TABU

Lääkeinformaatiota Lääkelaitokselta

Läkemedelsinformation från
Läkemedelsverket, Finland

Drug information from the National
Agency for Medicines, Finland

2 | 2005

TABU 2.2005

13. vuosikerta
13 årgången
13th Annual volume

På svenska

In English

ANNA-LIISA ENKOVAARA
Senior Medical Officer
National Agency for Medicines

Editorial

Traditional herbal medicinal products – changed monitoring within the EU

The Directive 2004/24/EC regarding traditional herbal medicinal products came into force on the 30th of April 2004. The Directive will become applicable in Finland at the same time as the reform of the Medicines Act, by the 30th of October 2005. Traditional herbal medicinal products are medicinal products which contain herbs traditionally used as medicines, such as valerian, hops or nettles. Such a product is intended for the alleviation of small complaints and may, in addition to herbal extracts, only contain vitamins and minerals. The preconditions are that the product has been used as a medicine for at least 30 years, a minimum 15 of them within the European Community, and that it has not been found to cause any harm during that time.

Traditional herbal medicinal products may be sold once they have been registered by the national authority. Compared with the drug marketing authorisation procedure, the registration system is simpler. No preclinical or clinical trials need to be carried out with the product if the authority considers that on the basis of experience of use for 30 years the minor effects and safety of the product are reliable. The quality requirements of traditional herbal medicinal products correspond to the quality requirements of conventional medicines.

EMEA already has an established committee, the Committee for Herbal Medicinal Products, HMPC. It started its work in the summer of 2004 with one expert member nominated from each of the 25 member countries. The aim of the Committee is to guarantee the safety of the herbal medicinal products sold within the Community area and to harmonise in the member countries the status of products containing medicinal herbs. For this purpose the Committee will compile a list of such medicinal herbal extracts and their compounds as fulfil the requirements of the Directive and which can be used in traditional herbal medicinal products. Within a couple of years, these lists will form the basis for national registrations and approval for registrations.

Since 1983 the Finnish legislation on medicines has contained regulations on products which were called 'products similar to medicines' at first, and now 'herbal medicinal products'. Marketing authorisations have been approved for the products by the National Agency for Medicines and their applications have been as bibliographic applications. Results of preclinical or clinical trials have not been required for the products if proof has been found in the scientific literature that the herb contained in the product has enjoyed 'an established status in medical use, acknowledged efficacy and approved level of safety'. An established status means that the product has been used as a medicine within the EU for at least 10 years. In other words, the marketing authorisation procedure for the present herbal medicinal products has already been a kind of less onerous version of the proper procedure.

While reform of the Medicines Act is taking place, a few of the present herbal medicinal products will be considered as traditional herbal medicinal products referred to in the new Act, for example, certain products containing ginseng. Some of the herbal medicinal products do not, however, fulfil the definition of a traditional herbal medicinal product, and consequently a number of products may also fall into the category of conventional medicinal products. Following the reform of the Medicines Act, depending on the composition, traditional use and therapeutic indications, a herbal medicinal product may be a subject either for registration as a traditional herbal medicinal product or for a marketing authorisation application as a conventional medicinal product.

ELINA KOLHO
MD, Specialist in Internal Medicine
HUS

Urinary tract infections in elderly institutionalised patients

Urinary tract infection is the most common bacterial infection in patients in long-term-care facilities. A prevalence study carried out in the USA showed that almost one in ten institutionalised patients had been prescribed a systemic antimicrobial. As many as half of these medications are indicated as having been for the treatment of urinary infections.

Asymptomatic growth of bacteria (bacteriuria) is a very common finding in the elderly population. Its prevalence increases with age as it is found in 20% of women aged 80 and over and in 10% of men in the corresponding age group. The risk of bacteriuria is also increased by reduced functional ability.

Bacterial colonisation in the periurethral area is of key importance in the development of bacteriuria. Bacterial colonisation is increased by oestrogen deficiency, a lack of bactericidal prostate secretions and faecal incontinence. Even though oestrogen deficiency is considered a risk factor for bacterial colonisation, oestrogen therapy has not been found to decrease the occurrence of bacteriuria in women in institutionalised care. Asymptomatic bacteriuria is found in 15–30% of men in institutionalised care, whereas the corresponding percentage in women is 30–50. Bacteria are detected in the urine of all patients with a permanent catheter in place for a minimum of two weeks (1, 2).

According to the literature, the frequency of symptomatic urinary tract infection is 0.1–2.4 per 1,000 days of treatment. The big differences between various studies are explained by the number of patient specific risk factors and the criteria used in the diagnosis of the infection. Symptomatic infections are more common in women, in whom the frequency is about four times that in men. Urinary tract infection with fever is nevertheless distinctly rarer and its frequency in different studies has varied between 0.05 and 0.10 per 1,000 days of treatment.

Factors exposing the patient to urinary tract infection include foreign objects in the urinary tract, e.g. catheters, and difficulty in emptying the bladder. Bladder emptying difficulties are usually due to prostate hyperplasia, uterine prolapse or neurogenic disorders of the bladder (1, 2).

