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Transdermal scopolamine for peripheral vertigo
(A double-blind study)

by

T. RAHKO and P. KARMA (Tampere, Finland)

Abstract

Transdermal scopolamine medication has been evaluated in 30 cases of acute peripheral vertigo. The double blind study revealed favourable effects, e.g. in Menière's disease. The best compromise between effect and side-effects was one active medication patch. The side-effects were those described for scopolamine, such as blurred vision and dryness of the mouth. Transdermal scopolamine seems to offer an alternative form of medication in acute peripheral vertigo.

Introduction

A frequent symptom of various diseases, vertigo can be very disturbing and sometimes it even impairs daily activities.

The various forms of medication currently available for the treatment of vertigo include antihistamines, vasodilators, anti-emetics and tranquilizers. Unfortunately, these drugs are not always effective.

One of the oldest products used in medicine, the belladonna alkaloid, has been tested for the treatment of motion sickness, because similar symptoms appeared in patients who were given cholinergic substances. Later observations have revealed that most of the drugs used for vertigo and related symptoms have an anticholinergic effect. The belladonna alkaloid blocks the synapse of the vestibular neuron at the nucleus (Shute and Lewis, 1963, 1965); connections between the reticular formation and the vestibular nuclei have been described. These connections are probably cholinergic; apparently the reticular formation has an excitatory cholinergic effect on the vestibular activation (Yules *et al.* 1966). Specific areas inhibiting and exciting vestibular function are found in the reticular formation. Through the reticular system, vestibular excitement can stimulate the vomiting center.

For a long time scopolamine has been commonly used for motion sickness, but the half-life of the drug is only about one hour and it has been difficult to find suitable dosage; furthermore, the doses recommended for the prevention of motion sickness may cause tachycardia, drowsiness and dryness of the mouth. This restricts the application of the drug.

Such problems have led to the development of a new way of administering scopolamine, *i.e.* by transdermal application. 0.5 mg of the drug in a gel is contained in a 2.5-cm^2, 0.2-mm thick multilayer patch with a reservoir. This is sandwiched between an impermeable backing layer and a rate-controlling microporous membrane. The epidermal side of this membrane is coated with a layer of adhesive gel which also contains scopolamine to secure a priming drug dose. The patch is placed on dry skin behind the ear.

This mode of application has been shown to be effective in preventing motion sickness, manifested by vomiting and vertigo (Graybiel and Knepton, 1977).

The purpose of our study has been to inves-

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tigate whether a drug which is effective for inhibiting motion sickness—transdermal scopolamine—could be effective in also preventing other types of vertigo of peripheral vestibular origin.

Patients and methods

The material consisted of 30 out-patients of the Department of Audiology of the Otolaryngology Clinic of Tampere University Central Hospital. Their ages ranged from 20 to 51 years (mean 39 years). Ten patients were men and 20 women. Sixteen patients had vertigo due to Menière's disease; eight had vestibular neuronitis; five had positional vertigo; and one patient had vestibular degeneration after streptomycin medication. The patients were randomly assigned to three different treatment groups. The nine patients in group A were given one active patch (with 0.5 mg of scopolamine) and one placebo behind the ear; the group B (11) patients received two active patches; and group C (ten) patients had two placebo patches. All these patches were similar in size and appearance and, before the end of the clinical follow-up, neither the patients nor the examiners knew to which of the groups the patients belonged. After three days the patients replaced the patches with a new set. After one week they came for a check-up which included registration of the heart rate and blood pressure. At home, the patients tallied their symptoms and any adverse effects. The patients were instructed to contact the clinic immediately if they had any adverse effects which might interfere with the test. All the patients who were accepted for the trial were otherwise quite healthy, with an apparently normal cardiovascular status. We excluded patients with psycho-neurotic states, hypertension, anemia, oculomotor disorders, hyperventilation syndrome, pulmonary disease, sensory ataxia, stroke, multiple sclerosis, tumour or other organic diseases in the central nervous system, glaucoma, pyloric obstruction, any psychotropic medication, or non-cooperative behavior.

Results

The effectiveness of medication was graded as: 1 = very good; 2 = good; 3 = poor; 4 = none, and the tolerance as: 1 = very good; 2 = good; 3 = moderate; 4 = poor. The results in different medication groups are shown in Table I. Group A, in which we applied one active patch, seemed to exhibit the greatest

TABLE I

THE EFFECT OF DIFFERENT DOSES OF TRANSDERMAL SCOPOLAMINE ON PERIPHERAL VERTIGO

A 1 active patch		B 2 active patches		C placebo	
Effect	Tolerance	Effect	Tolerance	Effect	Tolerance
2	2	4	1	4	1
2	2	2	1	1	1
1	2	1	2	1	1
1	4	discontinued	discontinued	1	1
1	1	2	3	3	1
3	1	1	2	discontinued	discontinued
1	2	discontinued	discontinued	1	1
3	1	discontinued	discontinued	4	1
1	1	4	4	1	1
		1	3	4	1
		discontinued	4		
$\bar{x}$ 1.7	1.8	2.1	2.5	2.2	1.0

Effect: 1 = very good, 2 = good, 3 = poor, 4 = none

Tolerance: 1 = very good, 2 = good, 3 = moderate, 4 = poor

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efficacy of the drug, with medium tolerance. The tolerance was poor in only one patient; in other cases it was assessed as good-to-very-good. The response regarding vertigo was poor in two cases, and good-to-very-good in the others.

