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Rapid and Severe Bone Loss Disorders

Pranjal Soni[1], Ravi Kumar Chittoria[2], Barath Kumar Singh P[3]

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Author Affiliation: [1]Junior Resident, Department of Surgery, [2]Professor, Head of IT Wing and Telemedicine, Department of Plastic Surgery & Telemedicine, [3]Senior Resident, Deartment of Plastic Surgery, Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry 605006, India.

Corresponding Author: Ravi Kumar Chittoria, Professor, Head of IT Wing and Telemedicine, Department of Plastic Surgery & Telemedicine, Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry 605006, India.

E-mail: drchittoria@yahoo.com

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Abstract

Acute, rapid, and severe bone loss (ARSBL) and a high fracture rate exceed postmenopausal and age related osteoporosis in many bone illnesses. Drug induced systemic disorders, weakness, immobility, and the sickness dominate these situations. Examples include GIOP, post-transplantation bone disease, stroke, and acute spinal cord injury immobility. These disorders cause 8% spinal bone loss and 5% hip bone loss annually. Effective management can reverse bone loss. This review covers quick and severe bone loss causes.

Keywords: Bone Loss; Disorders; Glucocorticoids; Bone Loss; Transplant; Management; Stroke.

INTRODUCTION

Acute, rapid, and severe bone loss (ARSBL) and a high fracture rate typically exceed postmenopausal and age related osteoporosis are common features of a range of bone disorders. Systemic diseases caused by pharmacological therapy, weakness, immobility, and the disease itself dominate these conditions.[1] Glucocorticoid induced osteoporosis (GIOP), post -transplantation bone disease, stroke, and acute spinal cord injury immobility are examples. In these conditions, spinal bone loss averages 8% and hip bone loss 5% year.[2] post-transplant osteoporosis fracture rates can reach 65% per year. Clinically, we must recognize this constellation of illnesses, its potentially devastating impact on the skeleton, and the rate of bone loss. Effective management can stop or reverse bone loss. In this review, we discuss about the various causes for rapid and severe bone loss.

MATERIALS AND METHODS

This investigation was done in a tertiary care plastic surgery department. This review article examines 30 papers on disorders related with quick and severe bone loss from Scopus, PubMed, Google scholar, and the internet.

RESULTS

Based on the inclusion criteria 50 articles were studied to discuss rapid bone loss under following headings:

1. Aetiology
2. Pathophysiology
3. Diagnosis
4. Management
5. Conclusion

DISCUSSION

Aetiology

The following aetiologies are identified based on the articles available:

a. Glucocorticoid Induced Bone Loss
b. Post Transplant Bone loss
c. Immobilization

Pathophysiology

Osteoporosis from Glucocorticoids

Most secondary osteoporosis cases are glucocorticoids. GIOP occurs in 50% of individuals treated for 6 months or more.[3] In long-term glucocorticoid users, the risk of hip fracture doubles, although the spine and rib fracture incidence are 34%. The dose and duration of treatment determine GIOP.[4] Oral dosages between 2.5 and 7.5 mg/day increase fracture risk. In haled glucocorticoids damage bone density, according to recent studies. Therapy increases fracture risk within 6 months but decreases afterward. In postmenopausal women without oestrogen replacement medication, fracture risk may remain high even after ceasing therapy if they have poor bone mass.[5,6] GIOP causes trabecular and cortical bone loss. Initial vertebral fractures are highest in trabecular bone. Two steps appear to cause GIOP-related bone loss. Phase one involves accelerated bone resorption. The main problem is likely decreased bone growth in the second phase.[7] There is strong evidence that glucocorticoid excess damages osteoblasts. Glucocorticoids also decrease osteoblast life span and ability to lay down new bone by increased apoptosis, which reduces bone mass and fracture risk.

Bone Disease after Transplant

This osteoporosis has emerged due to powerful immunosuppressive medications. As rejection events decrease, medications like Immunosuppressive agents prolong longevity but cause fractures.[8] Immobilization, poor nutrition, hypogonadism, and the underlying disease all contribute to post-transplant bone loss, but their roles are unclear. Glucocorticoids and CIs, especially Cyclosporin A and FK506, are the main culprits.[9] When taken in heavy doses soon after transplantation, glucocorticoids may damage bone the most. Calcineurin Inhibitors can cause significant bone loss without glucocorticoids. Because T-lymphocytes produce osteoprotegerin (OPG) and osteoprotegerin ligand (OPGL), Calcineurin Inhibitors may affect this system. Drug effects on the T-lymphocyte, which produces osteoclast stimulatory cytokines, may out weigh Calcineurin inhibitor effects on bone calcineurin.[10]

