Bone growth drug may reduce sudden infant death syndrome in children with common form of dwarfism

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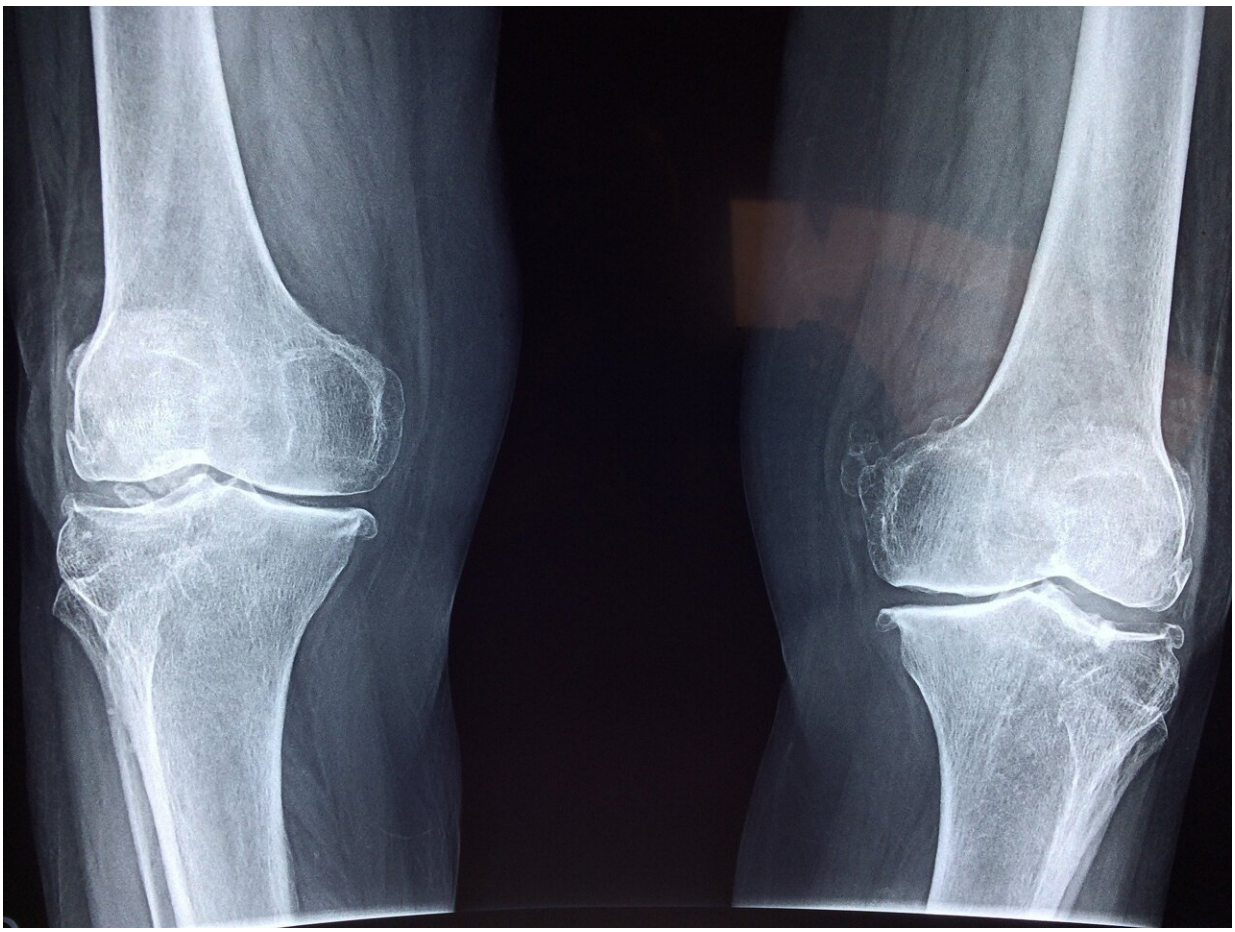

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A drug that boosts bone growth in children with the most common form of dwarfism may also reduce their chances of sudden infant death syndrome, sleep apnea, and needing surgery, according to a new study.

The international research trial, led by Murdoch Children's Research Institute (MCRI) and published in *The Lancet Child & Adolescent Health*, has showed for the first time that vosoritide treatment increases height, facial volume, and size of the foramen magnum, the hole at the base of the skull that connects the brain with the spinal cord, in children under five with achondroplasia.

