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LÄKEMEDELSINFORMATION FRÅN LÄKEMEDELSVERKET, FINLAND | DRUG INFORMATION FROM THE NATIONAL AGENCY FOR MEDICINES, FINLAND



Hannes Wahlroos

DIRECTOR GENERAL, PROFESSOR
National Agency for Medicines

Back to basics

In the business world, the above heading is an expression indicating a business' return to basic issues after they have been forgotten, or they have faded out for some reason. Considering recent observations, this expression is applicable to the expected tightening of food supervision in order to root out illegal and misleading information from the food market.

It is a well-known fact that the health market fares well. The border zone between medicinal and food products is an excellent example of this. With certain kinds of imagery and misleading information, the human mind is sensitised to desire a long and healthy life. Unfortunately, this is good business for some people. In developed countries, there is, however, a desire to prevent deception with foodstuffs.

Finnish food legislation is up to date in this aspect. The purpose of the food legislation is, amongst other things, to ensure the truthful and sufficient dissemination of information on food, and to prevent misleading information. The assertion or inference that any foodstuff owns prophylactic, therapeutic or healing attributes for human illnesses is particularly prohibited. Human food is meant to be food and not medicine.

Products that are more problematic than normal foods include the so-called nutritional supplements, which may be reminiscent of medicines due to their form, such as tablets, capsules, pills, powders, liquids, and other dosage forms. Their purpose is to complement the diet, or affect the nutritional or physiological functions of the human body in some manner or another. According to the decree issued by the Ministry of Trade and Industry in August, any claims or inferences to the effect that a nutritional supplement owns prophylactic, therapeutic or healing attributes for human illness are prohibited on packaging, in brochures, advertise-

ments, or in any other medium. Can it be put more clearly?

However, as is experienced in life in general, some kinds of foodstuffs and nutritional supplements will be foisted on the consumer, and the main promotional message of such goods will go against the aforementioned regulation. Consumers and patients are confused, but so are the traders, too. One can easily get the impression that there are two sets of regulations in the health market.

In Finland, according to food legislation, the administration of control belongs to the National Food Agency (EVI). The regional administrations and municipalities play a central role in the practicalities of the control. The nationwide food control program being prepared by EVI for implementation in 2004 covers a range of control projects. One of these projects, named the "Forbidden Health Assertions", has commenced already this year. The aim for the year 2004 is to carry out targeted strikes against health assertions in co-operation with officials of the regional authorities and municipalities. This enterprise is highly welcome. The deception of consumers and patients should be stopped.

In a category of their own are functional foods or foods beneficial for the health, for which there are neither definitions, evidence-based criteria nor regulatory system in the Finnish national legislation or in that of the EU. As long as the manufacturers or the marketers are allowed to decide for themselves whether a product is functional or beneficial to human health, then the food administration is expected to actively control the marketing practises.

Summary

Kari Ylitalo

Cardiological Department
Oulu University Hospital

Prophylaxis of atrial fibrillation

Prophylaxis of atrial fibrillation is probably the most common indication for the use of antiarrhythmic drugs. For the prophylaxis of atrial fibrillation, a physician may try beta-blockers, or, in certain circumstances, also ACE inhibitors and antagonists. Knowledge about the adverse reactions caused by other prophylactic drugs is nevertheless recommended, because at worst they may be life-threatening to the patient. Attention should also be paid to prophylactic drugs started earlier, such as quinidine and sotalol, and their benefits should be critically evaluated.

Atrial fibrillation (AF) is the most common type of cardiac arrhythmia that a physician will come across in his/her practice; its prevalence in the oldest patient groups is nearly 10%. AF is usually not an acute threat to the patient's life, but the subsequent symptoms may disable the patient. AF is also associated with a considerable risk of thrombo-embolic events, especially of a cerebral infarct, and it may exacerbate cardiac insufficiency in the patient (1). The results of long-term prophylactic treatment of AF are poor. In a one-year follow-up, AF recurs in 60–80% of the patients treated. Among the drugs in the Vaughan-Williams classification group those most often used in AF prophylaxis belong to the groups I A, I C, II and III (Table). The majority of studies on AF have been carried out with quite small samples of patients and there are no satisfactory comparative studies on the efficacy of various prophylactic drugs. According to the recommendations of AHA/ACC/ESC, prophylaxis of AF is justified in patients with severe symptoms. The patients most at risk, such as post-myocardial infarction patients, should nevertheless not be treated with proarrhythmic drugs (2).

Drug-free treatment

AF patients often ask whether their manner of life can affect the recurrence of AF. Even though all heart patients can be counselled to avoid smoking and to follow a correct diet, no answer supported by studies can be given to this question. A hangover may trigger AF in some patients, and the patients can naturally be advised to avoid hangovers.

