

Retrospective Study for Anticholinergic Blockade in Smoking Cessation

Abstract: A one year multi-center retrospective study examined the efficacy of Anticholinergic Blockade treatment for nicotine addiction. Two hundred patients were surveyed one year post treatment using the Welplex patented protocol. Data collected included current status of nicotine use (smoking vs. not smoking), or if currently smoking the length of abstinence post treatment. Other data collected included content of smoking pre-and post-treatment, qualitative data regarding levels of cravings for nicotine, and comparative success of other nicotine cessation treatments.

Background: The *Welplex*TM patent uses an anticholinergic blockade of central and peripheral nicotine receptors for the treatment of nicotine addiction. Intramuscular and subcutaneous injections of atropine, scopolamine and promethazine are used to block central nicotine receptors in the brain. The blockade is maintained for an additional 2 weeks through oral anticholinergic medications. Behavioral modification is accomplished through a series of video presentations and printed material focused toward the mechanical and habitual aspects of smoking. The patient is made aware of the mental triggers associated with cigarette smoking and given a series of diversions and alternative actions to aid in the mental habit portion of nicotine addiction. These messages are delivered in both a conscious and subliminal manner greatly adding to the overall success in smoking cessation.

Previously published data from 500 patients seen in a primary care setting treated with the anticholinergic medications showed successful abstinence from tobacco of 86% after two months and over 40% after a full year¹. This earlier study did not account for patients lost to follow-up and was passive in the data collection process. The current study examined the efficacy of the anticholinergic blockade by polling 200 active patients treated one calendar year earlier.

The Welplex approach is unique because it is directed at immediate saturation of the nicotine receptors. This saturation results in nicotine withdrawal without the characteristic cravings and irritability. The tremendously unpleasant side effects of nicotine withdrawal are eliminated, thus leading to a substantial increase in the success rate of cure from nicotine dependency.

Methods: the Welplex call center was utilized to contact a patient list provided from two treatment clinics. The treatment list was essentially chosen at random approximately taking the total clinic treatment population for the months of February through April 2004 until a total of 200 patient responses were obtained. All patient responses were documented on a standardized survey sheet. Data collected was subdivided based on the patient's current smoking status (smoking or not smoking). Those patients not smoking were polled as to the overall effectiveness of the Welplex Protocol using a scaled 1-10 complication / craving experience. Those patients who failed treatment and had resumed smoking were polled as to the length of abstinence, current and past level of nicotine use, factors contributing to the resumption of nicotine use and overall impression of the Welplex protocol. Other data collected from both groups included alternate methods of

smoking cessation used in the past and relative effectiveness compared to the Welplex protocol.

Results: Results are summarized in Table 1. The patients who failed the treatment were subdivided by months of smoking cessation (month 1-12). The total of patients who remained nicotine free for 60 days was 156/200 (88%). Total abstinence for 1 year remained at 56% (112/200). There was a linear progression from months 3 to 12 with the greatest failure proportion occurring by month six.

The greatest factor noted in the failed group for recurrence of smoking was stress related issues (family or work related). Of the early failures (less than 2 months) the most prominent reason stated was lack of motivation. Concurrently, the success of the treatment was rated high even in the treatment failure population in a majority of the patients (82%).

Quantitative consumption of nicotine was also decreased in the treatment failure population. The average nicotine consumption between the two groups (smoking vs. non-smoking was equal (29.2 cig/day vs. 28.8 cig/day p=.05). The post treatment failure group decreased overall cigarette consumption by 56% with the average current cigarette consumption at 16.1.

Discussion: Nicotine is a highly toxic alkaloid and is the principal pharmacologically active component in cigarettes and cigars. It is ubiquitous in western society and is found in measurable quantities in smokers and non-smokers alike. Nicotine exerts diverse psychopharmacologic effects and is thought to be the key component in tobacco responsible for habitual smoking¹. The initial site of nicotine's actions is the nicotinic acetylcholine receptor (nAChR). Nicotine's diverse psychopharmacologic effects likely relate to nAChR modulation of dopaminergic, serotonergic, adrenergic, glutamatergic, and endogenous opiate peptide pathways^{2,3}.

Tobacco was brought from the New World with Columbus. Reports from the crew describe the natives smoking the leaves of the tobacco plant and exhibiting a pleasurable reaction. The use of tobacco soon spread throughout the world, despite severe opposition and often draconian penalties. Currently in the United States approximately 25-27 % of the adult population smoke. In other parts of the world tobacco use exceeds 40% with concurrent increases in associated morbidity. Tobacco use was officially listed as form of drug dependence in the report of the Surgeon General in 1988¹.