Most spinal fractures are asymptomatic and discovered inadvertently. Hip fractures always cause symptoms, either spontaneously or after a fall or eccentric femur rotation. The severity of the underlying condition, time waiting for transplantation, medicines, starvation, and immobilization caused transplantation fractures before. The organ transplanted, the underlying condition, and the immunosuppressant dose used to avoid rejection affect bone loss and fracture rates after transplantation.[11]

Kidney and Kidney-Pancreas Transplantation:

Kidney transplants cause less bone loss and fracture than other organs. Renal physicians' considerable transplantation experience and modest immunosuppressant dosage may explain this. However, kidney transplant patients, especially those on long-term dialysis, usually have bone disease.[12,13] Renal osteodystrophy comprises osteoporosis, osteomalacia, secondary hyperparathyroidism, adynamic bone disease, and mixed bone disease. Most abnormalities resolve after transplantation, but hyperparathyroidism, hypercalcemia, adynamic bone disease, and avascular necrosis may persist.[14,15] Bone loss after kidney transplant ranges from 6% to 18% at the spine and 4% at the hip. Bone loss is usually in the first 6 months after transplant.[16]

Cardiovascular Transplantation:

Post-cardiac transplant osteoporosis causes substantial morbidity, with spine fracture risk ranging from 18% to 50% in cross-sectional studies. Most patients have significant spine and femur bone loss by transplantation.[17,18] According to WHO criteria, 8–10% of patients have osteoporosis

and 40–50% have osteopenia.[19]

Liver Transplantation

The same considerations apply as with other organ transplants, but the type of liver condition the patient has seems to have a major impact on fracture rates after transplantation. In the first year following transplantation, 65% of primary biliary cirrhosis patients had atraumatic spine, hip, rib, and long bone fractures. Immunosuppressants for liver transplant patients are usually higher than for renal and cardiac patients.

Lung Transplantation:

Before transplantation, 60% of patients have spine osteoporosis and 78% have hip osteopenia. Before transplantation, vertebral fracture prevalence is 25%–29%, while with cystic fibrosis, rib and vertebral fracture rates are 10 and 100 fold higher. Although calcium, vitamin D, and bisphosphonate are given, large immunosuppressant doses post-transplantation cause 37% fractures. The first six months after transplant consist mostly of trabecular bone loss.[20]

The histological image shows strong remodelling, with enhanced resorption and formation markers. These patients lose bone due to myeloablative regimens that cause hypogonadism, which can be treated with hormone replacement therapy in women. Allogeneic transplants may increase the risk of bone loss at the femoral neck and spine due to graft-versus-host disease.[21]

Loss of Bone due to Immobilization

Traumatic paralysis, poliomyelitis, multiple sclerosis, and cerebrovascular accidents induce acute and persistent immobility. Immobilization due to fracture can cause significant bone loss. Finally, a new field is forming around microgravity in space flight. Disuse causes weakening and muscle atrophy, reducing pressures and strains. The widely accepted explanation is that immobilization reduces bone canalicular fluid flow by reducing compressive mechanical stresses. Hypoxia of osteocytes, which transduce mechanical stimuli, stimulates osteoclastic activity.[22] Immobilization causes quick, severe bone loss. Bone loss may be localized or wide spread. This is localized to the damaged side or limb after spinal cord injury or poliomyelitis. Most bone loss happens in the first year following spinal cord injury but may last 15 years.[23] Trabecular bone suffers more than cortical bone. In paraplegic or tetraplegic individuals, hip bone loss is 2% per month for the first 6 months and then reduces to 1% per month. Over the first year, bone loss can reach 12%. Up to twice as much bone loss occurs in the tibia. Mechanical loading in the upright position may prevent lumbar spine density loss.

Stroke Bone Loss

After one year, stroke patients who do not retrain to walk can lose 9% bone mass due to demineralization and muscle atrophy on the paralyzed side.[24] If they cannot walk again, the non-paretic limb may also be harmed, and bone loss might reach 3% by year 1. Hemiparesis increases fracture risk with vitamin D insufficiency. In stroke patients with vitamin D levels <12 ng/ml, fracture risk is high.[25]