Beta blocking agents

Beta-blockers are the drugs of choice in the prophylaxis of AF. They are usually well tolerated and associated with a positive prognostic effect in patients with hypertension or ischaemic heart disease. Beta-blockers are not, however, notably effective in the prevention of AF. In a relatively extensive study, metoprolol was shown to reduce the occurrence of AF in only less than 20% of the patients during a 6-month follow-up (3). Comparative studies of the prophylactic effect of different beta-blockers in AF have not been conducted, and consequently, the benefit of beta₁-selectivity, combined alpha-beta-blocking, the ISA effect, or various fat/water solubility cannot be shown, but it is recommended that a couple of different beta block-

ing agents be tried before introducing other drugs.

Sotalol

It is easy to consider sotalol merely as a beta blocking agent, but according to the classification of Vaughan-Williams it is, in fact, a group III drug which prolongs the repolarisation of the cardiac cells and consequently the QT interval. A long QT interval exposes the patient to a life-threatening torsade de pointes tachycardia. According to the adverse reactions register maintained by the WHO, sotalol is clearly the most important one of the torsade de pointes tachycardia-inducing drugs. Since sotalol, according to studies, is no more effective than metoprolol or bisoprolol in the prophylaxis of AF, I do not think sotalol should be used in the prophylaxis of AF (4).

Flecainide

Flecainide, the I C group drug, is after beta-blockers the most commonly used drug in the treatment of AF in Finland. Its efficacy is comparable to that of other I A and I C groups of drugs, i.e. a one-year follow-up shows a recurrence of AF in about

Medicinal substances used in the prophylaxis of atrial fibrillation. The recommended drugs are indicated in bold.

<i>Medicinal substance</i>	<i>Advantages</i>	<i>Disadvantages</i>	<i>Important</i>
Beta-blockers	Safe, with a positive prognostic effect	Poor efficacy	
Flecainide	More effective than beta blocking agents	Not for patients with another heart disease	Severe cardiac arrhythmias even at small concentrations in 10% of patients
Amiodarone	The most effective one of the known prophylactics Other heart diseases do not prevent use	Adverse reactions: amiodarone-induced pulmonary reaction, hyperthyreosis, liver damage	Monitoring of diffusion capacity, liver and thyroid values
ACE inhibitors and angiotensin II antagonists	Safe Another useful profile of action	Insufficient proof of efficacy so far	
<i>Digitalis</i>		<i>Does not prevent recurrences of atrial fibrillation</i>	
<i>Quinidine</i>		<i>Increased mortality</i>	
<i>Disopyramide</i>		<i>Adverse reactions in 26% of patients</i>	
<i>Propafenone</i>		<i>Not for patients with another heart disease</i>	
<i>Verapamil, diltiazem</i>	<i>Inhibition of the atrial remodelling phenomenon</i>	<i>Importance in prophylaxis of atrial fibrillation unknown</i>	

40–50% of the patients treated (5). Due to its proarrhythmogenic properties, a reliable exclusion of structural heart defect, ischaemic heart disease, past history of cardiac infarct and cardiac failure in patients should be made prior to the use of flecainide. It is recommended that the flecainide therapy be started by a specialist and that, prior to the start of medication, the patient should undergo a cardiac ultrasound examination, including after careful consideration a clinical exercise test. It is recommended that after the introduction of the medication a resting ECG be checked at least and preferably also a clinical exercise test be performed to ensure that the QRS complex is not prolonged by more than 40–50%. A congenital slow metabolism of flecainide is found in 10% of patients and even small doses can cause proarrhythmogenic blood concentration. Fle-

cainide should always be used in combination with a beta-blocker for additional efficacy and safety.

Amiodarone

Amiodarone is the most effective and best known drug used in the prophylaxis of AF. In a 16-month follow-up, AF recurred in 35% of the patients treated, whereas in patients on propafenone or sotalol therapy, the recurrence was 64%. Adverse reactions leading to interruption of treatment were somewhat more frequent with amiodarone, however (6). Amiodarone can also safely be used in patients with ischaemic heart disease or cardiac insufficiency, and it does not expose the patients to life-threatening cardiac arrhythmias. However, other significant adverse effects are associated with the use of amiodarone, the most dreaded one of which is an

amiodarone-induced pulmonary reaction. Amiodarone can also cause hyperthyreosis or liver damage. Prior to the introduction of amiodarone that the patient's lung diffusion capacity should be established as well as liver and thyroid values. These values should also be monitored at intervals of 3–6 months for a year at first, and annually thereafter.

