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TABU

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TABU julkaisee lähinnä lääkevalvontaa, lääkehuoltoa sekä terveydenhuollon laite- ja tarvikevalvontaa käsitteleviä kirjoituksia. Julkaisu tarjoaa palstatilaansa myös lääkeasioista kiinnostuneille keskustelijoille. Lehdessä julkaistut kirjoitukset eivät edusta Lääkelaitoksen virallista kantaa, ellei nimenomaan toisin mainita. Kirjoitusten sisältöä voi lainata lähde mainiten. Kokonaisen kirjoituksen lainaamiseen tulee kuitenkin saada kirjoittajan lupa.

TABU publicerar närmast artiklar om läkemedelsövervakning, läkemedelsförsörjning samt övervakning av medicintekniska produkter. Också debattörer med intresse för läkemedelsfrågor bereds spaltutrymme. De artiklar som publiceras i TABU representerar Läkemedelsverkets officiella ståndpunkt om och endast om detta uttryckligen omnämns. Innehållet i artiklarna kan citeras med angivande av källan. För återgivande av en hel artikel erfordras emellertid tillstånd av artikelförfattaren.

TABU publishes mainly articles dealing with medicines control, pharmaceutical services, and the control of medical devices. The periodical also serves as a forum for debate or discussion input from authors sharing an interest in the subject matter. The articles published in TABU do not reflect the official views of the National Agency for Medicines, unless specifically stated otherwise. Any articles published may be quoted provided that the source is mentioned. An entire article may, however, not be reproduced without obtaining the author's permission prior to publication.

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Summary

Lehden artikkelien otsikot löytyvät aiheittain ryhmiteltynä Lääkelaitoksen kotisivulta ***www.nam.fi*** *kohdassa Julkaisut – TABU. Hakemistossa ovat mukana artikkelit ensimmäisestä numerosta (1.93) lähtien. Viimeisimmät numerot löytyvät kotisivuilta pdf-muodossa.*

Summary

Juhani Sivula
HEAD OF DEPARTMENT
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Editorial

Electronic services in the Internet

As a concept, "information society" first emerged in the public debate as long ago as the early 1990s. In those days, information society became a major target in renewing economic structures and the public administration in Finland. That development has been pursued in the form of several explorative and fact finding projects. The issue has been included in Prime Minister Paavo Lipponen's government policy and programme. In April 1999, the following items were added to the government programme: *"Finland will be turned into an information society, in which knowledge and skills are an essential part of education and culture, and the principal factor in production. Her policy on technology shall place Finland in the vanguard of developed nations. Finland wants to set an example for others in creating a humane and sustainable information society. That objective involves developing electronic services, and cultural and other informative content or substance that is safe and easy to access and use by everyone, whether the medium be a computer, digital television, or mobile telecommunication equipment."*

Building electronic networks to facilitate transactions between the citizens and the public administration has progressed relatively rapidly in various public organisations, departments, facilities and agencies, in keeping with the '*Nation in the Forefront*' objective. We have hardly earned a gold medal in this matter so far. There is still work to be done before the next Olympic Games. In facilitating electronic transactions, most organisation and government departments have advanced to the stage of having their own web pages in the Internet. The service they thus provide in the Internet is mainly informative in nature, enabling information searches. The opportunity to ask the Webmaster questions is often a part of this service. Public administration organisations are only now creating systems for producing actual electronic services. Some pilot projects have already created successful solutions. For instance those pertaining to statistics, address, and motor vehicle data systems. Commercial interests are clearly speeding up the development of electronic transaction systems for the citizens.

In terms of the information society objective, a citizen, individual, or organisation shall be able to initiate a process or matter with a public administration organisation through electronic media. Information safety is an important aspect of transactions with the public administration. Both the citizen and the public authority must be certain of the identity of the person initiating a transaction or raising a matter. Legislation controlling personal identification and the production of electronic signatures came into force at the beginning of December 1999. In this regard, the framework exists, but suitable applications and hardware are not yet commonplace.

The trend is obvious, and the speed of these developments is considerable. Information safety also means that both the citizen and the authority must be able to trust that the requirements of confidentiality of transactions are met even in electronic transactions between the parties. A closed network is not a comprehensive solution between client and authority, at least not in an open operating environment and with a large number of citizens as clientele.

