Summary

Literature search

Introduction: Osteoporosis (OP) is an important non-communicable disease, the incidence of which is increasing. It is a systemic metabolic skeletal disease characterized by reduced bone mass and changes in bone tissue quality. These disorders increase the risk of fracture and consequently have a considerable impact on public health. OP affects primarily postmenopausal women, but has recently become a great concern in men as well.

Among the most important preventive (and non-drug therapeutic) interventions are a diverse diet high in calcium, adequate physical activity, avoidance of exposure to toxic substances and fall prevention. Multiple therapeutic strategies are used in attempts to restore balance between the bone resorption and the bone formation. A first-line intervention is calcium and vitamin D supplementation. Specific drug therapies (anti-osteoporosis drugs) are classified according to the predominant mechanism of action into anticatabolic or antiresorptive drugs (bisphosponates, raloxifene, calcitonin) and formation stimulating, anabolic drugs (parathormones), and drugs with a dual mechanism of action (strontium-ranelate). The current treatment strategies reduce the risk of fracture by about half and have proved cost effective. As in other chronic asymptomatic diseases, poor adherence to OP therapy is a significant medical and economic concern.

Objectives: To provide a comprehensive review of the literature on OP drug therapy adherence and thus to put the adherence data in a wider context.

Methods: PubMed literature search.

Results: Poor adherence to therapy is a great public health concern. Adherence is defined as the extent to which the patient follows medical instructions. Pharmacokinetics and medication adherence are the most significant source of variation in the response to therapy. Generally, about half of patients only take adequate dose of medication needed to achieve the therapeutic effect. This fact results in increased morbidity, mortality and therapy costs. In most studies, medication adherence is either considered as synonymous to compliance or as an umbrella term for compliance (sticking to a prescription drug regimen) and persistence (staying on the medication for the recommended time). Non-adherence means principally two things: (1) the patient takes an inadequate dose of his/her medication (2) the patient takes the medication in an inadequate way.

Currently, there is no gold standard for medication adherence assessment and indirect methods are often used. Adherence correlates vary with population characteristics as well as with the definition and method used for the assessment. Sociodemographic factors usually have no effect on medication adherence. Important factors in this regard are the patient's motivation for treatment, health professional-patient relationship, psychiatric comorbidity, pharmacotherapeutic regimen and adverse events.

Successful strategies to promote adherence are interactive education of patients targeting the motivation for therapy, simple dosage regimens, phone consulting and reminders, case management, therapy monitoring and self-monitoring. Important factors are the quality of the relationship patient-health care professional, patient's realistic expectations of therapy outcome and feedback. Written information provided in addition to oral explanation and multiple sources of information were associated with higher adherence. Nevertheless, written information alone (distributed on leaflets) has low impact. Inappropriate advertising of over-the-counter medicines (paramedicines) can even have a negative effect on adherence to the prescribed drug.

Long-term therapy should be preferably taken not more than twice daily. A prolonged dose interval and use of depot and fixed-combination drugs proved effective. As adherence

correlates negatively with psychiatric comorbidity, early diagnosis and treatment of mental disorders can enhance adherence to treatment of somatic conditions. Higher adherence to co-pay therapy can also be achieved by promoting access to cheaper generic drugs. Helpful measures for combating spontaneous non-adherence can be matching medication times with daily routine activities and using medication dispensers, organizers and reminders.

Conclusion: The medication adherence monitoring should be an integral part of routine clinical practice, particularly in patients with chronic asymptomatic diseases.

Original part

Introduction: Improved adherence to antiresorptive OP therapy may significantly reduce osteoporosis-related fracture risk. Approximately 50% of patients do not follow their prescribed treatment regimen and/or discontinue treatment within 1 year. The asymptomatic nature of the disease is a factor contributing to non-adherence. In contrast to other "silent" diseases, there is a lack of options for patient self-monitoring, which can promote medication adherence. Some studies have shown that increased knowledge about OP is associated with greater adherence to preventive behaviours. Bisphosphonates (BIS) require particular attention with respect to compliance, as they need to be used in a special way to maximize gastrointestinal absorption of the drug and reduce risk of adverse effects. Although regimens with longer dosing intervals may modestly improve adherence (and persistence in particular) to BIS therapy, it should be understood that missed doses or improper dosing may have greater consequences with extended dosing intervals. The benefit from anti-osteoporosis treatment shown in large fracture end-point trials can only be achieved in calcium and vitamin D replete patients. Calcium and vitamin D supplementation is therefore recommended for all patients receiving anti-osteoporosis treatment.

Objectives: In women over 40 years of age followed up for OP in specialized centres: (1) to analyze OP drug therapy; (2) to estimate the rate of non-compliance with OP drug therapy; (3) to analyze correlation between OP drug therapy compliance, OP-related knowledge and other demographic and medical factors; (4) to find out and compare the extent of OP-related knowledge in followed up OP patients and women not treated for OP; (5) to study the factors influencing OP-related knowledge.

Methods: A cross-sectional study using a multicentre questionnaire survey (in 9 specialized centres in the Czech Republic).

The following subjects were addressed: (a) women diagnosed with OP (osteopenia) and currently treated for OP (group OS) and (b) a comparison group of first-time attendees (women referred for the assessment of OP). The compliance was analyzed at three levels: (1) drug compliance (based on the number of missed doses of antiresorptive drug over the last month), (2) calcium/vitamin D supplementation, and (3) for bisphosphonate therapy, compliance with the guidelines for safe drug use and good gastrointestinal absorption. The OP-related knowledge was assessed using the Osteoporosis Questionnaire (OPQ; Pande, et al., Maturitas 2000).

Results: A total of 474 women were studied, median age of 63 years; 306 subjects were assigned to OS group and 168 subjects to the comparison group. In OS group, 200 (65%) patients were treated with specific therapy, i.e. with alendronate (44.5%), risedronate (24.5%), raloxifene (18%) and calcitonin (13%). Calcium supplementation was reported by 73% of the patients and vitamin D supplementation by 62% of the patients. No significant difference in calcium/vitamin D supplementation was found between therapies. Supplementation was less frequent in the patients who had not provided the data on compliance. No correlation was found between the types of compliance specified above. The most frequently reported reason for non-compliance was „drug not handy". Compliance with bisphosphonate therapy was

higher compared to raloxifene and calcitonin. The mean compliance rates did not differ between once-daily and once-weekly bisphosphonates. Calcium supplementation was associated with obtaining information on OP treatment from other sources besides health care professionals (p = 0.038). Compliance with the guidelines for proper bisphosphonate use correlated strongly negatively with age (p < 0.001). The OP knowledge scores (median scores from the OPQ) obtained by OS and comparison group were 7 and 6, respectively. Statistical analysis adjusted for age revealed better OP-related knowledge in OS group (p = 0.019). Surprisingly, poor scores were obtained for the questions concerning life style (physical activity, diet, alcohol consumption). In both OS and comparison groups, OP-related knowledge correlated positively with education level and hormone replacement therapy use and negatively with age (p < 0.001 for each of the factors). OP-related knowledge was higher among women with better health than in women with poorer health in the OS group. None of the outputs describing compliance correlated with OP-related knowledge.

Conclusion: The study group showed inadequate OP-related knowledge and poor therapy compliance. The most relevant problems are: (1) poor awareness of the first-line therapeutic and preventive strategies to control OP, (2) low calcium and vitamin D supplementation in patients on specific therapy and (3) non-compliance with the guidelines for safe bisphosphonate use and absorption in older patients. Therapy adherence promotion needs to target the patient's motivation for therapy rather than the OP education alone.