Lack of Growth Hormone - does it matter?

Guest speaker Professor Ian Holdaway. Report written by Catherine Chan

Professor Ian Holdaway has been instrumental in our organisation. He is one of the few endocrinologists who specialises in acromegaly and pituitary diseases.

Deficiency in GH can occur in children and adults. In children GH deficiency can impair growth leading to short stature. Normal growth & height is restored by treatment with growth hormone and this treatment has been available for children in NZ for many years.

Adults who are growth hormone deficient have problems affecting many body systems, see chart on the right:

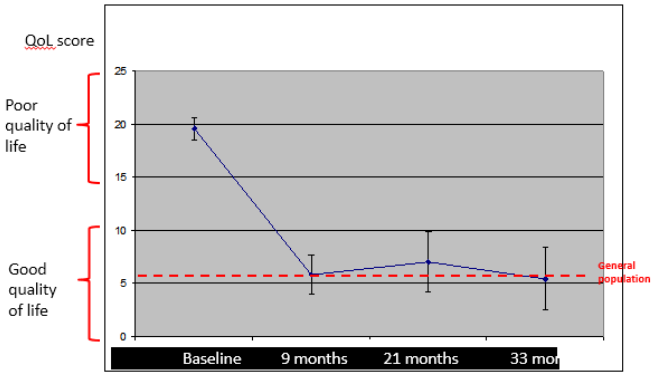
Clinical Consequence	Effect of GH Replacement
Body composition	
General and central adiposity	Decrease
Reduce lean mass	Increase
Reduced bone mass	Increase
Function	
Reduced exercise capacity	Improve
Muscle weakness	Improve
Impaired cardiac function	Improve
Hypohydrosis	Improve
Quality of life	
Low mood	Improve
Fatigue	Improve
Low motivation	Improve
Reduced satisfaction	Improve
Cardiovascular risk profile	
Abnormal lipid profile	Improve
Insulin resistance	Improves in long term
Inflammatory markers	Decrease
Intimal media thickening	Decrease
Cardiovascular and cerebrovascular events	Unknown
Laboratory	
Blunted peak GH to stimulation	
Low IGF-I	Increase
Hyperinsulinemia	Increase
High LDL- and low HDL-cholesterol	Improve
Longevity	Unknown

Studies show GH treatment improve quality of life in GH deficient adults. Four attempts to obtain funding for GH in deficient adults were made by the NZ Society of Endocrinology from the 1980s, before Pharmac decided in late 2009 to fund this. Criteria for treatment were developed in collaboration with a working party that included endocrinologists Prof Ian Holdaway, Assoc Prof Penny Hunt, Prof Patrick Manning, and Prof Wayne Cutfield. Pharmac used their tender process to obtain the lowest price for GH.

Applications for funded GH treatment of GH deficient adults commenced in April 2010, and as of April 2018 there were 571 patients on treatment. The expected number of adults with hypopituitarism in NZ would be about 2700, although the number with GH deficiency is unknown.

Data collected from those on GH shows the vast majority have a non-functioning pituitary adenoma as the initial diagnosis, with treated acromegaly causing GH deficiency in only a minority. Of interest Maori, Pacific Islanders, and Asian ethnicity were underrepresented in GH treatment.

This graph shows that within 9 months of GH treatment, quality of life improves and is comparable to that of the general population.



GH treatment also improved metabolic & body composition including reduction in waist circumference and cholesterol levels.

Studies have shown GH treatment in adults is safe, in particular there has been no pituitary tumour regrowth or new tumour development with its use. There has been no worsening in blood pressure or diabetes, and mortality rates are likely improved although longer experience is needed to prove this. Caution is needed when considering usage of GH in those with meningiomas, OSA, active malignancy, pregnancy, and those with rare syndromes.

For a person on the average dose of 0.3mg/day, growth hormone would cost $2389/year, compared to the cost of octreotide (sandostatin LAR) at 20mg/month which would cost $28296/year.
In order to qualify for funded treatment, the patient's serum IGF-1 must be more than 1 standard deviation below the mean for age and sex; and they should have very low growth hormone levels during tests which normally provoke GH release into the blood stream (e.g. an insulin tolerance test or glucagon stimulation test). In addition the patient should have poor quality of life, as defined by a score of 16 or more using the disease-specific quality of life questionnaire for adult growth hormone deficiency (QoL-AGHDA®). For an example of this questionnaire go to *www.imperialendo.co.uk/AGHDA.pdf*

The current subsidised brand of growth hormone in NZ is Omnitrope from Novartis.

