

LETTER to the EDITOR

Bone Health in Survivors of Lymphoma, Treated with High Dose Steroids - is there a Need for Clearer Guidelines on Bone Care?

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Dear Editor

Non Hodgkin's Lymphoma (NHL) is one of the five commonest malignancies worldwide and its incidence in the developing world is reportedly increasing. Data from Pakistan suggest a 19% increase in the males and a 23% increase in females over a period of 7 years (Bhurgri et al., 2006). High dose steroids form an integral part of most of the therapeutic regimens for non Hodgkin's lymphoma, the common chemotherapy regimens in lymphoma, depending on the type and subclass of the disease, almost always include high dose steroid (such as 50 mg² twice a day for 4-5 days cycle repeated 6-8 times). In all patients end up receiving about 800 to 1200 mg of steroids over the period of about 6 months. The adverse effects of using steroids in acute and chronic setting are well known (Robinson et al., 1997; Thornton et al., 1997). In fact, more than half a century ago damaging effects of steroids on bone were already recognized in 1932. Steroids have greater effect on trabecular than on cortical bone, thus the reduction in bone mass is more marked in the spine and proximal femur rather than in forearm or femoral shaft (Oak, 2008). However, current international clinical guidelines do not necessarily remind physicians of this risk, neither do they suggest taking preventive measures in this connection.

Osteoporosis refers to a systemic skeletal disorder that is characterized by low bone mass and disturbances of the micro-architecture of the bone tissue which entails an increased risk of fracture (1993). Our own experience is that in patients who develop steroid induced bone loss, the result can be compression fractures of the vertebrae. Such patients can be considered cured from the lymphoma but suffer from painful disability due to vertebral fractures.

Common fracture sites in osteoporotic patients are the femoral neck, radius, vertebral spine, and lumbar spine. The fractures of the vertebral bodies can be associated with chronic pain and loss of mobility, which in itself initiates a cycle of complications including the risk of dependency. Association of osteoporosis with cancer and its treatment is well established and one of the earliest recognized. Osteoporosis related to cancer treatment can result from hypogonadism from hormonal therapy such as in breast and prostate cancer, age related hypogonadism and chemotherapy such as in elderly patients with lymphomas and a combination of various factors in many other malignancies (Pfeilschifter and Diel, 2000). Bone loss secondary to effects of high dose steroids in

patients with lymphoma may result rapidly and become an emergency (Reid, 1997).

The median age at diagnosis for patients with lymphoma is 67 years, an age at which loss of gonadal hormones plays a significant role in bone decay. Administration of high dose steroids specially at this time generally provides the "hit effect" that results in severe osteoporosis and fracture (Pfeilschifter and Diel, 2000). Although direct effect of other therapeutic agents used in the treatment of lymphoma for example, alkylating agents, on bone mineral loss have been questioned (Brown, Ellis et al., 2006). Steroids remain the unequivocal culprit for increasing bone loss, this in addition to the fact that treatment population of lymphoma frequently is those of ageing patients is probably given less importance by the treating physician (C: 1997). Efforts are needed to take into consideration the essential bone care, as severe compromise in functions and quality of life may result when they are ignored. Effective ways have been suggested for patients receiving steroids for preventing bone loss including the use of calcium with Vitamin D, calcitonin, testosterone in men, The SERMs in females, and most effectively by use of bisphosphonates (Heaney, 1989; Reid, Hughes et al., 2000). Most recently the efficacy, safety and superiority of humanized monoclonal antibody Denosumab for Prevention of Fractures in patients with Osteoporosis has been established (Cummings et al., 2009; Smith et al., 2009). Assessment of the bone density is ideally done by bone mineral density, however if used appropriately a CT can also be render clinically useful images and in appropriate setting such as, CT-based finite elements study, can accurately predict bone strength (Besshoet al., 2007).

Compromised bone health has dramatic impact on general health, poses a significant burden on society and results in increasing cost of health care (Ethgen et al., 2003). Unfortunately proper emphasis on the issue is not suggested effectively by the general guidelines in cancer treatment which suggest high dose steroid therapies (NCC Network, 2009). It has been assessed that in patients with bony metastasis who have fear of fracture are generally more concerned about their quality of life then their health care providers, who generally attempt to handle current symptoms (Harris et al., 2009).