The mean efficacy of the drug seemed to be slightly better in group A than in group B, in which two active patches were used; in the latter group, treatment had to be discontinued in three cases owing to side-effects (Tables I and II). In one case the vertigo was aggravated despite treatment and it was therefore discontinued. The overall tolerance in group B seemed to be the poorest.

In group C, in which the patients received only placebos, four of the ten patients experienced poor or no efficacy; in five cases the placebo helped. The tolerance in this group was naturally very good.

No statistically significant inter-group differences could be shown. The pre- and post-treatment heart rates and blood pressures were the same. The test was discontinued because there was no effect (in one case), intolerance (in three cases) and increased vertigo (in one case) (Tables I and II).

TABLE II
THE SIDE-EFFECTS OF TRANSDERMAL SCOPOLAMINE TREATMENT

Patient No.	Group	
3	A	visual disturbances
8	A	visual disturbances
9	B	visual disturbances
10	A	dry mouth
13	A	visual disturbances
14	B	increased vertigo—discontinued
15	B	visual disturbances
17	C	went to emergency clinic with headache—discontinued
18	B	visual disturbances
19	B	dry mouth, itching—discontinued
20	A	dry mouth
21	B	dry mouth, visual disturbances—discontinued
23	A	dry mouth
25	B	drowsiness, dizziness
30	B	visual disturbances—discontinued

Table II lists the side-effects. The greatest number of patients with side-effects (a total of eight) was in group B. Most commonly these patients complained of blurred vision but some also had dry mouth, dizziness and drowsiness. Six patients in group A and only one in group C reported side-effects, half of them having a dry mouth.

Considering the patients in different diagnostic groups, the following was observed: in patients with Menière's disease (Table III), group A produced good or very good results in five out of six patients; group B produced good or very good results in three of the six patients. With the placebo group (C), two patients responded very well, one not at all. Group A seemed to show the greatest mean efficacy although, again, the differences were not statistically significant. The patients with other diagnoses were too few for inter group analysis.

Discussion

It has been known for some time that transdermal scopolamine can control motion sickness, but there are no corresponding studies on its influence on other peripheral vestibular disturbances causing vertigo.

Although there are no statistically significant differences between the treatment groups, the results in general are best in group A, with one active patch, and the tolerance is estimated to be between very good and good. A comparison with group B (with two active patches, in which the mean tolerance was only moderate and four patients had to be withdrawn) and with group C (with a placebo, in which one half of the patients obtained no help), seems to justify the view that the results of group A were the best.

This view is further corroborated by our results, as considered in accordance with the original diagnosis, *e.g.* in group A (with one active patch), the patients with Menière's disease show excellent results; on the other hand, because there happened to be only three Menière patients in the placebo group, any comparisons are difficult. The results in patients with vestibular neuronitis followed

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TABLE III
THE EFFICACY IN RELATION TO DIFFERENT CAUSES OF VERTIGO.

Group	Menière's disease	Vestibular neuronitis	Benign paroxysmal positional vertigo	Streptomycin vertigo
	Efficacy	Efficacy	Efficacy	Efficacy
B				
two	4	2	4 discontinued/increased	3
active			vertigo	
patches:	1	4 discontinued/ intolerance	1	
	2	1	1	
	1	$\bar{x} = 2.3$		
	4			
	4 discontinued/ intolerance			
	$\bar{x} = 2.7$			
A				
one	2	1	1	
active	2	3		
patch:	1	$\bar{x} = 2.0$		
	1			
	3			
	1			
	$\bar{x} = 1.7$			
C				
placebo:	1	1	1	
	4 discontinued/ no effect	4		
	1	4		
	$\bar{x} = 2.0$	$\bar{x} = 3.0$		

1 = very good; 4 = none.

roughly the same lines, although the numbers for comparison were very small.

Generally, the results suggest that medication with one active patch can be considered as a reasonable alternative to other forms of treatment in cases of acute peripheral vertigo, and that further comparative investigations should be undertaken.

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Address for correspondence:
Dr. Tapani Rahko
Department of Otolaryngology,
Tampere University Central Hospital,
SF-33520 Tampere 52, Finland

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