инфекции органов дыхания, каждый десятый ребенок имел анемию и неблагоприятный аллергический фон. Средняя продолжительность пребывания в стационаре детей всех возрастных групп составила 5 (3; 7) дней.

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OSTEOPOROSIS IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

Addipalli Maanasa

Scientific supervisor: Ph.D., Associate Professor *L. V. Krivitskaya*

Educational Establishment
«Gomel State Medical University»
Gomel, Republic of Belarus

Introduction

Osteoporosis is a disease characterized by low bone mass and microarchitectural deterioration of bone tissue. Osteoporosis is a devastating disorder with significant physical, psychosocial and financial consequences. Normal bone mass is defined by the World Health Organization as a Bone Mineral Density (BMD) within one standard deviation (SD) of the mean for young adults, osteopenia as increased bone loss with a bone mass between 1 and 2,5 SDs below normal, and osteoporosis as a bone mass ≥2,5 SDs below normal. There is no consensus about the definition of osteoporosis in paediatrics. Most bone specialists make a diagnosis of osteoporosis in children and adolescents only when BMD is low and there is at least one fracture. But Currently, Osteoporosis is receiving an increasing attention in paediatrics, since its importance in the late effects of children's with Acute Lymphoblastic Leukaemia (ALL) and its treatment because of their quality of life and its negative effect on the children's ability to perform developmentally appropriate activities. Leukaemia is the most common form of childhood malignancy, in which ALL accounting for approximately 75 % of cases. With an overall survival rate approaching 80 %, children with ALL have an excellent prognosis. The two major skeletal complications of leukaemia are osteoporosis and avascular necrosis. Therefore, in this article we will be describing how extensive the problem is and how to prevent and treat in a best way of osteoporosis in children with ALL and to increase their life expectancy and to decrease the global burden.

Goal

The purpose of this article is to carry out the prevalence and importance of osteoporosis in children with ALL, to rule out the evolving issues of ALL, establishing the early diagnosis and making an optimal treatment in order to decrease the mortality rate of this association and to improve the quality of life in children with ALL.

Material and methods of research

Information was collected from several databases. We searched articles published in MEDLINE, EMBASE, Online Library, Ncbi and PubMed searches (2020–2022) by using the keywords osteoporosis, ALL, epidemiology, bone metabolism, diagnosis and management were examined for appropriate references.

Results and discussion

According to the epidemiological database ALL has a global distribution. ALL, the most common form of childhood cancer, accounts for one-fourth of all child-

hood cancers. But there is a current cure rate which approaches 80 %, approximately 1,500 children in the U.S. are cured of ALL each year.

Bone metabolism: About 10 % of bone is normally replaced each year. Bone metabolism is a continuous cycle of modelling (resorption followed by formation at a distant skeletal site) and remodelling (resorption followed by formation at the same skeletal site). Osteoclasts (derived from cells of monocytic lineage) function to resorb existing bone, while osteoblasts (derived presumably from hematopoietic stem cells) lay down replacement bone matrix. But the metabolism of bone is quite changed in children with ALL. As there is a development of Osteoporosis, the Bone mineral density (BMD ≥2.5 SDs below normal) which indicates that there is a decrease in the BMD. The complex factors of bone metabolism like hormones, Interferons (INF), Interleukins (IL), Tumour Necrosis Factor (TNF) has significantly changed which is presented in table 1.

Table 1 — Changes in the complex factors of bone metabolism in ALL children with the development of osteoporosis

Complex Factors	**Levels**
Thyroid hormones (T3)	Increases
Estrogens	Decreases
Testosterone	Decreases
Prostaglandins	Increases
IL-1,6,7	Increases
TNF-α	Increases
IFN-γ	Decreases

Symptoms of osteoporosis in children with ALL: Among the symptoms related to decreased BMD are musculoskeletal pain, especially in the extremities, spine, and pelvis, abnormal gait, kyphosis and lordosis, unusual fractures, and decreased or delayed linear growth. Bone pain is a common presenting sign in children with ALL. It is not uncommon for an ALL patient, when first seen, to limp or even refuse to walk. Musculoskeletal pain has been reported in 21–59 % of children. Children with bone pain do not always have apparent radiologic lesions, and many children with skeletal changes do not have pain. Bone pain is caused by pressure from infiltration of leukemic cells into the medullary cavity or under the periosteum, while joint pain is usually thought to be referred from lesions of the periosteum. Fractures can occur at the time of diagnosis, as well as during and after ALL therapy, frequently long after cessation of therapy. Especially vertebral compression fractures are highly observed with the impairment of bone growth during the active disease process in children with ALL.