Diagnosis of urinary tract infection – a general approach

Asymptomatic bacteriuria in institutionalised patients should not be treated with antimicrobials except prior to elective urological procedures. According to three randomised, prospective studies, such treatment of asymptomatic bacteriuria did not reduce the prevalence of symptomatic infections or the mortality in institutionalised patients (3, 4) or the elderly (5). The unnecessary use of antimicrobials increases the costs and exposes the patients unnecessarily to adverse effects. Unnecessary use of antimicrobials should also be avoided because it increases the antimicrobial resistance. Several studies on long-term-care facilities have shown that preceding antimicrobial medication is a risk factor for the resistant microbial colonisation or consequent infection. It is difficult to spot the possibility of resistance in empirical treatment, and consequently the outcome of treatment for severe infections in carriers of resistant microbes may be poorer than in other patients. In long-term-care facilities, resistant microbes may be transmitted from patient to patient by contact infection. Copious use of antimicrobials promotes the selection of resistant microbes, which may easily result in an endemic of these organisms. In the hospital district of Helsinki and Uusimaa, the majority of the strains isolated from the urine in long-term-care departments are *E. coli* strains resistant to third generation cephalosporins (ESBL producing strains).

Since treatment of asymptomatic bacterial growth with antimicrobials is common in institutionalised patients, attempts have been made to create various combinations of definitions for the diagnosis of symptomatic urinary tract infection. The minimum criteria set at a US consensus meeting for urinary tract infections in cases where the institutionalised patient does not have a foreign object in the urinary tract are presented in Table 1. (6) If the

Table 1. Minimum criteria of urinary tract infections according to a US consensus meeting (6)

Dysuria, or
axillary temperature > 37.8° and at least one of the following:

- *Increased compulsion to micturate; either a new symptom or increased from previously*
- *Increased desire to micturate; either a new symptom or increased from previously*
- *Suprapubic pain*
- *Hypersensitivity in the renal region*
- *Macroscopic haematuria*
- *New urinary incontinence*

Table 2. Limit values of urinary culture in different types of infection

Uncomplicated urinary tract infection in women	*10^2 bacteria/ml (pyuria is expected)**
Complicated urinary tract infection in women	*10^5 bacteria/ml*
Lower urinary tract infection in men	*10^4 bacteria/ml (pyuria is expected)*
Pyelonephritis	*10^4 bacteria/ml (pyuria is expected)*

** the sensitivity level of a common urinary culture is 10^3 bacteria/ml*

Table 3. Inducers of urinary tract infections in long-term-care residents

Gram-negative rods
- *E. coli*
- *Klebsiella species*
- *Proteus species*
- *Enterobacter species*
- *Providencia stuartii*
- *Morganella morganii*
- *Serratie marcencens*
- *Citrobacter freundii*
- *Pseudomonas aeruginosa*

Gram-positive cocci
- *Enterococci species*

patient does not have a urinary tract catheter in place, the diagnosis of urinary tract infection according to these criteria always requires symptoms localised in the urinary tract, with an acute onset or acute exacerbation (6). If the patient has a urinary tract catheter in place, the symptoms of lower urinary tract infections are absent. The indication for therapy is a suspected upper urinary tract infection, the symptoms of which either in combination or alone include fever, fits of shivering, delirium or hypotension (6).

Unspecific symptoms in institutionalised patients, e.g. loss of appetite, tiredness, nausea and confusion are often suspected of resulting from a urinary tract infection. General symptoms are nevertheless seldom the result of a urinary tract infection. In practice, diagnosing and deciding on the correct treatment may be difficult, especially if the patient is suffering from numerous cognitive disorders, which makes it difficult to obtain from him/her a reliable history of urinary tract symptoms. If, due to unspecific symptoms, treatment of bacteriuria is indicated as the outcome of diagnosis, the symptomatic picture should be recorded prior to treatment, followed by a record of the response. This will help in the choice of treatment in future.

A Canadian survey looked into why treatment is so frequently given for asymptomatic bacteriuria. The survey comprised 16 nurses and 17 doctors with over five years' experience of working in long-term-care facilities. Urine culture was often done at the instigation of a nurse and on account of non-specific symptoms. The indications described by the nurses were, e.g.: "the patient was not quite right" or "the culture was done just in case". The doctors had started the treatment on the basis of urinary findings, because they were not actually in charge of the care and they believed that the cultures were done owing to symptoms, or they were uncertain about the interpretation of the urinary findings, or they were afraid that the asymptomatic bacteriuria would result in a severe infection (7).

Diagnosis based on laboratory findings

The diagnosis of a urinary tract infection is made not only on the basis of symptoms exhibited but also on the basis of significant bacterial growth found in the urine. New recommendations have recently been issued on the limits of significant growth. The new recommendations give different limit values to each type of infection (Table 2). These limit values have not been validated in long-term-care facility residents, in whom the limit of significant bacterial growth could still, as a rule, be considered to be 10^5 bacteria/ml (2). If the symptoms of a urinary tract infection exhibited by a long-term-care facility resident are unambiguous, the diagnosis of a urinary tract infection may nevertheless be considered confirmed even with a lower number of bacteria.