The development of electronic transaction systems in the field of medicines could be described in terms of an increasing volume and broadening coverage of information due to be become accessible in the informative web pages of National Agency for Medicines. With increasing volume, I am referring to the possibility that our clientele, partners and interest groups could link their own web pages to the already extensive body of data available through our web pages. As I understand it, broadening the coverage refers to making additional information available. The objective is to have the summaries of products characteristics (SPCs) and package inserts (PILs) of medicines accessible to all citizens on NAM's web pages.

The next, and far greater step in the development of electronic transactions, will be the adoption of a system, in which every stage from initiating the action, making an application, and its processing will all take place via the Internet. Information safety issues are the foremost problems still to be solved. The advantages for both the clients and the authorities are so significant that this objective is worth striving for.

Translation Liisa Fellman-Paul

Summary

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Medical treatment of psoriasis

Regular use of basic emulsion creams will moisturise the skin, prevent chapping of affected patches and relieve itching. Antihistamines are required if the rash is itchy.

Peeling off scale

Keratolytic treatment prepares the rash for effective treatment during the course of the disease. Forcible removal of scales is not recommended since disease activation is enhanced by damage to the lesions (Koebner phenomenon).

The most common keratolytic treatment consists of 2–10% salicylic acid in vaseline. A 2–3% concentration may be adequate for thin patches on the body and legs and arms, whereas a concentration of 5–10% is necessary for thick patches on the soles or palms, and for the scalp. The risk of overdose should be kept in mind when treating children and very extensive areas affected with psoriasis, since about 60% of the salicylic acid is absorbed from the skin. Salicylic acid/keratolytic therapy should not immediately precede phototherapy since it attenuates the effect of UV light.

Vaseline should not be prescribed to treat the scalp as it cannot be washed out of the hair. For peeling off scales of the scalp, for example, a 5–10% salicylic acid ointment or oil can be used, rubbing it into hair partings made over the scaling areas of the scalp and by leaving it overnight. The hair usually requires to be washed 2–3 times with a shampoo following scaling off treatment. Loose scales are either brushed or combed out of the hair.

Topical treatment

Tar has been used in the treatment of psoriasis for over a hundred years
Mild preparations containing coal tar *(Pyroleum lithanthracis)* or coal tar spirit (*Spiritus carbonis detergens)* are appropriate in the outpatient care and treatment of mild psoriasis, but due to their unpleasant odour and messy methods of application the use of more potent preparations is most practical in hospital.

Popular corticosteroids
Topical corticosteroid therapy is recommended in the short-term treatment of plaque psoriasis because it is easy to use and well tolerated. Absorption is more efficient from a fatty ointment than from an emulsion cream. General instructions include the use for 2–4 weeks of corticosteroid which has been chosen on the basis of the location and severity of the eruption. Thereafter the treatment is withdrawn gradually.

Moderate potent corticosteroid preparations are used on thin skin areas, and potent or very potent corticosteroids are used elsewhere.

The risk of systemic adverse effects should be kept in mind when large areas of skin are treated. Topical adverse effects include atrophy, striae (streak lines) and telangiectases. Tachyphylaxis or renewed flaring up of skin symptoms (rebound effect), induced by quick withdrawal of corticosteroids, may be associated with a prolonged course of treatment.

Calcipotriol a vitamin D derivative
Calcipotriols efficacy corresponds to that of corticosteroids of Group III. The amount of calcipotriol ointment used in one week should not exceed 100 g. The amount used in one week by children over the age of 12 should not exceed 75 g, and 50 g is the maximum weekly amount for children between the age of 6 and 12. At these dosages calcipotriol will not affect the body's calcium metabolism. The results will show typically in 6–8 weeks. Calcipotriol will not cause thinning of the skin or tachyphylaxis, but local irritation occurs in 5–25% of patients. Calcipotriol should not normally be used on the facial area, and its use in flexures should be avoided.

A patch of psoriasis may retain its redness following calcipotriol therapy. A corticosteroid may be used as a possible adjunct to calcipotriol treatment by using one drug in the morning and the other in the evening. This will produce a more complete remission of patches.