Diagnosis

Patients awaiting transplantation for years should have their Bone Mineral Density measured so treatment can begin. After transplantation, measure BMD at 6 months, 1 year, and 2 years. When starting glucocorticoids, the first BMD measurement should be taken. BMD should be measured at the time or soon after for various disorders. The hips and lumbar spine should be considered.[25] Because of quick and severe bone loss, therapeutic criteria must be stricter than for postmenopausal and involutional osteoporosis, and clinicians should be more aggressive with effective antiresorptive therapy. Urine and serum cross-linked telopeptides may help monitor these patients' therapy, but signs of resorption may be more useful than markers of creation (with GIOP as an exception). Few data exist to predict or assess their therapeutic response before or after organ transplantation. Blood tests include serum calcium and 25-hydroxy vitamin D can rule out vitamin D insufficiency. To rule out hypogonadism, sex steroids should be measured. Some patients may benefit from replacement therapy. Male testosterone levels initially drop but rise around 6 months following transplant, when immunosuppressants are discontinued. Thus, testosterone medication should be terminated and the patient reviewed for testosterone replacement.[26] Twenty four hours urine calcium levels may reveal the patient's calcium balance, especially in malabsorption syndromes such liver or intestinal disease. High urine calcium levels > 400 mg/24 h may indicate tubular leak from tacrolimus and cyclosporine. Glucocorticoids or excess vitamin D and calcium may also cause it. The general overview of management of Rapid bone loss summarized in Table 1.

Table 1: Management of acute and rapid bone loss

BMD Measurement	DXA before or at time of event, that is, awaiting transplantation, or at time of startingimmunosuppressive therapy.
	Repeat BMD measurements at 6 and 12 months, and then annually.
Medications	Decrease dose of immunosuppressants as rapidly as possible without compromising patient'sorgan survival
Exercise	Early mobilization and strengthening exercises
Biochemical Determinations, before and after Transplantation	Routine standard tests to exclude renal or hepatic impairment.
	25-Hydroxy-vitamin D
	Bone markers
	PTH if required, e.g., after renal transplant
	24-hour urinary calcium
	Gonadal hormones
Pharmacological Therapy	Calcium and vitamin D or analogs
	Hormone replacement if indicated
	Bisphosphonates: oral or intravenous
	Calcitonin
	SERMs?
	rhPTH

Management

Vitamin D and Calcium Analogues

Calcium is essential for primary and secondary osteoporosis prevention, according to place bo-controlled research. Chronic calcium deficit demineralizes bones and increases fracture risk. Patients with low baseline calcium consumption benefit most from calcium supplementation. The 1997 Consensus Development Conference on optional calcium consumption advised postmenopausal women to consume 1.5 g of "elemental" calcium daily, but intake must be personalized. Calcium supplementation has little risks, although those with a family history of nephrolithiasis must be tested with 24-h urinary calcium. Serum 25OH vitamin D should be measured, and results as low as 15 ng/ml may indicate subclinical vitamin D inadequacy. One must consume enough, yet avoid hypercalcemia.[26]

Calcitriol prevents bone loss following heart or lung transplantation but must be taken long-term.[27] Hypercalcemia necessitates regular serum calcium monitoring. To prevent high turn over bone loss, calcium and vitamin D therapy should be utilized with stronger antiresorptive drugs. Despite their extensive usage as adjunct therapy with anti-osteoporotic drugs, calcium and vitamin D and analogues are less effective than N-containing bisphosphonates in post-transplant and GIOP.

Calcitonin, Bisphosphonates were used in Glucocorticoid induced osteoporosis (GIOP). Nitrogen containing bisphosphonates prevented and treated GIOP better than etidronate.[27] Most convincingly, alendronate and risedronate increase BMD and minimize vertebral fracture in pooled studies.

Hormone Replacement

In Glucocorticoid induced osteoporosis (GIOP), oestrogen has bone sparing qualities. If a woman is amenorrhoeic and has no contra-indications, HRT can treat postmenopausal symptoms temporarily.[28] The recent Women's Health Initiative (WHI) report may make this option unfavourable unless postmenopausal hot flashes bother the patient. Hypogonadal men should get supervised and rogen therapy unless contraindicated. Male hypogonadism may be temporary, thus and rogen medication should be halted and reviewed post-transplant and post immunosuppressive therapy.[29] Due to physiological circulating levels, topical testosterone supplementation is preferred.

Recombinant Human Parathyroid Hormone

Recombinant human parathyroid hormone is a promising osteoporosis treatment. Anabolic rather than antiresorptive, this medicine has great potential in these conditions, especially where glucocorticoids are administered. When given intermittently and at low levels, PTH stimulates bone growth. Thus, it may reverse bone loss and restore GIOP micro architecture. Daily subcutaneous injections and the warning of osteosarcoma in rats following large and lifelong PTH dosages are drawbacks.[30]

CONCLUSION

The group of illnesses that produce rapid bone loss and fractures requires early detection and treatment. Bisphosphonates work best. Newer anabolic medications such recombinant human PTH may help osteoblastic abnormalities and poor bone formation induce rapid bone loss. Create and implement suggestions to prevent clinical symptoms and fractures with effective therapy.

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