Risk factors: Because the pathogenesis of decreased BMD in childhood cancer is multifactorial, a number of risk factors must be considered. Leukemic invasion of bone is not uncommon in ALL. Other risk factors for osteoporosis include corticosteroid and methotrexate therapy, local and cranial radiation, and deficiency of various hormones. Decreased activity because of limited exercise capacity and physical inactivity, as well as nutritional deficiency resulting in altered calcium, vitamin D, and magnesium metabolism, must be given consideration. Male sex and Caucasian race appear to be additional risk factors in childhood ALL.

Diagnosis: Beside carrying out the history, laboratory analysis, x-ray examination, the most important diagnostic tool in current use for diagnosing osteoporosis is Dual Energy X-ray Absorptiometry (DEXA), which assesses the mineral content of the spine while keeping the amount of radiation exposure low. The spine is largely made up of trabecular bone. DEXA is therefore more useful than single photon ab-

sorptiometry, which is limited to measuring cortical bone density. Clinically important sites for evaluation are the lumbar spine (L2–L4), femoral neck, and Ward's triangle, the latter describing a region of the proximal femur consisting predominantly of trabecular bone and radiographic evidence of osteopenia was reported as an initial finding in 13 % of ALL patients. During therapy 76 % developed radiographic evidence of osteopenia, and 64 % developed absorptiometry evidence of reduction in bone mineral content. The finding of osteopenia was attributed to leukemic infiltration, while the subsequent reduction in bone mineral content during therapy was attributed largely to chemotherapy in ALL children.

Treatment: Intervention designed to improve BMD should ensure sufficient supplies of calcium and vitamin D, include a weight-bearing exercise program and provide counselling for smoking cessation as well as avoidance of carbonated beverages in adulthood. Any hormone imbalance that is identified must be addressed, with replacement therapy if appropriate. Drugs currently used for treating osteoporosis specifically decrease bone loss by decreasing bone resorption. Calcitonin has recently been approved for administration by nasal spray for the treatment of osteoporosis in older women, but requires further study for use in children or adolescents. The bisphosphonates, a class of drugs that inhibit osteoclast activity, are useful in the treatment of osteoporosis. When children and adolescents receive experimental substances such as calcitonin and the bisphosphonates, particular attention needs to be directed toward the safety of their administration. Alendronate has received approval from the U.S. Food and Drug Administration (FDA) and is currently the most commonly used bisphosphonate for the treatment of osteoporosis. Because it is poorly absorbed, the drug should be taken on an empty stomach, with eating and drinking delayed for at least 30 minutes. Patients should avoid lying down for at least 30 minutes after ingestion because esophagitis and esophageal haemorrhage have been reported following its use. Its use is not recommended in the presence of renal insufficiency, and liver damage from alendronate. FDA approval of alendronate does not include children under the age of 18 years, nor does it include pregnant women and girls or women who may become pregnant. Among other bisphosphonates that are useful in treating metabolic disorders are etidronate and risedronate. A slow-release sodium fluoride is currently being studied because of its osteoblast-stimulating property, and low-dose parathyroid hormone is in an early stage of investigation for its anabolic potential.

Conclusion

In our article we determined the extent of osteoporosis among survivors of childhood ALL, who are at greatly increased risk for osteoporosis, and to ascertain which are effective measures for attaining optimal BMD. All childhood cancer survivors, especially survivors of ALL, should be monitored indefinitely for the appearance of possible cancer and treatment-related long-term effects, among them osteoporosis. Concerning general and specific intervention measures for prevention and treatment should be a part of all childhood cancer treatment programs. Counselling for a healthy lifestyle in order to minimize such effects, is an integral component of regular follow-up and that increase children life expectancy and decrease the financial burden.

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