Update on Treatment of Osteoporosis

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Biphosphonate was the first class of drugs shown to be effective in preventing non-vertebral fractures. They have been in the market for over ten years in Hong Kong. In recent years, several other classes of drugs have been introduced. Yet the age adjusted incidence of osteoporotic hip fractures in older people has not declined. This is in part due to the low usage of osteoporosis therapy. Barriers included the availability and costs of bone mineral density measurement (BMD) by Dual energy X ray Absorptiometry (DEXA) scan, the costs of osteoporosis medications, and the lack of awareness among attending doctors.

An important limitation of osteoporosis therapy has been drug non-compliance. Biphosphonates need to be taken with an empty stomach and in the upright posture, in order to prevent poor absorption and oesophagitis respectively. Compliance can be significantly improved with less frequent dosing regimes. Alendronate can be taken once weekly and has shown to be as effective as the once daily regime in increasing bone mineral density. This appears to be a class phenomenon and can be explained by their high affinity to bone and their apoptotic effects on osteoclasts. More recently, ibandronate has shown to be effective even when given once a month orally or once in three months if given intravenously. A very potent form of biphosphonate – Zolendronate can be given by a half hour infusion once a year, and this has been shown to be effective in improving BMD and preventing fractures in a randomised placebo trial. The infrequent dosing offers a distinct advantage in the older osteoporosis patients who already suffer from polypharmacy.

There have been concerns on the long term safety of biphosphonate therapy, because of its potent inhibition of osteoclastic activity. In particular, there have been rare reported cases of irreversible osteonecrosis of jaw which is devastating to patients. Orthopaedic surgeons have also reported cases of unusual fractures e.g. mid femoral fractures in those on long term treatment of biphosphonates. The significance and explanation of these case reports need further evaluations. On the other hand, the extension trial of the original FITS trial showed that alendronate therapy for ten years continued to show benefits in BMD and fracture rates.

In middle-aged postmenopausal women who have low absolute risks of non-vertebral fractures, selective oestrogen receptor modulators (SERM) may be a good alternative treatment. They are effective in increasing BMD and have been shown to prevent vertebral fractures. More importantly, they have protective effects against breast cancer, though risks of venous thrombosis and fatal stroke are increased. Hormonal replacement is no longer recommended as a treatment or prevention of osteoporosis in menopausal women because of the increase in relative risk of breast cancer. They may be prescribed if the women are willing to take the risk and undergo yearly mammogram.

Both biphosphonates and SERM work by inhibiting osteoclastic (bone resorptive) activities which are in relative excess of osteoblastic (bone building) activities. But the age related decline in osteoblastic activities is also a major factor of age related osteoporosis. Parathyroid hormone (PTH) has been well known to increase bone turnover, and persistent hyperparathyroidism has been associated with osteoporosis. However, intermittent PTH stimulates osteoblasts without significantly affecting the osteoclasts. This major finding led to the development of intermittent PTH therapy which has been shown to be very effective in increasing BMD and preventing osteoporotic fractures, particularly at the spine. Up to one fifth of patients may develop mild hypercalcaemia in the first six months, which usually resolves with dose reduction. Unfortunately, the high drug costs and the need to be given as once daily subcutaneous injections have meant that the indication for PTH is limited to those with severe osteoporosis (T score less than -4.0) and with high fracture risk. It is not recommended to continue with the treatment for more than eighteen months because of the concern over the risk of osteosarcoma.

Strontium is an interesting trace element which stimulates osteoblasts and inhibits osteoclasts at the same time. It has been shown to reduce the incidence of vertebral and non-vertebral fractures in older people. It offers a good alternative to biphosphonates particularly in those who have gastrointestinal side effects from biphosphonates, and its powder preparation also facilitates its use in frail elders who cannot swallow tablets.
Older people often have low calcium intake and have subnormal vitamin D status because of low level of outdoor activities and renal impairment. Any drug treatment of osteoporosis should be accompanied by calcium and vitamin D supplements. These supplements on their own can be expected to offer some protection against fractures in those with sub-optimal vitamin D and calcium status. Although Hong Kong is in the subtropical region, a local study showed vitamin D deficiency is also prevalent in older people.

To encourage more treatment of osteoporosis in people who are most likely to suffer from fractures, the WHO is advocating the use of absolute fracture risk when clinicians decide on drug treatment for osteoporosis. This was facilitated by a simple scoring system based on established risk factors of fractures. The instrument is currently accessible at the internet (www.shef.ac.uk/FRAX). DEXA is not an essential variable in the scoring system, but it is recommended for those who have access to it. Firstly DEXA adds to the predictive power. Secondly follow-up DEXA reassures clinicians and patients that the drug treatment is working. There is evidence that DEXA scan improves drug compliance.

High absolute fracture risk does not necessarily mean that osteoporosis therapy is indicated. That is because most fractures in older people occur in those with osteopenia, and there is no evidence so far that osteoporosis therapy is effective in preventing non-vertebral fractures in high fracture risk populations without selection for osteoporosis. However fracture risk estimation may prompt clinicians to screen for osteoporosis by DEXA, fracture history or simple algorithm. Among Asian women, a simple formula based on age and weight has been validated. If body weight (kg) minus age (years) and then multiplied by 0.2 is smaller than -1, there is an increased risk of osteoporosis in Asian women.

Older men are also at risk of osteoporosis and fractures. The risk factors are similar to those of women. But androgen deficiency is an additional consideration.

Osteoporosis screening by DEXA, followed by osteoporosis treatment, has been shown to be cost effective in men aged 65 years or over and with fracture history, and in men aged 80-85 years.

In summary, there is wide range of effective drug treatments for osteoporosis. Clinicians should be alert to their patients' fracture risk, and actively screen for osteoporosis particularly in those with high fracture risk. The choice of treatment will depend on the age, sex, comorbidities and individual tolerance to drugs. A more proactive approach is required to make a significant impact on the fracture rates of the older population.

References