended dose

is 2mg. The dosing schedule is to dissolve one lozenge in the mouth every 1-2 hours,

with a minimum of 9 lozenges used daily, for 6 weeks, then one lozenge every 2-4

hours for 3 weeks and finally one lozenge every 4-8 hours for 3 weeks. Duration of

therapy is recommended for 12 weeks. An advantage of lozenge use includes patient

control of amount and time of dosing, which can be accomplished on demand. In

addition, when compared with equal dosing of nicotine gum the lozenge has to offer

about 25% more nicotine replacement (Shiffman, Dresler, Hajek, Gilburt, Targett, &

Strahs, 2002). Patients are to avoid eating and drinking 15 minutes prior to and during

use of the lozenge and are to minimize swallowing. Adverse reactions include mouth

and throat irritation, headache, hiccups, dizziness, upset stomach, hypertension and

dizziness (Murphy, 2004).

Non-nicotine Replacement Therapy

Bupropion Hydrochloride

Bupropion hydrochloride has been used in the United States for about 15 years as a treatment for major depression (Rennard & Daughton, 2004). Though there is a strong correlation between tobacco users and past history of depression, bupropion appears to be equally effective in patients, regardless of past history of depression. This implies that its ability to aid in smoking cessation is not related to its antidepressant effects (Hurt, 1999; Sutherland, 2002). Classified as an atypical antidepressant, its exact mechanism of action in regards to aiding smoking cessation is unclear, but it has been proven effective in double-blind placebo controlled trials (Martinez-Raga, Keaney, Sutherland, Perez-Galvez, & Strang, 2003). It has been hypothesized that bupropion works to ameliorate nicotine withdrawal symptoms by inhibiting the reuptake of the neurotransmitters norepinephrine, dopamine, and to a lesser degree serotonin. However, a recent study suggests that instead of inhibiting reuptake, bupropion may directly stimulate the release of norepinephrine, which in turn mounts an excitatory effect on serotonin releasing neurons, not dopamine releasing neurons. This suggests that the major action of bupropion is on the serotonergic system (Martinez-Raga et al., 2003). Bupropion is the first and only non-nicotine containing FDA approved medication used to treat nicotine dependence (Martinez-Raga et al., 2003; Dale et al., 2000). It gained FDA approval in 1997 and is available by prescription only in a 150mg sustained release formulation (bupropion SR) (Gold, Rubey, & Harvey, 2002; Murphy, 2004). Initial dosing for patients that are at least 18 years of age is 150mg daily for 3 days, then 150mg twice daily thereafter. Maximum daily dose should not exceed 300mg and each

dose should be separated by at least 8 hours time. Patients are to set a quit day within 1-2 weeks of initiating therapy. Therapy is recommended for 7-12 weeks duration, although the exact, most efficacious duration of treatment is unknown (Murphy, 2004; Rennard & Daughton, 2003). Current recommendations state that continuation of treatment for an additional 6 months or indefinitely is a reasonable option for patients that were able to quit successfully after the standard treatment regimen (Sims & Fiore, 2002; Barringer & Weaver, 2002). Conversely, if patients are still smoking after 7 weeks of treatment with bupropion, the medication should be discontinued at that time.

Following administration of a single 150mg dose of bupropion SR, peak plasma concentrations of the drug are achieved in about 3 hours (Martinez-Raga et al., 2003). Bupropion is an effective treatment option for patients who desire non-nicotine containing therapy or could not tolerate or failed NRT (Okuyemi et al., 2001; Sutherland, 2002). Adverse effects associated with use of bupropion are mild and may include insomnia, dry mouth, anxiety, headache and rash (Sutherland, 2002). There is a seizure risk associated with use of bupropion. Although the estimated risk of seizure is similar to that of other antidepressant medications bupropion is contraindicated in patients with a history of seizure disorder (Peters & Morgan, 2002). Scenarios in which a patient's seizure threshold may be lowered are also contraindications to the use of bupropion. This may include use of medications such as monoamine oxidase (MAO) inhibitors, or the existence of the following conditions: eating disorder, alcohol abuse, CNS tumor, history of head trauma, type 1 or 2 diabetes, cirrhosis, or bipolar disorder (Martinez-Raga et al., 2003). The approximate cost of bupropion SR is $1.60/150mg. Therefore, the first 3 days of therapy with once daily dosing of 150mg will cost $1.60/day.

Treatment thereafter, with twice daily dosing (300mg) will cost $3.20/day (Watts et al.,

2002).