A urinary culture is an important method of examination when a urinary tract infection is suspected in a long-term-care facility resident, since the range of factors likely to cause infection is wider than that in outpatient care (Table 3). A urinary culture confirms the correct choice of medication. A urinary bacterial culture makes it also possible to monitor the prevalence and pathogenesis of urinary tract infections in the care facility or department. Monitoring

will also reveal any epidemics of infection and any resistance problems present.

The urine sample is usually taken from a midstream urine. It is unclear whether washing of the periurethral area reduces the bacterial contamination significantly. Catheterisation on a single occasion only to obtain a urine sample in women is justified if it proves impossible to take the urine sample in any other way. If the patient becomes symptom-free with antimicrobial therapy, monitoring of the urinary culture is not necessary following the treatment (1, 2, 8).

Other urinary examinations in long-term-care patients are less beneficial. Absence of leukocytes in the urinary sample usually excludes any significant bacterial growth reliably enough, unless the patient is neutropenic. Even if the number of leukocytes present in the blood is greater than normal, the finding does not necessarily portend significant bacteriuria, because as many as a third of long-term-care residents are found to have pyuria without significant bacterial growth. Asymptomatic bacteriuria also produces an inflammatory response in the urinary tract, which is why 90% of patients with asymptomatic bacteriuria also have pyuria (1, 2, 8). A number of leukocytes in the urinary sediment of more than 10 leukocytes in the field of vision is significant; less than 5 leukocytes is a normal finding whereas 5–10 leukocytes are found in indeterminate instances.

Examination of the urinary sediment is laborious, and consequently, most places use a strip test for screening. A strip test assesses the leukocyte esterase to detect pyuria and the nitrite test is used as chemical marker for bacteriuria. The sensitivity and specificity of a strip test to detect pyuria (over 10 leukocytes in the field of vision) are relatively good; the sensitivity is 75–96% and the specificity is 94–98%. The specificity of the nitrite test is good, but its sensitivity to detect a significant bacteriuria is below 30% and in long-term-care residents it is likely to be even poorer. In theory, the nitrite test is positive if the urine contains a significant number of bacteria, which produce nitrite, provided that a sufficient amount of nitrates are obtained from food. All the pathogens, such as enterococci and *Pseudo-monas aeruginosa*, which are the common causes of urinary tract infections in long-term-care residents, do not, however, produce nitrite. A nitrite test not positive either unless the urine has stayed in the bladder for at least four hours, because a shorter time is not long enough for the bacteria to transform nitrate into nitrite.

Classification and treatment of lower urinary tract infections

Urinary tract infections are classified as uncomplicated or complicated. A urinary tract infection is complicated if the patient suffers from obstructive uropathy or a bladder retention amounting to over 50 ml. A urinary tract infection is also classified as complicated if the patient suffers from renal impairment, because the secretion of antimicrobials in the urine may be reduced. The division is important, because uncomplicated urinary tract infections can be treated with a 3–5 day course of antimicrobials, depending on the drug, whereas a complicated infection requires a course of treatment lasting for 7–14 days, rarely even longer. Occasionally, a complicated urinary tract infection will not clear up, and the only way out is a long suppressive therapy. Normal therapeutic doses for urinary tract infections, instead of prophylactic doses, are applied in such treatment. The urinary culture is monitored at one month intervals during treatment to ensure that resistance is not developing to the drug used, and that other strains which would be resistant to the drug used will not be selected.

A relapse of a urinary tract infection implies that a symptomatic infection caused by the same microbe is found two weeks after the completion of the antimicrobial therapy. The usual cause of relapse is an ineffective antimicrobial therapy or an insufficiently long course of treatment. Reasons for antimicrobial therapies being too short include, for example, that the patient's infection has been a complicated one after all, or that the patient suffers from a bacterial prostatitis. It might also have been an upper urinary tract infection with a short course of drug therapy or with insufficient concentrations of the chosen drug in the renal tissue. An infection fulfilling the criteria of a relapse may of course sometimes, in reality, be a re-infection. A suspected relapse always requires to be somewhat more closely examined.

It is hoped that the choice of an antimicrobial will be made easier by a Finnish Current Care Recommendation which is being updated at the moment. In the choice of medical treatment for long-term-care residents the general guidelines are only indicative, since the choice should take into consideration the pathogens responsible for the patient's previous infections, the history of antimicrobials used so far, and the endemic microbes of the institution or the department and their situation with regard to sensitivity.