It remains a challenge to make the bone health assessment of patients who present for cancer care an integral part of management so that an essentially

preventable and treatable condition like osteoporosis is dealt with before it causes a sequence of complications originating from poor bone health. Improvements in the treatment of cancer therapies have resulted in many long term survivors from the disease, which put emphasis on control of long term toxic effects from the treatment of cancers, before they cause substantial damage. (Pfeilschifter and Diel, 2000) Some of the drastic late outcomes could question the very effect on survival by virtue of compromise on quality of life (Brown et al., 2006).

References

- Anonymous (1993). Consensus development conference: diagnosis, prophylaxis, and treatment of osteoporosis. *Am J Med*, **94**, 646-50.
- Bessho M, Ohnishi I, Matsuyama J, et al (2007). Prediction of strength and strain of the proximal femur by a CT-based finite element method. *J Biomech*, **40**, 1745-53.
- Bhurgri Y, Bhurgri A, Nishter S, et al (2006). Pakistan--country profile of cancer and cancer control 1995-2004. *J Pak Med Assoc*, **56**, 124-30.
- Brown JE, Ellis SP, Silcocks P, et al (2006). Effect of chemotherapy on skeletal health in male survivors from testicular cancer and lymphoma. *Clin Cancer Res*, **12**, 6480-6.
- Cooper C (1997). The crippling consequences of fractures and their impact on quality of life. *Am J Med*, **103**, 12S-9S.
- Cu Cummings SR, San Martin J, McClung MR, et al (2009). Denosumab for prevention of fractures in postmenopausal women with osteoporosis. *N Engl J Med*, **361**, 756-65.
- Cushing H (1994). The basophil adenomas of the pituitary body and their clinical manifestations (pituitary basophilism). 1932. *Obes Res*, **2**, 486-508.
- Ethgen O, Tellier V, Sedrine WB, et al (2003). Health-related quality of life and cost of ambulatory care in osteoporosis: how may such outcome measures be valuable information to health decision makers and payers? *Bone*, **32**, 718-24.
- Harris K, Chow E, Zhang L, et al (2009). Patients' and health care professionals' evaluation of health-related quality of life issues in bone metastases. *Eur J Cancer*, **45**, 2510-8
- Heaney R P (1989). Nutritional factors in bone health in elderly subjects: methodological and contextual problems. *Am J Clin Nutr*, **50**, 1182-9; discussion 1231-5.
- Network NCC (2009). Clinical practice guidelines. V 1, 2009.
- Oak J (2008). Preventing steroid induced osteoporosis. *Indian J Dermatol Venereol Leprol*, **74**, 5-7.
- Pfeilschifter J, Diel IJ (2000). Osteoporosis due to cancer treatment: pathogenesis and management. *J Clin Oncol*, **18**, 1570-93.
- Reid DM, Hughes RA, Laan RF, et al (2000). Efficacy and safety of daily risedronate in the treatment of corticosteroid-induced osteoporosis in men and women: a randomized trial. European Corticosteroid-Induced Osteoporosis Treatment Study. *J Bone Miner Res*, **15**, 1006-13.
- Reid IR (1997). Glucocorticoid osteoporosis--mechanisms and management. *Eur J Endocrinol*, **137**, 209-17.
- Robinson RJ, Iqbal SJ, Whitaker RP, et al (1997). Rectal steroids suppress bone formation in patients with colitis. *Aliment Pharmacol Ther*, **11**, 201-4.
- Smith MR, Egerdie B, Hernández Toriz N, et al (2009). Denosumab in men receiving androgen-deprivation therapy for prostate cancer. *N Engl J Med*, **361**, 745-55
- Thornton MJ, O'Sullivan G, Williams MP, et al (1997). Avascular necrosis of bone following an intensified chemotherapy regimen including high dose steroids. *Clin Radiol*, **52**, 607-12.

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