EDITORIAL

Neurological Disorders, Corticosteroids, and Fracture Risk: Hiding in the Hindsight!

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Corticosteroids are one of the most frequently used groups of medications, advised by all clinicians across all medical specialties. Steroids are used widely for various indications in neurology. Specifically, with the advent of "Neuroimmunology" as a branch and recognition of many immune-mediated neurological disorders, the need for steroid use has substantially increased. Neurological disorders like myasthenia gravis, chronic demyelinating radiculoneuropathy, multiple sclerosis, neuromyelitis optica spectrum disorders, autoimmune encephalitis, etc. require recurrent and mostly long-term steroid use.

Bone loss is a well-recognized and common complication of long-term steroid use. Osteoporosis is defined as a state of reduced bone mass and microarchitectural deterioration of the bone tissue which leads to bone fragility and enhanced risk of sustaining fractures.[1] Corticosteroids are known to cause a reduction in bone mass due to increased bone resorption and reduced formation. The inhibition of intestinal calcium transport, increased urinary calcium excretion, increase in osteoclastic activity, induction of interleukin–6 receptors in the skeletal cells, decreased level of osteocalcin, alterations in growth/gonadotropin hormones, and complex actions on skeletal cell-gene expression have been implicated.[2]

An acute phase of rapid bone loss followed by a comparatively slow but ongoing decrement in bone mineral density is noted in patients with prolonged steroid exposure underscoring the importance of periodic assessment in the patients who require long-term treatment.

While with the advancing evidence, the guidelines are often clear on the use of steroids, the strategies to contain the fracture risk are underrated and are often ignored while taking care of the primary neurological disorder.

While the exact risk of fractures depends upon multiple factors like duration of treatment, daily and cumulative steroid dosage, baseline bone health, patients body mass index, patient's functional status etc., chronic exposure to glucocorticoid can cause fractures in as high as 50% of patients.[3] More so, steroid dosage as low as 10 mg per day has an adequate potential to cause an early and substantial bone loss.

Patients with neurological disorders have an additional risk of developing bone loss. Interestingly, neurological patients have been poorly represented in trials on preventive treatments for osteoporosis despite their increased risk.

Many disorders like various neuromuscular diseases, Parkinson's disease, etc. are associated with an increased risk of falls. Falls are more common as age advances and up to 5% of falls in the geriatric population are known to cause fractures.[4]

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Neurological conditions causing immobility like strokes, spinal cord diseases, neuromuscular diseases, myopathies further cause an increased risk of bone loss by altering the skeletal loading mechanism.

Patients with epilepsy not only have an increased risk of falls but are often at higher risk because of exposure to medications like phenytoin, phenobarbital, carbamazepine, valproic acid, etc.[5,6]

While the use of steroids is unavoidable on many occasions, precautions should be advocated to minimize the risk. Patients who require prednisolone at a dose of 7.5 mg or more daily for 6 months or more, should be considered at high risk for the development of early osteoporosis.

Sites with high trabecular bone content (lumbar spine, ribs, etc.) demonstrate the earliest signs of osteoporosis. Assessment of fracture risk by measuring bone mineral density is a reliable and convenient method. Ideally, the assessment of bone mineral density should be done at the onset of the treatment, 6 months after the initiation of the therapy, and subsequently at yearly intervals.[3]

Preventive treatment should specifically be considered in specific patient groups like elderly, postmenopausal patients, patients requiring high daily doses of steroids, steroid-dependent patients, etc.

The management entails discontinuation of glucocorticoid therapy but this is usually not a feasible option. Bone sparing steroids or steroid analogs like deflazacort appear to have lesser detrimental effects for an equivalent anti-inflammatory dosage. Parenteral (intravenous) high dose, pulse (3–5 days monthly) steroids are considered a lucrative option to avoid complications associated with regular use of oral steroids. The use of steroid-sparing agents should be considered earlier in therapy if possible.

Based upon the available data, bisphosphonates (alendronate, risedronate, zoledronic acid, etc.) seem to be

one of the most effective agents to prevent osteoporosis and hence reduce the fracture risk. Early supplementation of vitamin-D [calcitriol (1,25-dihydroxyvitamin D) and alfacalcidol (1α-hydroxyvitamin D)] with calcium is an easy and convenient option. Antiresorptive agents like calcitonin have also been avidly studied and found effective. Hormone replacement therapy should be considered in postmenopausal patients requiring long-term steroids. The use of sodium fluoride has also been shown to enhance bone function. Teriparatide with its anabolic effects has been considered highly effective in patients at risk of developing fractures.[7]

Roughly 50 % reduction in fracture rate can be obtained if a judicious and timely treatment is adopted. Nonpharmacological therapies like balance and gait training, use of hip protectors, weight-bearing exercises can substantially potentiate the prevention of fractures in these patients. Lifestyle modification with alcohol and smoking cessation should be advised to all patients initiated on corticosteroids.

The ultimate functional status of patients with neurological disorders depends upon multiple factors. While steroid treatment is a cornerstone for therapy in many immune-mediated neurological diseases, timely prevention of osteoporosis may offer a better disease course with a better quality of life.

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