Combination Therapy

A number of studies have been published within the past 10 years evaluating the effects of combination therapy on smoking cessation. Suppression of nicotine withdrawal symptoms as well as smoking cessation rates are usual primary outcomes of interest of the studies. Employing the use of 2 NRTs simultaneously has been reported to increase cessation rates an additional 5-10% (Gold et al., 2002). Though current product information does not endorse the simultaneous use of different NRT formulations, there is a pharmacological basis for employing combination NRT (Peters & Morgan, 2002). Especially combining therapies that couple a long acting formulation (nicotine patch), with a shorter acting formulation (nicotine gum, nicotine nasal spray, or nicotine inhaler), the latter being used on an as-needed basis (Hurt, 1999). Efficacy is improved using combinations such as these (Okuyemi et al., 2001). Another rationale for employing combination NRT is that dual therapy provides enhanced withdrawal control, as current NRT formulations used alone provide less than half of the nicotine plasma concentrations moderate to heavy smokers are familiar with from cigarettes (Cinciripini, 1999; Stapleton, 1999). Further studies have investigated the merit of combining NRT (nicotine patch) with bupropion. There is rationale to combine these medications, as each act on different parts of the brain (Hurt, 1999). Current recommendations suggest reserving combination therapy for moderate or highly dependent smokers who were unable to quit with a single agent and suffered significant withdrawal (Okuyemi et al., 2001; Peters & Morgan, 2002). Special attention must be made when considering combination therapy as the use of two agents simultaneously could be cost prohibitive (Watts et al., 2002).

Nicotine patch + Nicotine gum

Nicotine patch in combination with nicotine gum has been shown to increase smoking abstinence rates as well as reduce nicotine withdrawal symptoms compared with either treatment alone (Sweeney et al., 2001). The average nicotine substitution for the combined therapy has been found to be 61.7% versus 39.8% replacement for patch only therapy. Abstinence rates for the combination therapy have been demonstrated to be up to 50% greater than patch only therapy and are statistically significant up to 24 weeks (Kornitzer, Boutsen, Dramaix, Thijs, & Gustavsson, 1995).

Nicotine patch + Nicotine nasal spray

Blondal, Gudmundsson, Olafsdottir, Gustavsson, and Westin (1999) found that using combination nicotine patch for 5 months with continued use of nicotine nasal spray for one year resulted in greater efficacy for smoking cessation versus using patch only therapy. Abstinence rates for the combination therapy were doubled and tripled during the active treatment phase of the study. Furthermore, long-term follow up abstinence rates of study subjects who received the combination therapy were doubled. Subjects receiving combination therapy were afforded nicotine replacement greater than 50% of smoking concentrations (Stapleton, 1999). Another study by Croghan et al. (2003), found that combining the nicotine patch with the nicotine nasal spray was more efficacious for achieving smoking abstinence compared to either therapy alone, though the results were only significant for a short time.

Nicotine patch + Nicotine inhaler

In accordance with the dual therapies described above, nicotine patch in combination with nicotine inhaler has also been reported to be a more effective method for improving smoking abstinence rates versus use of the nicotine inhaler only. As described by Bohadana, Nilsson, Rasmussen, & Martinet (2000), short (6 weeks) and long (12 months) term abstinence rates were consistently higher in subjects who received both forms of NRT. The combination was also reported to provide greater than 50% nicotine replacement of prior smoking levels (Bohadana et al., 2000).

Nicotine patch + Bupropion

Bupropion SR in combination with the nicotine patch has demonstrated abstinence rates superior to that of therapy with nicotine patch alone or placebo in a randomized clinical trial. However, these findings were not significant when compared with abstinence rates achieved with the use of Bupropion SR alone. (Jorenby et al., 1999). In a similar more recent naturalistic study, Gold et al. (2002) found comparable abstinence rates across treatment groups with again the combination therapy achieving the highest abstinence values.

Methodology

A review was undertaken of the relevant smoking cessation literature from 1995-present. Journal articles were searched using PubMed, Medline, CINAHL, and UpToDate databases using key words such as: Nicotine, Nicotine Replacement, Smoking Cessation, Combination Therapy, & Combined Modality Therapy. Selection of articles was limited to those printed in the English language.

Discussion

Based on the current literature, there is evidence to support NRT products as equally effective therapies for the treatment of tobacco dependence that improve abstinence rates as well as alleviate nicotine withdrawal symptoms. Bupropion SR, a nicotine free therapy, has also proved to be an efficacious medication for the treatment of tobacco dependence. It alleviates withdrawal symptoms and as with NRT approximately doubles abstinence rates (Fiore, 2000). The efficacy of combining therapies has also been established and has demonstrated cessation rates that are double those of single therapy regimens. These results demonstrate efficacy comparable to monotherapy versus placebo (Stapleton, 1999).