Nicotine Addiction

The addictive qualities of nicotine are generally accepted; however the actual severity of the addiction is often ignored. Fully 80% of adult smokers express a desire to stop smoking. The success rates for smoking cessation vary with approach. The classic "cold turkey" has the lowest success rate with only 5%-8% of smokers succeed. Of those who actually succeed, an average of 7 attempts are needed to become smoke free. The single

most stated reason for not stopping or even attempting to quit smoking is the fear of the withdrawal symptoms^{1,2,4}.

While addiction to nicotine is different from that of cocaine and amphetamine addiction, nicotine appears to involve similar pathways in the pleasure/reward centers of the brain. The pathways of the central nervous system (CNS) are complex, but are believed to involve the pleasure centers of the limbic system as well as pathways associated with hunger (smokers are on average 5-10% thinner than non-smokers⁴). Overall CNS and peripheral nervous system (PNS) effects include stimulating the following areas: the adrenal medulla, central nervous system, cardiovascular system (from the release of catecholamines), gastrointestinal tract, salivary and bronchial glands, and the medullary vomiting center⁷.

Nicotine replacement therapy (NRT) became available in the 70's with only marginal increases in smoking cessation approaching 10% - 15%. NRT carries with it its own problems and concerns. Individuals who continue to smoke while using NRT products are at significantly increased risk for nicotine toxicity. In addition, repeated attempts with NRT are less successful after the first failure. As NRT's only substitute the nicotine delivery system, the actual addiction to nicotine remains intact. It is presumed that this will allow for modification of the ritual (i.e. habit) component of the addiction with subsequent gradual withdrawal of the nicotine. Not surprising, the most common concern expressed by smokers is the fear of developing dependence for the NRT itself after smoking is discontinued⁴.

Various pharmacologic neurotransmitter modulators have been used as an adjunct for smoking withdrawal. Tricyclic antidepressants, anxiolytics, central receptor modulators, and direct nicotine agonist have all been used with varying degrees of success. Currently Welbutrin (Zyban), a serotonin, adrenaline uptake inhibitor has the highest success rate of 22%. The common factor of the pharmacologic treatments has been the diminution of the nicotine cravings and the subsequent reduction of the distress (both physical and psychological) experienced by the individual.

Previous studies on the use of ACB in Nicotine addiction

In 1987 a patent was issued for the use of anticholinergic blockade in the treatment of nicotine addiction. A subsequent patent was developed in 2000 which expanded the original work to include a regimen of medications to provide a low level of anticholinergic effects for the duration of nicotine withdrawal in conjunction with behavioral modification. The current patent uses three drugs in a series of injections which use the anticholinergic properties of these medications to block central nicotine receptors in the brain. The data from 500 patients seen in a primary care setting treated with the anticholinergic medications showed successful abstinence from tobacco of 86% after two months and over 40% after a full year. This approach was unique in that it was directed at immediate saturation of the nicotine receptors resulting in withdrawal without the characteristic cravings and irritability. Patients report that after the treatment their cravings for nicotine simply weren't there. The tremendously unpleasant side effects of

nicotine withdrawal were eliminated thus leading to a substantial increase in the success rate of cure from nicotine dependency.

Anticholinergic Blockade Vs. Conventional Treatments

Anticholinergic blockade of nicotine receptors offers clear advantages to other treatment modalities. Most notable is the immediate cessation of nicotine cravings instead of the gradual withdrawal of Nicotine Replacement Therapies and Serotonergic treatments (Zyban). Compared to the most successful conventional modality, the Welplex methodology offers the potential success over four times that of Zyban and six times that of abrupt nicotine cessation or NRT. As previous studies have shown it is the cravings as well as the fear of cravings responsible for the failures of smoking cessation. The Welplex method’s overwhelmingly high success rate is directly correlated to the immediate reduction in cravings for nicotine. This allows for modification in behavior without the compounded factors of physical and psychological cravings.

Summary

This study clearly demonstrates the advantages and overwhelming success of the Welplex method for the treatment of nicotine addiction. While nicotine addiction remains one of medicine’s most difficult and frustrating problems, the Welplex method offers a novel approach opening new avenues for nicotine treatment.

	2 months	3 months	4 months	5 months	6 months	7 months	8 months	10 months	11 months	12 months
Non-smoking N (200)	156	152	149	142	134	128	120	117	115	112
Percent Non-Smoking	88%	76%	74.5%	71%	67%	64%	60%	58%	57%	56%

Table 1: Patients summary by month. Total patients N=200. Data is actual patients remaining abstinent from tobacco up to and including the particular month documented.

	Initial (Pre-Treatment)	12 month
Cigarettes / day	29.2	16.1
Range	80 - 10	60 - 4

Table 2: Pretreatment and Current Cigarette Consumption in the Failed Group (N= 88). Consumption ranged from 4 packs/day (80 cig/day) to ½ pack/ day for the Failed Group prior to treatment. Post-treatment smoking consumption ranged from 3 packs per day (1 patient) to a low of 4 cigarettes per day. (Key: 1 pack per day =20 cigarettes.)