Tazarotene a vitamin A derivative
Tazarotene is a synthetic retinoid, only less than 5% of which is absorbed through the skin. In practice, the most common adverse effect is irritation of the skin. Tazarotene therapy is most appropriate for a patient with a maximum of 10% of skin area, involving the body, legs and arms, affected by plaque psoriasis. The gel is applied in the evening, thinly and only on the areas of rash, avoiding any healthy skin, flexures and the face. The symptoms of irritation include redness of the skin, pruritus, burning sensations and even pain in the skin.

If the psoriasis is severely inflamed, a two-week course of treatment with a very potent corticosteroid is recommended, and tazarotene therapy is continued thereafter. To improve the effectiveness

and toleration a potent corticosteroid may be used on alternate days, with tazarotene or as adjuvant therapy once a day. The typical duration of tazarotene therapy is 12 weeks. The drug must not be administered to women who are planning pregnancy or are pregnant or breast-feeding. Tazarotene may be combined with methotrexate and cyclosporin therapy, but not with systemic retinoid therapy with acitretin.

Disregarded dithranol
The disadvantages of dithranol include irritation of the skin and staining. The "minutes method" is appropriate in outpatient care; the cream only applied to affected skin areas for 10–30 minutes once a day, after which it is washed away. The use of an acid detergent will reduce staining. The eyes, mucous membranes and the neighbourhood of flexures must be avoided. Administration of dithranol is suitable for children and during pregnancy. No tolerance is developed.

The tools of a dermatologist include systemic treatment

Systemic antipsoriatics are considered for the treatment of rash affecting extensive skin areas if other treatment is inadequate or the patient suffers from treatment exhaustion. Erythrodermic generalised pustular and arthritic psoriasis usually require internal drugs. Intermittent therapy reduces the long-term risks of medication.

Methotrexate has been used for treating psoriasis over half a century
In the treatment of psoriasis, methotrexate is administered once a week. Patients like methotrexate therapy because the response is achieved quickly and they usually notice no adverse effects.

Methotrexate is excreted mostly via the urine, and consequently, even mild renal insufficiency needs to be taken into consideration when administering the drug. The risks of leucopenia and thrombocytopenia are increased by e.g. sulphas, NSAIDs, tetracyclines, penicillins, phenytoin, diphenylhydantoin, furosemide, corticosteroids, barbiturates and probenicid. The treatment is contraindicated in bone-marrow dyscrasias and in patients with active or recent gastric or duodenal ulcer. Folic acid therapy can be given to prevent nausea and the bone marrow toxicity of methotrexate.

The biggest risks of long-term administration are chronic hepatitis and cirrhosis. Liver biopsy (1.5g total dose intervals) or measurement of the serum levels of aminoterminal propeptide of type III procollagen are recommended as a means of monitoring.

Acitretin produces excessive scaling in psoriasis
Acitretin is exceptionally teratogenic, and it should not be administered to a woman of child-bearing age unless reliable contraception is used during, and for two years after completion of, the treatment. Acitretin is used in the treatment of extensive erythrodermic, topical, generalised pustular psoriasis. Acitretin is contraindicated in patients with severe hepatic or renal insufficiency.

At the start of acitretin therapy the affected areas produce more scales and seem increasingly inflamed for 6–8 weeks. The after effect of retinoid therapy is long-lasting, and the patient may stay symptom-free for months following completion of therapy. Adverse effects include dryness of mucous membranes, loss of hair and infection of the nail folds.

Adverse effects associated with long-term use include hepatoxicity, increased levels of serum triglyceride and cholesterol, and skeletal changes. Retinoid therapy which has lasted for several years may be associated with skeletal malformation.

Cyclosporin acts as a brake on immune processes
Cyclosporin is kept specifically for the treatment of severe psoriasis in cases where other treatment is ineffective or inappropriate. Cyclosporin therapy should not be introduced in patients with untreated infections, immune deficiency or a history of malignancy. Induction of cyclosporin therapy requires careful consideration in patients who have received large amounts of UV phototherapy, lest it increases unnecessarily the risk to the patient of light-induced cancer.