MCRI is the largest vosoritide clinical trial site in the world and is led by Professor Ravi Savarirayan whose research team has previously shown how the drug improves bone growth development in patients, aged between 5-18 years, with achondroplasia. This latest study found the drug produces similar results in children and infants as young as four months.

Achondroplasia, a genetic bone disorder affecting one in every 25,000 children, is caused by a mutation in the FGFR3 gene. The condition slows bone growth in children's limbs and spine and narrows the base of the skull, putting pressure on the spinal cord. Patients under age five with achondroplasia are 50 times more likely to die due to complications of this narrowing, which causes spinal cord compression and breathing difficulties.

The randomized controlled trial involved 75 children aged under five years from Australia, the US, Japan, and the UK, who underwent 52 weeks of vosoritide treatment.

The study found vosoritide led to an increase in the foramen magnum, which was more pronounced in children aged six months and under.

Professor Savarirayan said these findings would not only vastly improve quality of life but could ultimately save lives.

"Children with achondroplasia have abnormalities at the base of their skull, which causes sleep-disordered breathing and brainstem compression, all major contributors to sudden death in these young patients," he said.

"These findings may lead to a decrease in sudden infant death syndrome, sleep apnea, and the necessity for neurosurgical decompression at the base of the skull."

Professor Savarirayan said the trial reported no serious side effects and discovered changes in height and facial and sinus volume.

"The management of achondroplasia is evolving from purely treating the symptoms to identifying drugs that improve skeletal growth," he said. Improved growth may also reduce the need for facial surgery and corrective orthodontic treatments, which are often required later in life."

The study found the annual growth rate was 0.78cm in treated children under five compared with 1.57cm in those five years and older who undertook previous clinical trials.

"The smaller height rise could be because, in very young children with achondroplasia, there is rapidly declining growth, where a small difference in age can have a big impact on growth measurements," Professor Savarirayan said. This height deficit accumulates rapidly up to the age of two and then follows a more gradual decline."

Earlier this year, the Federal Government listed vosoritide, manufactured by BioMarin Pharmaceutical Inc, on the PBS for treatment of achondroplasia. Vosoritide is the first and only approved

medicine on the PBS that targets the underlying cause of the condition.

The eligible age to first access vosoritide therapy for achondroplasia varies between countries. The US recently dropped the age from five to birth, based on the results of this study. In Australia, the drug is listed on the PBS from birth.

"The study findings will be crucial when relevant authorities are deciding whether to lower the age from which vosoritide can be taken with the first few months of life the time where we expect to see the greatest potential medical benefits," Professor Savarirayan said. "It will also be of considerable use to pediatricians and other health care specialists who are assessing the risks and benefits of starting vosoritide treatment in young children with achondroplasia."

Daisy and Justin's son Casper, 4, was diagnosed with achondroplasia as a newborn.

"During my pregnancy, it was suspected that Casper had the condition, which we had confirmed through genetic testing when he was 10 days old," she said.

"I was filled with worry and anxiety when we received the diagnosis. As a first-time mum, you are going through all the emotions of learning how to care for a baby, and then having this unfamiliar condition to get your head as well as a lot to digest. It was a huge learning curve for us trying to understand what his future would look like."

But to try and give Casper the best start to life, Daisy enrolled him in the vosoritide trial at MCRI when he was five months old.

Daisy said it was remarkable to see the positive changes in Casper.

"Casper has no spinal compression, his limbs are more proportionate, and his legs are less bowed," she said. He is healthy and happy, and a lot of that we contribute to the vosoritide treatment."

Daisy said the latest MCRI research came as a huge relief and would be life-changing for families.

"We did a lot of research into the condition when Casper was born, and there were some very sobering statistics," she said. To learn children with achondroplasia are at risk of severe complications throughout their lives and are 50 times more likely to die before the age of five than other children was terrifying.

"But it's reassuring to learn that vosoritide can help improve the quality of life of young children with achondroplasia and ultimately avoid some of the long-term health complications."

More information: Ravi Savarirayan et al, Vosoritide therapy in children with achondroplasia aged 3–59 months: a multinational, randomised, double-blind, placebo-controlled, phase 2 trial, *The Lancet Child & Adolescent Health* (2023). DOI: 10.1016/S2352-4642(23)00265-1

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