

TRANSDERMAL NICOTINE ADMINISTRATION

This note takes account of discussions at the Scientific Research Group (SRG) Meeting, Montreal, Canada, 7th May 1992.

1. As a method of administering nicotine.

Neither the standard nicotine patch (e.g. Nicotinel) nor the "Stowic" patch match the delivery pattern of smoke inhaled from a cigarette. They do, however, match more closely the pattern of some other forms of tobacco usage, e.g. pipes, cigars, and snuff, although there is some debate on the actual importance of the peaks and troughs in nicotine levels associated with inhaling cigarette smoke.

It should also be noted that the patches deliver "free" or unreacted nicotine. Nicotine is a basic compound and combines with acids if smoke is acidic (for example in flue cured cigarettes). Nicotine absorption is fastest when it occurs in the "free" state and, as is well known, the smoke from pipes and cigars is frequently alkaline leading to rapid absorption.

While delivering nicotine, patches do not mimic any of the other facets of smoking. In addition, as presently developed they are a totally automatic delivery system and have none of the flexibility of tobacco usage, both as to amount and timing of delivery.

Nicotine containing patches are potentially considerably more dangerous than cigarettes: they can be easily misused or tampered with and as currently manufactured they can be mistaken for plasters by the elderly or the young. The total nicotine content of individual nicotine patches can be as high as 51 mg, roughly equivalent to the lethal dose for a man of average weight. By contrast the tobacco rod of a filter tip cigarette (850 mg weight, 2% nicotine) contains about 17 mg nicotine. Direct nicotine intake from a cigarette requires ingestion: and this is demonstrably rare. Nausea usually occurs when attempts are made to consume cigarettes.

2. Status of Products

Because of their development by pharmaceutical companies patches may be seen as a general drug delivery system, a view confirmed by the likely use of patches to

deliver a wide spectrum of pharmaceutically produced drugs. Although this classification may not apply in all countries, marketing of nicotine containing patches by tobacco companies would be seen as move towards tobacco companies being regarded as pharmaceutical companies.

3. Effectiveness of Product in Smoking Cessation

The evidence produced by the makers of Nicotinell (Ciba Geigy) is not particularly convincing and does not indicate substantial advantages compared to placebo. This may simply reflect poor quality scientific studies: sales in New Zealand have been better than the makers expected and, incidentally, are very profitable.

4. Nicotine in Relation to Neurodegenerative Disorders and Other Diseases

Current advice from consultants to BAT is that the epidemiological basis of a negative association between smoking and incidence of Alzheimer's disease is hardening: there is also good evidence that smoking alleviates the symptoms of Alzheimer's disease. The situation with regard to Parkinson's disease is similar but rather more certain. These observations are widely believed to be due to nicotine but this has not been substantiated--although the view is consistent with current pharmacological knowledge. One adviser, Dr. S. Wannacott (University of Bath), is of the opinion that nicotine has unique properties and 'protects' nerve cells against damage leading to neurodegenerative disorders. On this basis she believes that the pharmaceutical companies will not easily be able to develop a drug to replace nicotine in relation to Alzheimer's disease. In relation to alleviating symptoms of Parkinson's disease the position is different and another material (l-dopa) is preferred. This is because different regions of the brain are involved.

It has also been suggested over the years that nicotine may be implicated in some smoking-associated diseases, more especially cardiovascular disease. This possibility has not been disproved although Wald and Froggatt (1989) do not find the evidence persuasive.

Finally, it should be noted a paper was published (April 29, 1992) suggesting that a gene which protects against cancer may be a risk factor for Parkinson's disease.

Generally speaking this area of work is likely to increase the interest in nicotine administration, especially since Alzheimer's disease is likely to be a major health issue in the next century, as life expectancy increases and birth rates fall.

5. Possible Developments

The possible development of more sophisticated patches can be foreseen, for example in which compounds other than nicotine could be co-administered. Patches containing reduced amounts of nicotine (and shorter useful contact times) are obviously possible, as are user-controllable patches.

6. Future Activities

- a) Meeting with Stovic Resources (May 19th) - to ascertain their views on their product.
- b) Informal meeting with Chairman of U.K. Committee on Safety on Medicines (Professor M. Rawlins, University of Newcastle, May 21st). To hear the views of the Chairman on the probable approach to nicotine patches in the U.K.
- c) Behavioural efficacy of nicotine patches. Brief behavioural study to compare patches with smoking in a vigilance task. Summer 1992 - subject to ethical approval from University of Reading (Professor D. M. Warburton).

7. Scientific Conclusions

- 1. Nicotine patches deliver nicotine: the nearest equivalent smoking habit is probably snuff-taking. As a means of delivering nicotine they are quite different to cigarettes, particularly when the smoke is inhaled. There are many problems associated with nicotine patches.
- 2. Nevertheless we should continue to investigate the potential of nicotine patches, particularly against the possibility that improved patches are developed.

3. We should support research in relation to Alzheimer's disease in view of the probable importance of nicotine with regard to this condition.

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