

OSTEOPOROSIS EVALUATION AND THERAPY IN PRADER-WILLI SYNDROME

Consensus Statement of the PWSA | USA Clinical Advisory Board

Many individuals with PWS have osteoporosis (low bone mineral density). This condition is most often diagnosed in adolescence and adulthood. The cause(s) of the osteoporosis is not totally clear, but it is thought to be primarily due to the growth hormone and sex hormone deficiencies that occur in PWS. Hypotonia is probably a contributing factor as well.

Bone mass typically accumulates until around the age of 30, with the maximum accrual time for bone mineral density being in adolescence. Puberty is often delayed or incomplete because of a deficiency in sex hormones in individuals with PWS. This interruption of normal puberty in combination with growth hormone deficiency probably results in less bone mineral mass being accrued during adolescence in individuals with PWS compared to the normal population. However, the process may begin earlier than adolescence due to other hormonal abnormalities which affect bone mineral density.

Physical inactivity and limited weight bearing also play a role in the onset and exacerbation of osteoporosis. Exercise is an essential part of the life style for all individuals with PWS, and the health benefits of exercise must continue to be emphasized. Also, recent studies suggest that the use of psychotropic medications may play a role in the genesis or exacerbation of osteoporosis. It is well known that individuals receiving anticonvulsants for seizures or mood stabilization are at greater risk for osteoporosis. Adults receiving selective serotonin reuptake inhibitors (SSRIs) have greater bone loss and lower bone mineral densities. Children and adolescents receiving SSRIs are at risk for decreased bone mineral accrual and bone formation. Given the large number of individuals with PWS who are receiving psychotropic medications, extra care for evaluation and management of these individuals is required.

Osteoporosis is diagnosed with a dual-energy X-ray absorptiometry (DEXA) scan. A DEXA scan is a painless low dose X-ray procedure. DEXA scans of children and

adolescents should be interpreted only by experts experienced in scoring these scans in pediatric patients. DEXA scans which are interpreted compared to adult standards (T-scores) often overestimate the presence of osteoporosis in children and adolescents. Although the normative pediatric databases are small, the interpretation of the DEXA scan should contain an age-, gender-, and race-matched Z-score. Frequently radiologists or other individuals who evaluate DEXA scans do not have access to this information. A Z-score (or T-score for adults) that is between 1 and 2 standard deviations below normal is considered osteopenia (weak bones), while a Z- or T-score that is more than 2 standard deviations below normal is considered osteoporosis. You should ask your physician to provide you with the Z-score (if you are under 18 years of age) or T-score (if you are an adult). DEXA scans should be monitored every one to two years in adolescents and adults with PWS.

Other assessments that are valuable for individuals with osteopenia or osteoporosis include measurements of serum calcium, phosphorus, magnesium, parathyroid hormone (PTH), alkaline phosphatase, 25-hydroxy-vitamin D levels (calcidiol), and 1,25(OH)₂-Vitamin D (calcitriol). Many individuals in the United States are deficient in dietary intake of vitamin D and calcium. These nutritional deficiencies play a big role in the development of osteoporosis. Other laboratory measurements should include evaluation of thyroid function, prolactin, sex hormone levels, and growth hormone levels.

If osteopenia or osteoporosis is present on DEXA scan, the primary treatment is maximizing vitamin D and calcium intake in the diet. A nutritional consult should be obtained to assess current dietary intake of calcium and vitamin D. Current recommendations for adults (note that pediatric standards vary according to age) are that dietary calcium for individuals with low bone mineral density should be at least 1,500 mg per day and vitamin D intake should be at least 600-800 IU per day. Some studies indicate that even these amounts may be inadequate to significantly improve bone mineral

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density. Ideally, serum 25 vitamin D levels should be followed, with the desired concentrations being at least 30-32 ng/ml in order to improve bone mineral density.

In many cases the dietary intake is inadequate and supplementation of calcium and vitamin D is necessary. It is important to know that most calcium supplements are calcium carbonate which is only 40% bioavailable (meaning that a calcium supplement which contains 500 mg of calcium carbonate only provides 240 mg of elemental calcium which can be used by the bones). Vitamin D can be purchased over-the-counter without a prescription in 200 – 1,000 IU capsules or may be purchased at higher doses with a prescription. The best way to give calcium supplementation is with food, no more than 600 mg of elemental calcium at a time, and no more often than every 2 hours to allow maximal absorption.

Although medications called bisphosphonates (e.g., Fosamax, Actonel, and others) are commonly used in adults with osteoporosis, the use of these medications in adolescents and young adults remains controversial. Some experts in pediatric bone disease recommend

that these medications not be started in young people with osteoporosis until they have had a fracture. The long term risks of these medications are unknown at this time. However, there have recently been reports of an increased incidence of jaw necrosis after dental procedures associated with these medications. Bisphosphonate therapy may be considered in adolescents or young adults once vitamin D and calcium supplementation are maximized. More research is needed to identify the long-term risks that may be associated with these medications in adolescents and young adults.

Other important treatment options for osteoporosis include hormone replacement therapy (such as estrogen, testosterone, thyroid hormone and growth hormone). These treatments have been shown to improve bone mineral density in individuals with PWS. Starting these therapies before adolescence, if possible, should be most beneficial. Supplementation of vitamin D, calcium, sex hormones and any other modality of treatment for osteoporosis should be monitored by a physician.