Weight gain is a common association and concern with regards to smoking cessation. Average weight gain upon stopping smoking is between 8-11 pounds. All of the NRTs have been shown to delay but do not prevent weight gain (Diefenbach & Smith, 2003; Rennard & Daughton, 2004). In addition, a randomized, placebo-controlled trial found that patients treated with bupropion for one year experienced less weight gain over time versus those who received placebo (Rennard & Daughton, 2004). Furthermore, Jorenby et al. (1999) reported patients treated with the combination of nicotine patch and bupropion experienced the least amount of weight gain compared with treatment groups that received either monotherapy or placebo. These results were statistically significant for 7 weeks of therapy. Regardless of weight gain, the advantages of quitting smoking are far greater than the disadvantages associated with a modest amount of weight gain (Rennard & Daughton, 2004).

Conclusion

Smoking cigarettes and the use of tobacco products in general are known

causative agents for significant unfavorable health and welfare conditions, not only for

users but also for those who are environmentally exposed to tobacco. Nicotine

dependence is the most common psychiatric disorder and is recognized as a chronic

addiction (Martinez-Raga, 2003). As brief intervention from a health care professional

has been reported to increase smoking cessation rates, it is our responsibility to

routinely screen for tobacco use and determine smoking status of all patients. It is even

recommended that smoking status be incorporated into the vital signs so to assure this

assessment is conducted routinely (Sutherland, 2002). This is critical information

because smokers do not generally seriously attempt quitting smoking more than once

per year (Jamerson et al., 2001). Complete abstention from tobacco products must be

encouraged as the harm reduction of smoking fewer cigarettes is unknown (Peters &

Morgan, 2002). It has been reported that 97% of quit attempts are unsuccessful without

the aid of therapy (Shiffman et al., 2002). With the exception of certain patient

populations who may require special consideration before employing pharmacotherapy,

any of the FDA approved therapies for smoking cessation should be utilized to aid

patients who are motivated to quit. Exceptional patient populations include, those with

medical contraindications to pharmacotherapy, pregnant or breast feeding women,

adolescents and patients smoking less than 10 cigarettes per day (Fiore, 2000).

It is important to remember and acknowledge that nicotine has mood modulating

effects. Smokers would not continue smoking if nicotine did not have this capability.

Tobacco users rapidly experience feelings such as a heightened sense of alertness and

pleasure, which is powerfully reinforcing (Cinciripini, 1999; "New Tools to help you quit

smoking," 1999). Following smoking cessation, the maximum intensity of withdrawal

symptoms peaks in 24-48 hours and gradually declines over 2 weeks (Thompson &

Hunter, 1998). Combination therapy may be especially useful in these first couple

critical weeks following smoking cessation because of its increased capability to

suppress nicotine craving and withdrawal symptoms by providing higher concentrations

of nicotine replacement (Haustein et al., 2003; Stapleton, 1999). Patients and clinicians

must equally understand that pharmacotherapy will help alleviate withdrawal symptoms,

not eliminate them (Campbell, 2000). Following cessation, ex-smokers can expect the

desire to smoke to persist for months to years (Thompson & Hunter, 1998).

Experimentation with smoking should be strongly discouraged, as it more often

than not results in relapse (Cinciripini, 1999). Unfortunately, these factors most likely

account for the unfavorable statistic that, regardless of intervention and initial success,

80% of smokers will relapse within a 12-month period (Jamerson et al., 2001). Despite

this figure, understanding that nicotine addiction is a true dependence, visiting smoking

status routinely, utilizing the most effective smoking cessation strategies currently

available, and ensuring prompt, repeated follow-up care are all things clinicians can do

to continually promote and increase smoking cessation rates.

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Abstract

Objective. Review current smoking cessation literature to determine the most effective strategies available to increase smoking cessation rates. Method. Relevant articles from the past 10 years were obtained and reviewed. Results. All six FDA approved first line therapies available to aid patients in smoking cessation are efficacious and improve cessation rates. Combination therapy has demonstrated greater efficacy for smoking cessation over monotherapy. Conclusion. Smoking cigarettes poses an extraordinary hazard not only to those that smoke but also to persons who are exposed to environmental tobacco smoke. Smokers must be routinely identified and encouraged to quit. Nicotine replacement therapy and bupropion are effective therapies to benefit smoking abstinence. Utilizing combination therapy as first line treatment for smokers who are motivated to quit, especially in the first few critical weeks following smoking cessation, may provide greater relief of withdrawal symptoms and improve long term cessation success.