Literature

1. Nicolle LE. Urinary tract infection in long-term care facility residents. Clin Infect Dis 2000; 31: 757-61.
2. Nicolle LE. Urinary tract infection in geriatric and institutionalized patients. Curr Opin Urol 2002; 12: 51-55.
3. Nicolle LE, Bjornson J, Harding GKM et al. Bacteriuria in elderly institutionalized men. N Engl J Med 1983; 3209: 1420-1426.
4. Nicolle LE, Mayhew JW, Bryan L. Prospective randomized comparison of therapy and no therapy for asymptomatic bacteriuria in institutionalized elderly subjects. Am J Med 1987; 83: 27-33.
5. Abrutyn E, Mossey J, Berlin JA et al. Does asymptomatic bacteriuria predict mortality and does antimicrobial treatment reduce mortality in elderly ambulatory women? Ann Intern Med 1994; 120: 827-833.
6. Loeb M, Bentley DW, Bradley S. et al. Development of minimum criteria for the initiation of antibiotics in residents of long-term-care facilities: results of a consensus conference. Infect Control Hosp Epidemiol 2001; 22: 120-123.
7. Walker S, McGeer A, Simor AE et al. Why are antibiotics prescribed for asymptomatic bacteriuria in institutionalized elderly people? A qualitative study of physicians' and nurses' perceptions. Canadian Medical Association J (CMAJ) 2000; 163: 272-277.
8. Wilson ML and Gaido L. Laboratory diagnosis of urinary tract infections in adult patients. Clin Infect Dis 2004; 38: 1150-1158.

TAPANI VUOLA
Senior Medical Officer

LEENA SOMMARBERG
Researcher

TINNA VOIPIO
Researcher

National Agency for Medicines

Reports received by the Adverse Drug Reaction register in 2004

In reporting of adverse drug reactions another record was made last year, a total of 1,118 reports having been received. Almost half of the reports were of serious reactions, i.e. ones which either resulted in or prolonged hospitalisation, caused a permanent injury or reduced the functional ability, or were life-threatening or fatal.

Conclusions about differences among the drugs cannot be made directly on the basis of the number of reactions they caused: frequent use will generally generate a higher number of adverse reactions and a greater number of reports are received on new drugs – which is the way it should be. There are usually more frequent reports on drugs figuring in the media headlines, and the zeal with which the pharmaceutical companies themselves record the reactions they have been made aware of may perhaps manifest itself in the increased numbers of reports of adverse drug reactions.

Cholesterol-lowering drugs

The largest number of reports of adverse drug reactions this year were made about rosuvastatin (by the trade name Crestor); a total of 38 reports. About half of these were of myalgia or a combination of myalgia and elevated creatine kinase. There were also reports of elevated liver values. The sales of rosuvastatin were equal to those of fluvastatin (Lescol), which was the subject of 9 reports, but fluvastatin was introduced on to the market year 1996, whereas rosuvastatin was only introduced year 2003. Six reports of adverse reactions of fluvastatin were of liver effects.

Atorvastatin (Lipitor), which was the drug mostly used in this group, was reported 18 times as having been associated with various symptoms, among which pancreatitis is the one that figures most prominently (4 reports). Simvastatin was reported 15 times regarding the variety of adverse reactions it caused, mostly elevated liver values or myalgia.

Anti-inflammatory and antirheumatic agents

The second highest number of reports of adverse reactions received concerned valdecoxib (Bextra); 31 reports in total. They do not focus directly on any one particular reaction: haematoma, liver reactions and urticaria were each reported 4 times, and, at a quick glance anyway, the rest of the reactions appear to be sporadic.

Etoricoxib, or Arcoxia, was reported to NAM on 26 occasions. Five of them were about elevated liver values, 3 about oedema of the feet and 2 about facial oedema. Celecoxib (Celebra) appears 20 times in last year's records; three of the cases concerning an allergic reaction, two anaphylaxis and five some form of skin reaction.

Fourteen reports were received on rofecoxib (Vioxx, Vioxxakut) with no specific emphasis on any single effect. Only a couple of adverse cardiac reactions were mentioned in the coxib group, even though there was an outcry about these reactions in other countries. However, the reports on coxibs include four cases of ulcer.

The coxibs were introduced on to the market relatively concomitantly followed by insignificant differences in their sales figures and the number of adverse reactions reported. The majority of the reports were about valdecoxib, which was also the drug mostly sold. It is not possible to draw any important conclusions about these adverse effects.

Only occasional reports were received concerning conventional anti-inflammatory analgesics.

As in previous years, the majority of the reports in the antirheumatics group were about infliximab (Remicade); a total of 16 reports. Etanercept (Enbrel) and leflunomide (Arava) were each reported 12 times, and adalimumab (Humira) 8 times. There does not seem to a special focus on any individual drug

"TOP 20" LIST

Medicines	Number of ADR reports
rosuvastatin	38
valdecoxib	31
levofloxacin	28
clozapine	26
vaginal ring with etonogestrel and ethinylestradiol	26
etoricoxib	26
bupropione	25
celecoxib	20
atorvastatin	18
iomeprol	18
infliximab	16
simvastatin	15
terbinafine	15
venlafaxine	15
quetiapine	14
lamotrigin	14
mirtazapine	14
combination preparation with nitrofurantoin and ascorbic acid	14
rofecoxib	14
telithromycin	14

this time, except for the five cases of skin rash reported in association with the use of etanercept. The entire group contains 7 reports of blood count changes, 4 of vasculitis and 3 of pulmonary fibrosis.