Long-term treatment carries the risk of nephropathy. Other drugs causing renal toxicity should not be used during treatment.

What is UV phototherapy and with what treatment can it be combined?

UV phototherapy is classified into types UVA and UVB. The healing effect of ultraviolet rays on psoriasis is restricted on the erythematogenic UVB band, and the treatments (UVB and SUP) have an anti-inflammatory and immunosuppressive effect. In photochemotherapy, i.e. PUVA therapy, the skin is sensitised both internally and externally with a psoralen-containing preparation and exposed to UVA radiation (psoralen + UVA). UV phototherapy is given to psoriatics under the supervision of a specialist.

Outlook

A better understanding of the causes of psoriasis will make it possible to develop and improve the direction of therapies towards the various phases of the aetiology. Active research is focussed on genetics, immunology, intercellular signals and transcription factors. New analogues of vitamin D_3 (tacalcitol and 22-oxacalcitriol, i.e. liver calcitol) are developed for topical treatment of psoriasis. Research among retinoids has focussed on systemic bexarotene for the treatment of moderate and severe psoriasis. Liarozol is an imidazole derivative which inhibits the metabolism of cytochrome P450-dependent retinoic acid and thereby increases the blood retinoic acid concentration. The focus of research within immunotherapy is concentrated on e.g. immunosuppressive interleukin-10 and human monoclonal anti-IL8 antibody. Combinations of treatments are also being developed to include the systemic treatments of psoriasis available today, e.g. rapamycin (sirolimus) combined with cyclosporin therapy in small doses. Information obtained from genetic research may even make gene therapy of psoriasis possible in the future.

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Difficult introduction of a new antirheumatic drug

A new drug for the treatment of rheumathoid arthritis, etanercept (Enbrel) is a TNF-modulator. It has been granted marketing authorisation in the EU centralised approval system, but so far has been prescribed in Finland for only a small number of patients. A total of 80.000 patients world-wide have been treated with etanercept.

In clinical trials the drug was well tolerated, and the most severe adverse reaction was increased susceptibility to infections. New features have emerged since the drug has been introduced on the market. An abstract recently published at a meeting of the American College of Rheumatology discusses four cases which indicate that etanercept may be associated with exacerbation of multiple sclerosis.

Recent world-wide reports on the use of etanercept include three cases with associated aplastic anemia and seven cases of pancytopenia; in five of these cases the patient died of sepsis. The drug treatment in these cases had lasted between two weeks and five months, and some of the patients had had either previous or concurrent treatment with known myelosuppressive drugs such as methotrexate, leflunomide, 6-mercaptopurine, cyclophosphamide or azathioprine.

It is recommended that patients on Enbrel therapy be advised to seek medical treatment at once should unexpected liability to bleed or bruise, or susceptibility to infections, supervene.

Ventricular arrhytmias associated with antipsychotics

Ventricular arrhythmias associated with the use of various drugs have recently been discussed widely (in TABU 6/1999, 4/2000), the most recent case being cisapride. Many neuroleptic drugs, including thioridazine, haloperidol and sertindol have been alleged to prolong the QT interval and cause the ventricular tachycardia known as torsade de pointes (wave-burst arrhythmia). Consequently, authorisation for the marketing of sertindol has been cancelled temporarily. Among the older neuroleptic drugs, thioridazine has been the first to undergo closer scrutiny; this has resulted in the USA last summer, and in Finland this autumn, in restriction of the indications for thioridazine, which is now prescribed only as a secondary drug in the treatment of psychosis.

Reassessment of all neuroleptic agents with regard to their potential for causing arrhythmias has meanwhile begun in the CPMP Working Party on Pharmacovigilance.

Tendinitis associated with fluoroquinolones may be prolonged

This year the National Agency for Medicines has so far received two reports on Achilles tendinitis commencing during ofloxacin therapy of usual duration; the condition has lasted more than a year in one case, and five months in the other. Tendinitis associated with fluoroquinolones is usually cured relatively quickly, but according to the literature the condition is known to be prolonged in about 10% of such patients. Long-term lesions have also been found in animal models.

Translation Mervi Moisander