ACE inhibitors and angiotensin II antagonists

In recent years, the possibility of using angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers in the prophylaxis of AF has emerged. In a TRACE study, prophylaxis with ACE introduced following a myocardial infarction reduced the frequency of AF by over 50% compared with a placebo (7). When amiodarone was combined

with an angiotensin II antagonist, irbesartan, the sinus rhythm was retained in 83% of the patients during a 9-month follow-up, whereas the sinus rhythm was retained in 52% of the patients on amiodarone therapy alone (8). ACE inhibitors and angiotensin II antagonists are considered to inhibit the structural changes of the atria, primarily the fibrotisation. In animal studies it has also been found to prevent electrophysiological changes, which may be a result of the prevention of structural changes (9). So far, no randomised studies have been made on the efficacy of ACE inhibitors or angiotensin II antagonists in the prevention of AF, but they can already be recommended in patients with hypertension, cardiac insufficiency, mild mitral insufficiency or in patients who exhibit some atherosclerosis.

Other drugs

Among the drugs of the I A group, quinidine has previously been extensively used in the prophylaxis of AF. Compared with a placebo, however, quinidine causes a three-fold increase in patient mortality, and consequently its use should be avoided (10). Disopyramide and propafenone have also been used in the prophylaxis of AF, but their efficacy is not superior to that of any other prophylactic agents and their use is associated with an array of adverse reactions and restrictions. Digitalis does not prevent the recurrence of AF, but it can be used together with a beta-blocker to reduce the pulse level in that condition. Digitalis is especially useful in patients with cardiac insufficiency. Calcium channel blockers have been found to have a positive effect with respect to the electrical changes caused by AF; their benefit in the prophylaxis of AF has not been adequately studied, however. Recurrence of AF can be prevented by dofetilide, but the drug is not yet available in Finland. In the future, azimilide and dronedarone may also be used in the prophylaxis of AF (11).

The adoption of pulse control and invasive treatment

We often come across a situation where, despite several trials with prophylactic agents, the patient continues having recurrent AF events requiring cardioversion. A discussion with the patient is recommended in this case to see if AF can be tolerated together with adequate pulse rate control by taking a beta blocker and digitalis as necessary. According to an AFFIRM study, in the more elderly patients at least this practice is even safer than repeated cardioversions (12). It is recommended that certain, carefully chosen patients should also consult a cardiologist in view of the possibility of ablation therapy for their AF.

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Summary

Matts Lenck

Gynaecologist and Obstetrician

Valkeakoski

My observation of an adverse drug reaction Tibolone and carpal tunnel syndrome

Carpal tunnel syndrome is characterised by compression of the median nerve in the carpal tunnel of the wrist. The main symptoms include numbness of the thumb and the index and middle fingers and a tingling sensation and pain especially at night. The syndrome is more common in women than in men. Gynaecologists are familiar with the condition because it is seen fairly often towards the end of pregnancy and spontaneously disappears after delivery. According to the literature, hormone therapy during menopause, especially oestrogen-induced fluid accumulation in the tissues, is considered one of the risk factors for carpal tunnel syndrome (1, 2).

My first patient was an otherwise healthy female, except for migraine which had troubled her for years during her menstrual periods. Due to menopausal symptoms, a cyclic therapy with oestrogen-progestogen was introduced at the age of 50. The symptoms disappeared, but due to migraine associated with withdrawal bleeding, treatment with tibolone which does not induce bleeding was suggested to the patient when she was 54. With the customary dose of 1 tablet a day, menopausal symptoms and migraine were totally avoided. Within a couple of months, severe pains started occurring in the hands, especially at night, to the extent that the patient had been admitted for examinations on the suspicion of rheuma-

tism. Weight increase was not confirmed, but she felt swelling in the fingers. Clinically, no swelling was found. As carpal tunnel syndrome appeared likely, tibolone therapy was withdrawn and the patient was transferred to a continuous combined therapy of oestrogen and progestogen at a fixed dose. Pains in the hands disappeared immediately, but due to bleeding problems, tibolone therapy was tried once more, this time by halving the daily dose. Severe symptoms in the hands followed again, and tibolone therapy had to be stopped, after which the patient again became symptom-free. Subsequently, an appropriate therapy was found by using the above-mentioned continuous combined therapy, without bleeding or other problems. I should perhaps mention that the outcome of the examinations for rheumatism was negative.