Antimicrobials

The third highest number of reports last year were about levofloxacin (Tavanic), which took the first place in the list the previous year. Except in a couple of instances, the reports were about the typical effect of the drug, i.e. inflammation and/or rupture of the Achilles tendon. A colleague, Marja-Leena Nurminen, reviewed the situation in the article on ADRs in 2003 (TABU 2/2004): elderly men (76%) on concomitant corticosteroid therapy appear to be especially predisposed to this reaction. This can also indicate that the drug is used with careful consideration in severe cases. Individual cases have also occurred without concomitant medication with corticosteroids, and consequently, whenever tendinitis is suspected, the use of the drug should be stopped immediately. A couple of reports of adverse effects on the Achilles tendon were also received in association with the use of moxifloxacin (Avelox) and ciprofloxacin (several products).

Telithromycin (Ketek) was reported 14 times last year. Three of the reports concerned visual disturbances, the rest being various. The combination product of nitrofurantoin and ascorbic acid was also reported 14 times. Half of these concerned the well-known adverse pulmonary effects of nitrofurantoin, pulmonary infiltration or pulmonary fibrosis.

Terbinafine (Lamisil) indicated for the treatment of fungal infections was the cause of 15 reports, half of which were about either the lack of or disturbance of the sense of taste, which is a well-known adverse effect of the drug. Only sporadic reports were received on the rest of the antimicrobials.

Hormones

The fourth position on the list of adverse reactions last year has a contraceptive ring (NuvaRing) which contains etonogestrel and ethinylestradiol. It was reported 26 times, and except for the six reports that were about various reactions, as many as 20 concerned the problem of unintended pregnancy.

In proportion with the sales figures, a contraceptive patch (Evra) containing ethinylestradiol and norelgestromine caused about the same number of reports of adverse reactions, i.e. nine, eight out of which were cases of unintended pregnancy. Contraceptive pills (Yasmin) containing ethinylestradiol and drospirenone were the object of reporting 8 times. Two of these reports concerned pulmonary embolism, two others were about cerebral embolism and cerebral infarction. The use of all hormonal contraceptive products is associated with increased risk of venous and arterial thrombosis. It is not known at present, how high the risk is with these more recent products in comparison with the older ones.

Tibolone appears among other hormone products; it was reported 10 times, 5 of the cases were of endometrial cancer, one of breast cancer and one of ovarian cancer. Evaluation of these cases is nevertheless difficult; the likelihood of cancer grows with age, and before tibolone was introduced for the treatment of menopausal complaints, all the women except for one had for years used other hormone therapies. Consequently, the summaries of product characteristics of all products of this group include very comprehensive warnings.

Antipsychotics, antidepressants and bupropione

The fourth and fifth positions on the list are held by clozapine and bupropione, respectively. A total of 26 reports were about clozapine, 17 of which were about its already long and well known adverse effects on blood. Among the antipsychotics in this list, quetiapine (Seroquel) figured 14 times. A variety of reactions were reported, but those most typical of antipsychotics included: three cases of malignant neuroleptic syn-

drome, 2 of granulocytopenia, one of dystonia and one of tardive dyskinesia, plus a variety of other individual cases, such as hyperglycemia, prolongation of QT-interval and hepatitis. Olanzapine (Zyprexa) and risperidone were reported 7 times, including various adverse reactions typical for antipsychotics.

Bupropione (Zyban), used to help people to stop smoking, was reported 25 times. The majority of the cases were associated with various mental reactions (7 in all), but urticaria (4) and skin reactions (4) were also reported.

Among antidepressants there are 15 adverse drug reaction reports about venlafaxine (Efexor) and 14 reports about mirtazapine. In the case of venlafaxine, attention is drawn to QT-interval prolongation, which was the reason for reporting on four occasions. In the case of mirtazapine the focus is on the 7 reports of epileptic seizures. The adverse reactions are mentioned in the summaries of product characteristics of both.

Among the more recent antidepressants, escitalopram (Cipralex) received 9 reports, focusing on a variety of reactions. Milnacipran (Ixel) was reported 7 times, four of which were about hypertension.

Contrast media

'Lasting favourites', as it were, among reportees appear to be the commonly used iomeprol, iopromide and iohexol, which were reported on 18, 13 and 11 occasions, respectively. These iodine-containing contrast media do not appear to differ from one another in respect of their adverse effects. The most commonly reported reactions in this group included urticaria, allergic reaction, nausea and anaphylactic reaction.

Individual medicines

Some individual drugs appeared on the list of the most commonly reported drugs: an antiepileptic agent, lamotrigine (Lamictal) was reported 14 times, half of which concerned cases of various skin reactions of which there also are warnings in its summary of product characteristics. An anticancer drug, capecitabine (Xeloda) was mentioned 11 times, four cases of which referred to a cardiac adverse reaction. Candesartane was a drug under suspicion a total of 10 times in the list of reports. There does not appear to be any particular trend in these reports.

