Managing bone health in Rett syndrome

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What is meant by bone health?

Bone health typically relates to the density of bone. Low bone density can lead to weaker bones and a greater susceptibility to fractures. Bone health is important to everybody, particularly in individuals who are older.

Why is bone health an issue in Rett syndrome?

Bone density and mass are lower in individuals with Rett syndrome compared to females in the general population. Consequently, the rate of fracture is nearly four times that of the general population. Fractures can occur spontaneously because of trivial trauma or a fall, and they often occur in the long bones of the arms and legs. Fractures of the spinal bones are also common in Rett syndrome and are usually associated with osteoporosis. Unfortunately, these are often undetected and may escape medical attention. Bone density can be low in girls with Rett syndrome from as young as three to four years of age. Many individuals with Rett syndrome live into adulthood and so it is imperative that their bone health be appropriately managed, across the life span.

Individuals with Rett syndrome often have less muscle mass and their bones are smaller which can affect bone density, especially in those who cannot walk. Some anti-epileptic medications can be associated with decreased bone density. Problems with nutrition and growth may also lead to bone health issues. Delayed puberty is common in Rett syndrome and may affect bone development as oestrogen plays an important role in bone formation during puberty. This is often further delayed if girls are underweight (also common in Rett syndrome) or in individuals with the more severe p.Arg168* *MECP2* mutation.

How common are bone health issues in Rett syndrome?

Fracture represents a substantial burden on those with Rett syndrome and their caregivers. Fractures can be difficult to recognise, given that some individuals have reduced sensitivity to pain and find it difficult to communicate any discomfort. Bone health issues are not uniform across all individuals with Rett syndrome. There is a higher risk of fracture in those with p.Arg168* or p.Arg270* mutation, in the presence of epilepsy, and if certain anti-epileptic medications are used. Fracture is closely linked with mobility levels and capacity to bear weight – those with less mobility and limited weight bearing capacity are more likely to fracture.

How can families manage this at home?

Family members and other caregivers must be aware of the commonality of fracture in Rett syndrome so that they can provide adequate supervision for activities and minimise the risk of accident or fall, including when using equipment and during transfers. Families can support their daughter's bone health through increasing physical activity as possible, and ensuring adequate calcium and vitamin D intake.

For those who are wheelchair dependent, supported standing during transfers and using a standing frame for at least 30 minutes per day should be encouraged. For those who are able to walk,

caregivers can aim to increase the distance and/or length of time walked each day with a goal of 2 hours per day if possible. Assisted walking is recommended for those where mobility is limited. Planning with all caregivers including schools is important to identify schedules for physical activity that are safe.

Are there established treatment/ management options?

Clinical assessment of bone health should start early on in life and continued as necessary, particularly during puberty. Routine risk factors should be taken into account – the ability to walk, the presence of mutations associated with greater severity (in particular p.Arg168*, p.Arg255*, p.Arg270* or p.Thr158Met), prescribed anticonvulsant medications, and prescribed oral and intramuscular progesterone medications. Previously having had a fracture is associated with higher risk of having a subsequent fracture. Where risk factors are identified, baseline bone mineral density measurements should be performed, and then monitored as necessary into the future.
Bone mineral density can be assessed using either a DEXA scan or quantitative ultrasound. Clinical assessment can review BMI, mobility level, sunlight exposure and dietary intake of calcium and Vitamin D.

What are the initial treatment options?

Non-pharmacological interventions include two major avenues for improving bone health: through increasing physical activity to strengthen muscles and raise bone density, and through calcium and vitamin D supplementation. Given the variability in physical capabilities for girls and individuals with Rett syndrome, referral to a physiotherapist is recommended for development of a physical activity plan tailored to the needs of the individual. If calcium intake is low, this can be increased with calcium-rich or calcium-fortified foods. If calcium intake is unable to be increased via diet alone, a doctor may prescribe calcium supplements to meet the local recommended daily intake level. Regular blood tests can be used to assess Vitamin D levels and if found to be lower than 75nmol/L, your doctor will recommend following the local protocol in terms of safe and adequate sunlight exposure and supplementation. Plans should include realistic expectations for increasing weight bearing activities, calcium and vitamin D intake, considering needs and capabilities.
Pharmacological interventions are considered when there is a combination of low bone density and a history of previous fracture. Bisphosphonate medications may be useful although there is little published literature in relation to Rett syndrome at the current time. Bone density should be reassessed one year after bisphosphonate therapy to check if the medication has been helpful and to guide whether continued use is appropriate.

What follow-up is needed?

Other medications may impact on bone health. Families should be aware of this and query any uncertainties with their daughter's doctor. All prescribed medications should be identified at each clinical visit. Some medications that regulate the menstrual cycle increase the risk of fracture. Some anti-epileptic medications have been shown to increase fracture risk in Rett syndrome, comparative to the risk associated with using no or other prescribed antiepileptic medications. If bisphosphonate therapy is being undertaken, regular follow-up and monitoring (i.e. after one year of treatment) is recommended given the uncertainty of this treatment's effectiveness in girls and women with Rett syndrome.

Reference

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