Due to hot flushes, my second patient was started on cyclic oestrogen-progestogen therapy so that withdrawal bleeding occurred every three months. Since the bleeding was always associated with migraine, tibolone was introduced when the patient reached 61 years. Menopausal symptoms did not recur, and the patient had no migraine. Within a couple of months the patient's weight had nevertheless increased by 5 kg. There was no swelling, clinically or subjectively. Due to a severe tingling sensation and numbness in the hands, however, the patient's night-

time sleep was disturbed. Based on the experience gained from the treatment of the first patient, tibolone was withdrawn, and symptoms in the hands thereupon disappeared. A smaller dose of tibolone was not tried in this patient, especially as the appropriate treatment for her, too, was found to be the continuous combined therapy of oestrogen and progestogen at a fixed dose.

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Summary

Hanna Saari

M SCIENCE (PHARM)

Vantaa 9 Pharmacy

Ulla Närhi

PH D (PHARM)

Safety and Drug Information

National Agency for Medicines

The article is based on a study (Pro Gradu) by Hanna Saari at the Department of Social Pharmacy of the University of Helsinki: Oiremarkkinointi suomalaisten kuluttajien lääkeinformaation lähteenä. (Illness related marketing as the source of medical information available to Finnish consumers.)

Internet and medical information

Consumers are, to an increasing degree, searching through the Internet for medical information. Illness related marketing is one way of disseminating medical information.

Illness related marketing refers to the information on offer to the consumer regarding illnesses/symptoms and associated means of treatment. The aim should not be the marketing of a drug preparation, but creating awareness of an illness and supplying information on the use of medicinal preparation. Information should be given even-handedly on all treatment alternatives.

The initiator of illness related marketing is usually a pharmaceutical company, but it may also be some other commercial enterprise, e.g. a health centre or a pharmacy. The Internet is the most popular medium for illness related marketing. Several pharmaceutical companies maintain web pages with information on the illnesses treated with the company's products, symptoms of the illnesses and various drug and alternative therapies.

The aim of a survey carried out in the spring of 2003 was to outline the Finnish consumers' search for information on the Internet pages of illness related marketing. The purpose was to establish what kind of information consumers are looking for on the pages and what information they believe they do receive, whether the consumers are satisfied with the information received and what follow-up measures they were encouraged to pursue.

The material was made up of a 28-day review of seven different web pages of illness related marketing maintained by pharmaceutical companies. The illnesses involved on the web pages included migraine, erection

disturbances, diabetes, nocturnal enuresis, pain and hair loss in men.

The key subjects in the survey consisted of consumers who used pages of illness related marketing as their source of information. The sample form was single random sampling. The selected persons were those who completed all the queries in the review. The questionnaire appeared on the screen when the consumer logged on to the Internet pages. A total of 672 replies were received.

Results

Those selected in the sample corresponded to the Internet user profile of medical information established in international surveys. The respondents were mainly women, highly educated, living in towns of over 50,000 inhabitants and aged under 50. Among the total group of respondents the women were on average better educated than the men, whereas the men were older than the women. This was due to the areas of indication within which the review was done: men were the predominant sex only on the web pages involving erection disturbances and loss of hair.

The respondents were mainly seeking information on medical treatment, causes of illnesses and symptoms of illnesses (Fig. 1).

When respondents were asked how they valued the importance of various elements of medical treatment (scale: 1 not at all important – 5 very important), the highest scores concerned the effects of medical treatment (4.59) and the adverse reactions caused by medication (4.41). The lowest score obtained con-

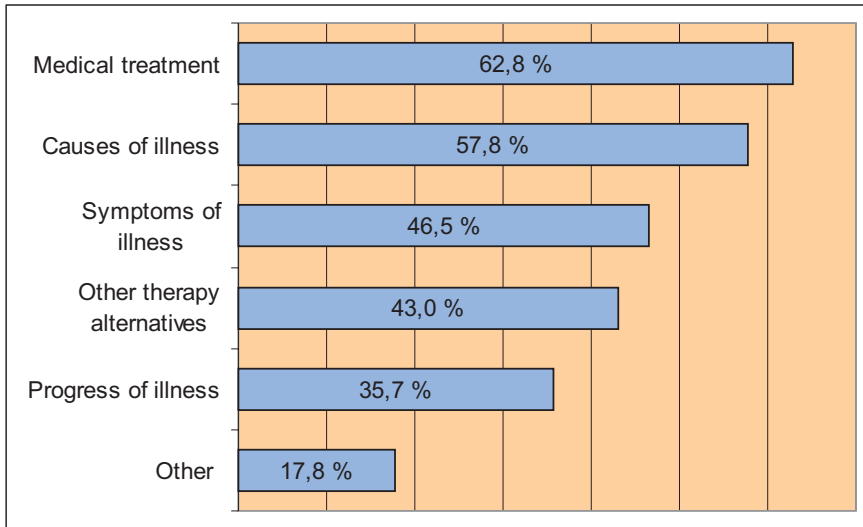
cerned the costs of medical treatment (3.84). The area in between was covered by various alternative prescription drugs, interactions of various medications and alternative OTC preparations. The standard deviation for each alternative was small.