Reporting of adverse drug reactions

The reports play an important role in the evaluation of safety profiles, especially those of the more recent drugs. Prior to introduction on to the market, a drug has always undergone testing with a small group of patients who are usually very carefully selected. It is not until large numbers of patients have been exposed to a drug that its real safety in use can be established. Consequently, special interest at NAM is focused on new types of adverse reactions, new drugs, adverse reactions exhibited in new patient groups and any changes occurring in the frequency of the reactions. It would also be useful if interactions with new drugs were reported.

To make reporting easier, we have released a form in Finnish, which is available for filling in and forwarding on the Internet. It can be found at: http://hava.nam.fi (please note: no www-prefix).

JUHANI OJAJÄRVI
DM, Specialist in Clinical Microbiology

Small sterilizers in Finnish health care

The purpose of sterilization of medical devices is to prevent infection through contamination. In primary health care sterilization is usually done using small sterilization equipment: hot air chambers or small steam autoclaves. The responsibility for the sterilization procedure and associated supervision lies with a competent user. By law, a professional user is an operative unit within social welfare and health care.

The method of steam sterilization is to be preferred to hot air sterilization. A European standard (SFS-EN 13060:2004) defines small sterilizers as steam sterilizers with a chamber capacity not exceeding 60 litres. It is customary to classify the small autoclaves according to the programmes they use (Table 1).

A large number of small sterilizers in use do not yet fulfil the requirements of the standard SFS-EN 13060. Old autoclaves do not have a pre-vacuum phase, and their programmes are therefore similar to the type N programmes referred to in the standard for small steam sterilizers. For the purposes of this article, type N autoclaves fulfilling the requirements of the standard and old autoclaves have both been dealed here as 'type N autoclaves'. Cassette autoclaves of the type used in dentistry do not have a pre-vacuum phase either. They are primarily used for sterilization of instruments.

Purpose of the study

The Finnish Agency for Medicines carried out a project in 2003–-2004 with the purpose of mapping out the existing selection of small autoclaves in primary care in Finland and details of their use. Initial details of a total of 1,003 small autoclaves were received from the biggest suppliers of equipment before the actual start of the study. The majority of devices sold in recent years comply with the standard SFS-EN 13060 on small steam sterilizers.

The survey comprised 272 health care centres or municipal health centres and 1,090 private doctor's surgeries. The health care centres also included units with exclusively dental care services.

The outcome

The survey questionnaire was completed by 90% of the care units. Information was gathered about 1,519 sterilizers from 730 care units. 86% of the health care centres and 45% of the private care units had a sterilizer. A couple of units reported of having outsourced their sterilization operations. Small sterilizers used solely in dental care numbered 182 (12%).

The majority, i.e. almost a third, of the devices were hot air sterilizers (Fig 1). Among table top autoclaves, the proportion of type B autoclaves (with pulsating pre-vacuum) and type N autoclaves was equal, about 22%.

The average age of the devices was about 12 years, but the age distribution was conspicuously wide (Fig 2). The oldest hot air chamber had been in use for 48 years. The average age of hot air chambers was 17 years, and that of small autoclaves 10 years. The number of small sterilizers older than 20 years was 231, 133 of which were hot air chambers and 76 small autoclaves.

The sterilizers were mainly used to sterilize instruments. 106 steriliz-

Table 1. Small sterilizers

- *The type B autoclave is appropriate for all types of sterilization. Expulsion of air from the autoclave is done through fractionated pre-vacuum phases after which the chamber is filled with saturated steam. Type B autoclaves are also appropriate for sterilization of textiles.*
- *The type N autoclave is only appropriate for sterilization of unwrapped solid items. This type of autoclave does not contain a vacuum pump. The sterilized items may not be wrapped, and the items must be used immediately after sterilization. These autoclaves must not be used for sterilization of textiles or hollow or tubular devices, because any residue air can jeopardize the success of sterilization.*
- *The type S autoclave incorporates a number of special programmes for the sterilization of hollow, porous or wrapped devices. These autoclaves can be used to sterilise wrapped items, textiles or tubular items only if the autoclave contains an appropriate programme for doing so.*

ers were used to sterilize textiles despite the fact that they did not incorporate a pre-vacuum phase. Wrapped instruments were also incorrectly sterilized in 269 autoclaves without a pre-vacuum phase, and in 68 cassette autoclaves.

Variations including actual deficiencies were also found in the monitoring of the sterilizing efficiency of the sterilizers. A process indicator, an autoclave colour tape, for example, should be included in every run, but this was only included in 70% of the runs. An autoclave tape glued on to the items was often the only indicator used; this would not give an indication of a successful sterilization process, but instead only of the fact that the item has been in an autoclave. An autoclave leak detection test was carried out at least once a week in only about 12%, and a Bowie & Dick test to measure the air expulsion capacity only in 9%, of the type B table top autoclaves. Nearly 10% of the survey participants reported that they carried out this test on type N autoclaves, despite the fact that the test cannot be carried out on this type of autoclave.

