Medical Options for the Treatment of Acromegaly

Guest Speaker Professor Ian Holdaway

Written by Dr Catherine Chan

This year due to popular demand, we have invited Prof Holdaway again to discuss the medical (non-surgical and non-radiotherapy) options for the treatment of acromegaly. Prof Holdaway is an endocrinologist with a special interest in acromegaly. He is based in Auckland and works in the public and private sectors.

We began with a quick reminder on the hormones involved. The pituitary gland produces growth hormone (GH). GH in turn stimulates the liver to produce IGF-1. IGF-1 has growth-promoting effects on almost every cell & tissue in the body.

Going through the history of medication treatment for acromegaly. Starting off in the 1970’s, progestins (e.g. Depo provera, currently used in contraception) was shown in a study to reduce GH levels. However later studies could not replicate the findings so this treatment quickly went out of favour.

Oestrogens, which have been around for a long time, was shown in a new study in 2012 to produce up to 45% cure level of IGF-1. This can be taken in the form of oestrogen tablets or patches for ladies. For the guys, who obviously would not like the side effects of oestrogens such as breast development, oestrogen-like agents such as Raloxifene (a selective oestrogen receptor modulator) would be more suitable. More studies are needed before this treatment will be adopted into the mainstream, so watch this space!

Dopamine-like agents are more familiar to a lot of us. Bromocriptine has now been largely superseded by Carbegoline, which has a longer duration of action, with a very low rate of side-effects compared with bromocriptine. There is now good evidence that carbegoline can be used on its own or together with octreotide, with ~50% achieving normal IGF-1 levels.

Moving onto somatostatin look-alike agents. Most of us are familiar with octreotide depot injections monthly as an excellent medical treatment that is fully funded for acromegaly in New Zealand. Octreotide has also been shown to shrink the pituitary tumour in 53% of individuals by more than 20%. See the diagram in the right, there are 5 different types of somatostatin receptors on the cell wall, octreotide acts mainly on the SR 2 receptor only.
In recent years several new variants of somatostatin look-alike agents have been developed. Of note is Pasireotide, which is currently available in Australia under special application, but is not yet available in NZ. Pasireotide LAR patients were shown in a study to be 63% more likely to achieve normal IGF-1 than octreotide LAR. See the diagram on the right, pasireotide has a broad range of action on several receptors include SR1, 2, 3, and mainly SR 5. A major side effect of pasireotide unfortunately is that it can adversely affect diabetes.

Staining is not available in NZ yet as it is very expensive, but this is probably going to be the trend for the future.

For those of you who have had surgeries in the past, rest assured that most laboratories store a sample of your pituitary tumour tissue, and this can be brought up and tested once staining becomes available in the future.

How does selective treatment work?
For example, if staining of an individual’s tumour shows predominantly SR 2 receptors then octreotide would be the most suitable medication. Whereas another individual’s tumour may show predominantly SR 5 receptors on staining, indicating pasireotide would be a better treatment option.

Another research project currently running is oral octreotide, it is currently undergoing phase 3 trials overseas to evaluate its effectiveness and safety profile. This could mean swapping the monthly injections for a few tablets in the future! Keep an eye out for this!

Finally another medication of a different class all together, Pegvisomant, is a new designer drug. Pegvisomant is different to all of the previously mentioned medications in the way it acts. It blocks the GH receptors directly stopping its action on the rest of the body.

Currently pegvisomant is only available in New Zealand under a special application to Pharmac known as ‘Named Patient Pharmaceutical Assessment’, previously known as ‘Exceptional Circumstances’. To date we know of 2 or 3 patients who have successfully obtained this in New Zealand.
What of the future?

- We may have an effective oral octreotide, replacing regular intramuscular injections.
- As the cost of medical treatment goes down, and their effectiveness increases. Medical treatment may become the first line treatment option for acromegaly, bypassing surgery.
- Treatment with a drug linked to a chemotherapy or radioactive agent to kill the tumours cells.
- Combination of agents leading to ease of use e.g. a combined carbegoline/octreotide agent

All in all, it is exciting to hear so many research efforts are being put into the medical treatment of acromegaly. I can see brighter days for fellow acromegaly patients in the future!

Thanks again to Professor Ian Holdaway
(Endocrinologist, Greenlane Hospital, Auckland)
For an excellent presentation.