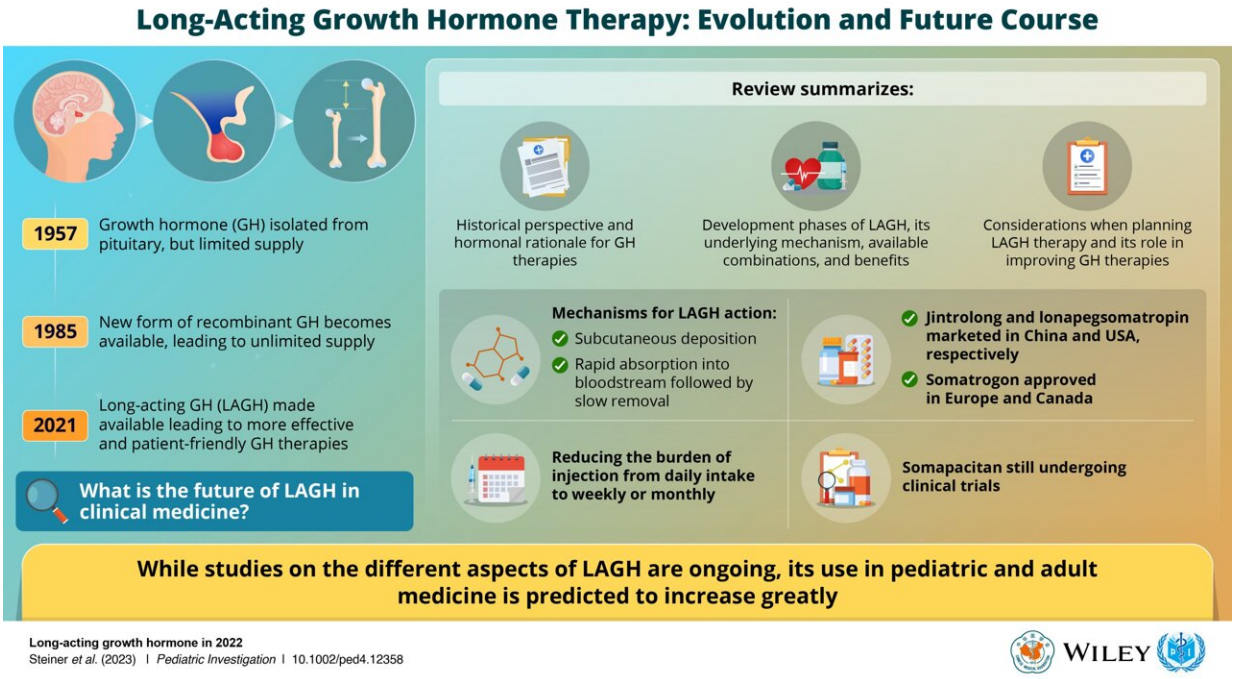
Pediatric review takes stock of history and current status of long-acting growth hormone therapy

March 13 2023



The growth hormone somatotropin is directly involved in regulating growth in children, and continues to play a role in adulthood. Long-acting growth hormone is now available in most global markets and will positively impact growth hormone therapies by reducing the treatment burden on the patient. Credit: Pediatric Investigation

In 1957, Maurice Raben successfully isolated and purified the growth

hormone (GH) from the pituitary gland, opening up a potential avenue of GH therapies. Children who were born with a deficiency of this hormone could now receive medical intervention in the form of daily injections to substitute the product into their body, thus avoiding the ill-effects of GH deficiency.

However, given that it was a product that had to be meticulously extracted from the pituitary of dead bodies, and was time-consuming as well as labor- and resource-intensive process, it remained available only in limited quantities, wherein only a few patients could be treated.

A few years later, in 1985, recombinant-DNA generated GH became available that could be produced in laboratories and in much larger quantities. As a result, it became more easily available and accessible for treating children with GH deficiency. However, one drawback these therapies suffered from was the need to take daily injections of the hormone to ensure that it was available in appropriate concentrations in the blood.

A recent review article published in *Pediatric Investigation* has now taken stock of the clinical development in GH therapy since its isolation, outlining how far we have come and where we are headed with the use of GH therapy.

"The physiological regulation of GH involves a complex mechanism that depends on several age-related and metabolic factors. This regulatory mechanism releases GH doses into the bloodstream every three hours. While this mechanism remained a theoretical interest from clinical perspectives, researchers tried to synthesize a recombinant GH that could integrate itself seamlessly into the mechanism," explains corresponding author Dr. Paul Saenger, who is a professor at NYU Long Island School of Medicine.

"The goal was to produce a pharmaceutical product that would remain active in the body and mimic this pulsatile release of the hormone such that a daily dose would not be necessary."

A prototype of such a long-acting growth hormone (LAGH) was developed by LG Life Sciences in 2014 and the research data were made publicly available. Over the next few years, multiple research labs and pharmaceutical companies have fine-tuned this original prototype, developing many LAGH products.

The review begins with a discussion on the clinical evolution of GH therapy from a historical perspective, followed by a deep dive into the hormonal rationale for GH therapies, development phases and mechanisms involved in these different LAGH products. It then goes on to highlight the considerations patients and their families must keep in mind when planning a LAGH therapy, and its overall role in improving GH therapies.

The mechanisms underlying novel LAGH action involve either a formulation that forms a subcutaneous deposit to allow the release of native/modified GH hormone in a pulsatile manner similar to the actual GH release patterns in the body, or injecting it as a substance that can be easily absorbed in the bloodstream but is removed slowly such that the same pulsatile release can be maintained.

With these developments, LAGH therapies now only require a weekly or monthly dose instead of a daily intake, greatly reducing the burden of injection on the patient. This, in turn, is likely to improve patient compliance. LAGH-based products like Jintrolong and Lonapegsomatropin have already cleared phase 3 trials and are being marketed in China and USA respectively, while Somatrogon has been approved in Europe and Canada.

"The clinical use of GH is an exciting success story. We are now entering a new era of LAGH therapy with new formulations of GH, which will predictably be the preferred form of therapy for years to come. Additionally, the availability of new safety data will further establish its use in clinical medicine," comments Dr. Saenger.

While further research on dosage regulation and timing is still underway for other forms of LAGH, their availability in international markets certainly paints a bright picture.

More information: Margaret Steiner et al, Long-acting growth hormone in 2022, *Pediatric Investigation* (2023). DOI: 10.1002/ped4.12358

Provided by Cactus Communications