Figure 1. Types of sterilizers

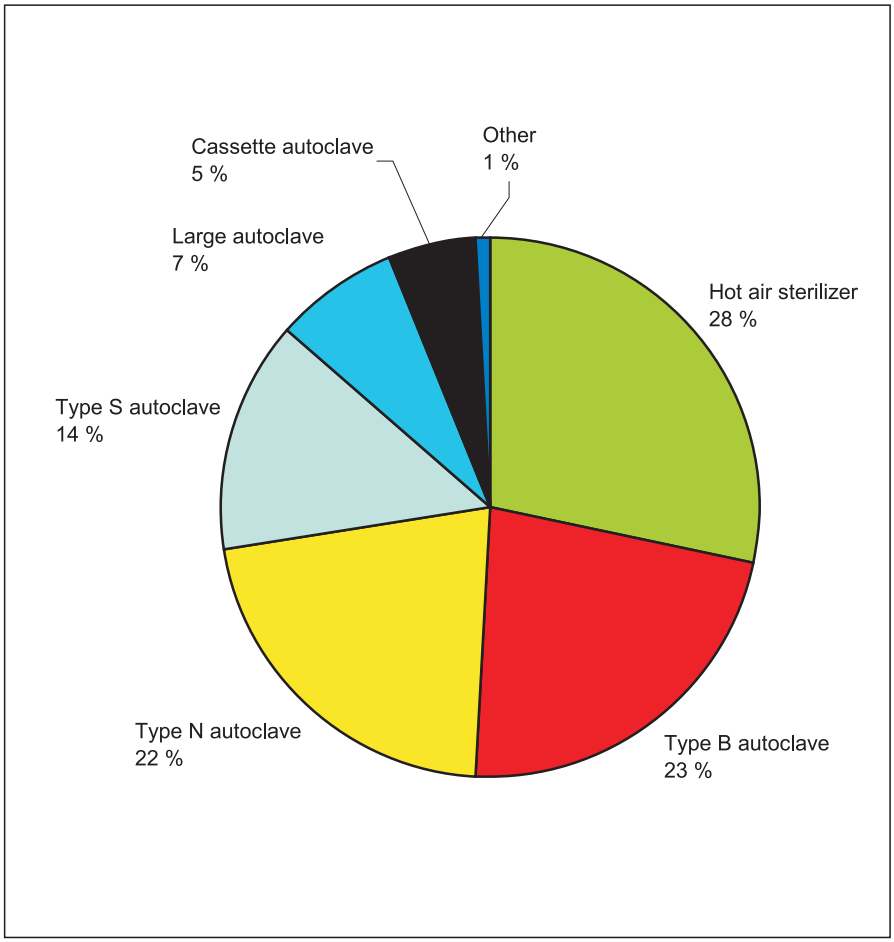

Figure 2. Age of sterilizers

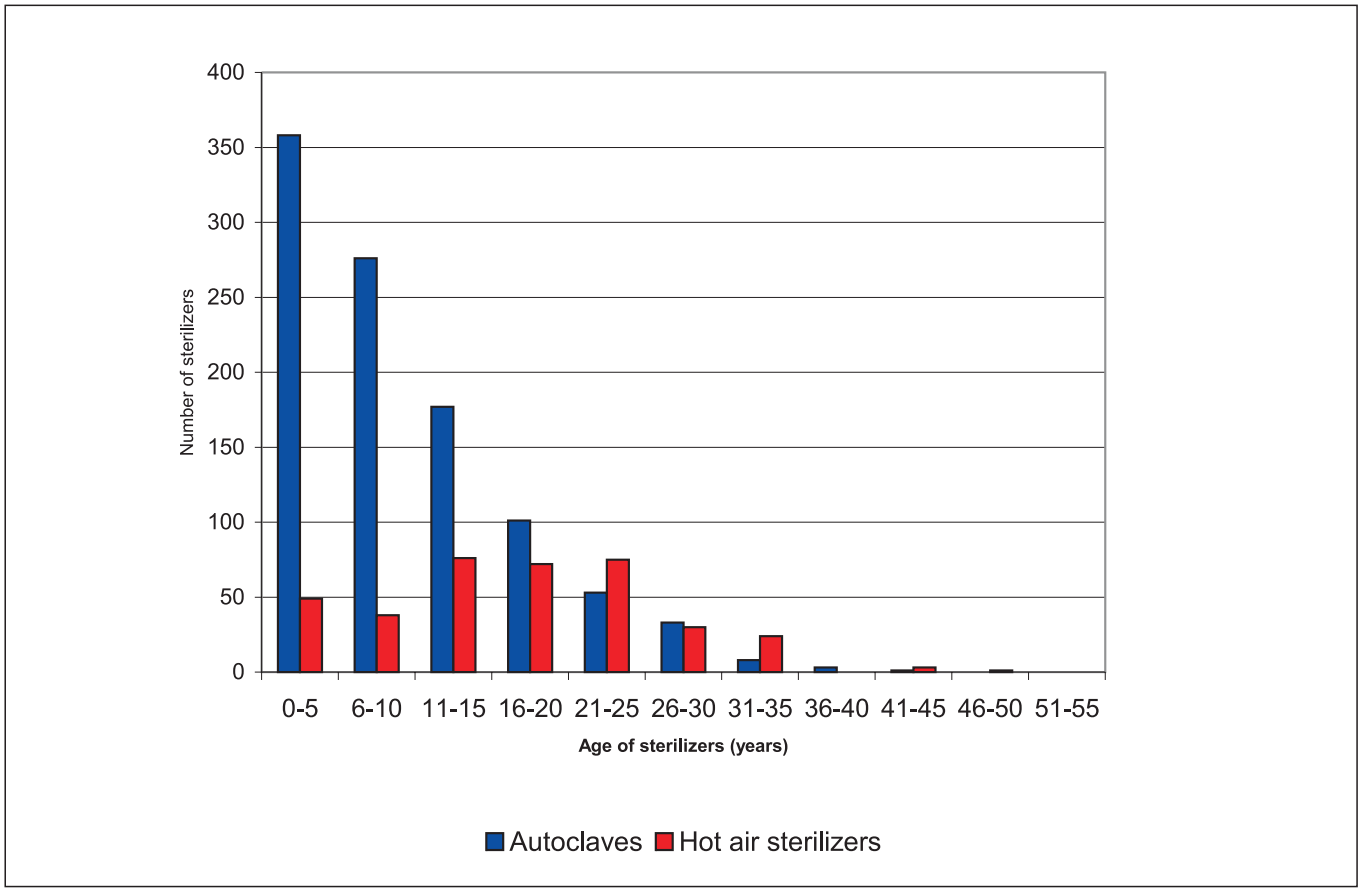

Table 2. Small sterilizers with total lack of monitoring*)

Type of sterilizer	*%*	*number*
Hot air sterilizer	*22,3*	*96*
Type N autoclave	*12,0*	*40*
Type S autoclave	*11,5*	*24*
Cassette autoclave	*7,5*	*8*
Type B autoclave	*4,1*	*14*
Total		*182*

**) no process or biological indicators, no sterilizer leak testing, no Bowie Dick test or equipment calibration carried out*

The status of hot air sterilizers was equally poor: the temperature, time and pressure were monitored in about 42% of the runs and an autoclave colour tape was used in about every other sterilization run. Only about 7% of the thermometers were calibrated as recommended, i.e. at least once a year. 48% of the thermometers had never been calibrated. Biological indicators were used at least every 6 months in only about 12% of the equipment.

A total of 182 (13%) of the small sterilizers had no monitoring of efficiency at all (no autoclave colour tapes, biological indicators, leak detection tests, Bowie & Dick tests or calibration of equipment were used) (Table 2). Hot air sterilizers were found to have the relatively poorest monitoring status: 96 (22%) of them were not monitored at all.

The frequency of maintenance of the equipment varied greatly. Sterilizers underwent maintenance after between 40 and 2,500 uses. Some equipment had never undergone maintenance, even though they had been bought as long ago as in the 1970's.

Conclusions

Finland lacks a comprehensive database of small sterilizers. The survey revealed that the selection of equipment in use is often considerably old. Sterilizers older than 20–25 years are no longer necessarily reliable and require more service and maintenance to work as properly as new sterilizers which comply with the standard for small steam sterilizers. The use of small sterilizers older than 20 years should actually be totally abandoned. The alternatives consist of introducing single use products or buying sterilizing services from an external equipment service.

The new type B autoclaves, which comply with the standard for small steam sterilizers and which can be used for sterilization of wrapped items and textiles, were found in about 23% of the units of the survey. They will gradually replace the old autoclaves in which the residual air is not removed by vacuum.