The majority of respondents (60%) were satisfied with the information they received from the web pages of illness related marketing. The respondents who were not satisfied with the information they received (40%) were asked about the areas on which they would like to have more information. More information was wanted mainly on medical treatment (54%), alternative treatments (50%) and causes of illness (48%). More information regarding medical treatment was wanted mainly on the alternatives among OTC preparations (70%), effects of medical treatment (65%) and various alternatives among prescription drugs (64%).

The respondents reported a doctor, and other Internet pages, as their most important additional sources of information (Fig. 2).

27% of the respondents reported that they would contact a doctor as a follow-up measure. Equally 27% were not able to tell whether they would seek follow-up treatment or not. 19% reported being under adequately good treatment as it was. 42% of the respondents reported that the information they had received on the Internet pages had no effect on their decision about follow-up treatment measures, 32% were unable to say whether the pages had any effect or not, and 26% replied that they did have an effect. The respondents' opinion on the effect of the pages had a statisti-

Fig. 1. Areas of interest in which the respondents were seeking information on the web pages of illness related marketing



cally important effect on the decision about follow-up treatment.

Conclusions

The increased need for information among consumers on their illnesses and associated treatment is not a phenomenon independent of the surrounding community; rather it is part of an overall change leading towards the information society. Finland can be considered an "information society No 1" for various different reasons, and consumers in Finland have excellent opportunities to receive medical information from various sources. One of the most used and debated new sources is the Internet.

According to international surveys, medical information is the sec-

ond most often searched subject area on the Internet (1). At least two percent of the web pages discuss issues associated with health (2). An average of 40% of Internet users have at some point sought medical information on the Net (3). It is certain that both the demand for and the supply of medical information are constantly increasing (4).

Consumers appreciate the Internet as a source of medical information because information can be searched for at times most suited to them (5). As a source of information, the Internet is varied and searches can be made anonymously; it is common to use the Internet for searches associated especially with sensitive subjects.

The level of quality of web pages offering medical information varies

and evaluation of quality is difficult. It may also be difficult to draw a line between drug information and drug marketing. It remains unclear at present how consumers choose and evaluate the medical information they find on the Internet and what effect the information has on their choices (6). Nevertheless, the role of the Internet as the source of medical information and the benefits offered by and disadvantages attached to it are the subject of several extensive surveys being carried out in Europe at present.

According to this survey, the amount of medical information that Finnish consumers search for on the Internet is great and varied. Furthermore, they also value highly the information they receive. Pages of illness related marketing appear to encourage the consumers to seek help for their symptoms and especially to make an appointment with a doctor to discuss them. Companies involved in marketing by symptoms have a high degree of responsibility: the contents of the pages should not have marketing characteristics, but the information offered should instead be varied, of good quality and correct.

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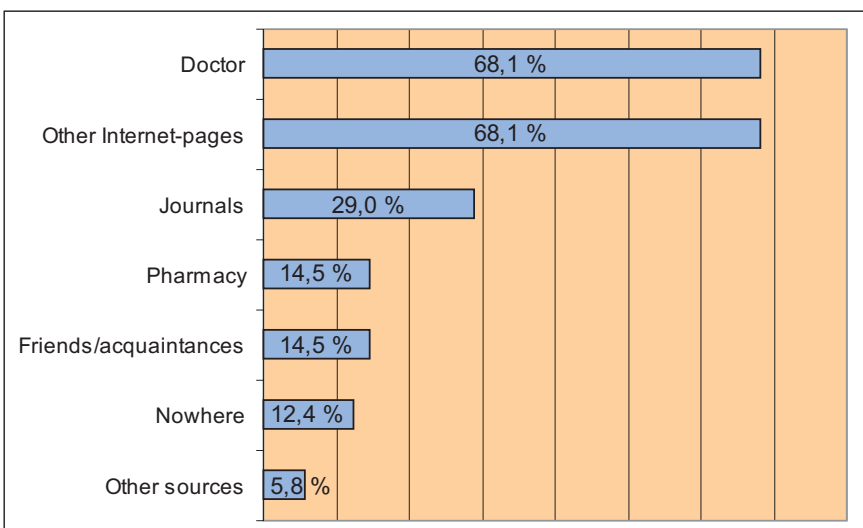


Fig. 2. Sources from which the respondents aimed at getting additional information