Questions & Answers from Professor Holdaway:

We had several members send in questions for Professor Holdaway and we were delighted to have these answered.

1) Who detects new cases of acromegaly?

In the last 5 years the following groups/individuals diagnosed 43 cases of acromegaly in the Auckland region:

- 12 cases diagnosed by GPs
- 7 diagnosed by endocrinologists (1= raised prolactin, 2 = thyroid clinic, 1 = ward patient, 2 = patients referred with pituitary adenomas, 1=McCune Albright syndrome)
- 4 by General Physicians
- 4 by gynaecologists (3 = irregular periods, I = husband accompanying his wife!)
- 3 by respiratory physicians (obstructive sleep apnoea)
- 2 diagnosed by the endocrine registrar
- 2 by ENT surgeons (obstructed upper airway)
- 2 by neurologists (headache investigation)

- 1 each by: sports physician, diabetes dietician, wife, gastroenterology registrar, general surgeon (haemorrhoids), psychiatrist, diabetologist

2) Are the diagnosis rates increasing?

Expected rates of new diagnoses of acromegaly from 20th century studies = 3 per million/year.
i.e. in a country with a population of 1 million there would be 3 new individuals with acromegaly diagnosed per year. The numbers of new diagnoses of acromegaly in Auckland in the last 5 years 2013-2017:

Year	no of cases	population (millions)	**cases/million**
2013	7	1.42	5
2014	12	1.42(?)	8
2015	8	1.42(?)	6
2016	7	1.42(?)	5
2017	11	1.53	7

There thus appears to be significantly more individuals diagnosed with acromegaly per head of population than expected from pre- 2000 estimates.

3) Travelling with Sandostatin and minirin/desmopressin

Ask your travel agent for advice (unusual destinations), or the respective Embassy about taking ampoules and an injection device. Your local endocrinology nurses can usually assist.

- Always keep the medication in its original box with the pharmacy label on it
- Transport the medication in your carry on baggage
- Take with you a copy of your most recent Endocrine clinic letter
- For some countries a note from your GP or specialist listing the medications you take may be useful
- Take up to 90 days of medication; if away longer get additional meds couriered or mailed

Sandostatin injections (LAR Octreotide):

- can be kept at 25 degrees for up to 25 hours, then can be safely put back at 4 degrees in the fridge
- if longer time of travel can purchase a small chiller bag with a slicker freeze pad to go in it

Desmopressin (ddAVP) nasal spray:

- normally store upright at 2-8 degrees in the fridge. Once in use, can store at up to 25 degrees.
- Alternatively obtain Desmopressin (Minirin) tablets which are stable at room temperature.

Growth hormone/somatropin injections (Omnitrope):

- The medication cartridge should remain in the injector pen and has to be kept between 2 to 8 degrees in a refrigerator.

An excellent recommendation from Tania (endocrine nurse from Waikato) for those travelling overseas with chilled medications is the iCool Medicube. This bag is designed to keep your medication between 2 and 8°C for 36 hours. They also have a range of smaller bags available for shorter trips. For details visit:
medactiv.com/en/transport-of-medication/38-medicube.html

This is available from their NZ distributor at www.mediray.co.nz for around $120.

4) Is longevity influenced by chronic ailments in acromegaly?

- The key factor influencing longevity in acromegaly is the blood GH and IGF-I level after treatment.
- The main ailment or complication of GH excess affecting longevity in acromegaly is hypertension. However, effective treatment (as with ordinary hypertension) should reduce this increased mortality back to the expected level.
- Other “complications” of acromegaly have not been shown to reduce longevity, but it would nonetheless be sensible to treat conditions such as diabetes and obstructive sleep apnoea effectively.
- Does possible body damage pre-diagnosis affect longevity? Yes, the longer the time from “first symptoms” to diagnosis and treatment the greater the effect on longevity.

Our sincere thank you to Professor Ian Holdaway for another excellent presentation.