There are still small autoclaves in Finland in which the residual air is not removed by a pre-vacuum phase. There is usually no system of pre-removal of residual air in the cassette autoclaves either. However, 81% of those taking part in the survey reported that they sterilized wrapped devices and items with these autoclaves as well.

There are big deficiencies in the monitoring of the sterilization processes. The temperature, time and pressure are monitored in only less than 50% of the sterilization processes. The biggest cause for concern arises from the fact that the sterilization process in about 13% of all small sterilizers is not monitored in any way at all. This shows the lack of knowledge about the sterilization process and associated responsibilities in those people answerable for the sterilization.

The Act on Medical Devices includes general requirements with respect to competent professional use and obligations regarding quality assurance and the safeguarding of reliable operation. A competent professional user, in this case a health care unit, is answerable for the safety and use of the medical device. The use of old autoclaves includes risks of unsuccessful sterilizations, possible infections and risks involved with the use of pressure vessels. The quality assurance systems of health care operational units require the use of sterilizers which comply with the standard mentioned earlier, or the introduction of disposable products.

Proposals for future measures

The use of sterilizers older than 20 years is not recommended, because guaranteeing their sterilizing capacity is a complex matter. The measures for servicing old equipment become costly, and this applies also to the organisation and maintenance of staff training. The time spent on servicing the equipment could often be better spent on other duties.

The survey revealed the need for training and information among the staff of the equipment service. Training should be arranged regionally, for example, in association with each hospital district's own training. Measures need to be taken to redress the apparent deficiencies detected in the monitoring of small sterilizing equipment and the need for training among the users.

Translation Mervi Moisander