



IPWSO
International
Prader-Willi Syndrome
Organisation

IPWSO Health ECHO abstract

April 20, 2021: Endocrinology

Please note this document is abridged from audio transcription of the Zoom session. Some errors resulting from the transcription process may be present.

IPWSO hosts: Georgina Loughnan (GL) and Tony Holland (TH)

Presenters: Dr Charlotte Höybye (CH) and Dr Tania Markovic (TM)

Video link

[Dr Charlotte Höybye: Prader-Willi syndrome: Adolescent and Adult Endocrinology](#)

[Q&A Following Dr Charlotte Höybye's Presentation](#)

Q: Hormone replacement for pubertal induction – what behaviour problems have people seen and how is that managed? Do they just not have hormone treatment if they struggle with it or do you use adjusted doses?

CH: In only a few patients have I seen this increased sexuality which can be expressed in many ways and sometimes it can be difficult because you don't know if the patient understands. It has been discussed very much what happens if they get more aggressive. I don't think they do. We know some patients can better express what they feel or are more aware. In my experience this has only been in a few patients and this can usually be managed.

Q: And would you stop the treatment or give them a smaller dose?

CH: I would try and figure out what the problem is and if it can be managed in other ways. If it isn't possible to change the behaviour and this leads to conflicts all the time, I would reduce the dose.

TM: In my experience having normal Androgen levels affects behaviour. Parents often worry but I have shown examples of a patient in psychiatric care for his behaviour when his testosterone was 0. The only affect I've seen testosterone have is that it's made boys want to masturbate which is normal (as long as in appropriate private setting).

CH: You can also speak to parents about the adverse effects of low sex hormones in the body. Adults with PWS can have mood swings. Sometimes when they get sex hormone treatment mood become more stable. It doesn't have to become worse.

Q: What is the appropriate FT4 level for treating hypothyroidism with Levothyroxin?

CH: Exactly the same as in everyone else.

Q: What factors should affect my decision to start sexual steroid replacement?

CH: There are a lot of indications. We know it is good for the muscles, for body composition and skeletal. In women you will need to discuss birth control.

TM: In women, up to the age of 50 you should always have estrogen. If we have pre-menopausal levels the advice is to have estrogen up to the age of 50 otherwise it has an adverse effect on cardiovascular health.

Participant: I am a paediatric endocrinologist, but we also care for adults. We sometimes give testosterone to young adults with PWS. Our experience is that often parents do not agree to start at the normal age when puberty is introduced so we often have a discussion over years and introduce it at 14 or 15. At the time we are to stop the growth hormone this is a good time to discuss that testosterone can have effects on muscle mass. We like to start with testosterone gel so it can be started at low doses. There were only bad experiences when the patient used the gel excessively like shower gel so his levels were sky high. When this was discovered, the dosage was adjusted and his levels became fine.

CH: In Sweden we have the gel and the injections. Most of the adults are in group homes where they are not comfortable treating with gel so usually men have injections. This is a depo injection so it not as easy to control the levels.

Participant: After time we also switch to injections. At the time when the family is not comfortable with the idea of giving testosterone we say if you feel something wrong it is easier to stop rather than an injection for 4 weeks so that is why we start at low levels with the gel.

Participant: I need to disagree a little bit. As a psychiatrist we have the experience of young adults getting treated with testosterone. They sometimes show more temper outbursts. It is nothing I can justify with numbers but I discussed it with a colleague a few days ago. We both have patients who receive injections and in the first week after the injection we find the patient has higher arousal and are more likely to get some temper outbursts. That's true for those living with their families and also living in groups. It is not always the case but we have 8,9, patients where we lowered the dose of testosterone and the patients got better. I don't know how it is in children because we only treat adults.

TM: I don't think we disagree with you – this dose should not be too high. This is why we use the gel so as to control the dose. With the injection you can get high levels. What the endocrinologist needs to do is make the gap longer. There are 2 types of injections, 1 that is slow release and in slimmer people can last up to 6 months and then there is the older one that lasts 2-3 weeks and that really does cause really high

levels initially and that certainly could affect mood. Done the right way where you are getting results in the middle or middle to high normal range it should not affect behaviour.

Participant: That is a question we always have. Does the level have to be mid-range to upper range, or can it be in the lower range?

CH: If the level is 0 or close to 0 when you start the treatment, the same as when we see other adults who have had pituitary tumours and have been at low low levels for a long time, when you replace the testosterone they will change in mood as well. It's just a physiological reaction. It may be more positive and stable but it does cause a difference.

TM: Often parents conflate testosterone with behaviour outbursts that are to be expected in PWS. Though testosterone affects other things it is not usually what is causing difficult or unpleasant behaviour.

Q: Do you give Hydrocortisone in severe acute illness or before surgery?

CH: I don't but I only see adults. It's a chronic disease so we would have known about symptoms before. I check regularly for cortisone levels.

Q: Do you perform Metirapone test to prove that kind of deficiency to all of your patients?

CH: Yes this is a test you have to use to see central adrenal insufficiency but you should only do it if you have a clinical suspicion. In my daily clinic I only check morning cortisol.

Poll Results

1. Do you treat adults with PWS with thyroid hormones?

11 responses Yes (79%). 3 responses No (21%).

2. Do you treat adults with PWS with GH?

9 responses Yes (56%). 7 responses No (44%).

Challenge presentation (Abridged)

GL: Tania Markovic is an Endocrinologist and the Director of Obesity Services at the Royal Prince Albert Hospital in Sydney, Australia which is a tertiary teaching hospital and we have one of the few specialised clinics for adults with PWS in Australia.

TM: 52 yr old man with PWS under our care since 08/2002

- deleted, diagnosis in childhood

- lived at home with parents (father radiologist) and siblings aged 34, fridge locked, was working; moved to first PWS group home in Australia aged 34 in 2003

- initial weight 106.9 kg, height 1.72 m, waist 116 cm, BMI 36.1

- since 2005 his weight has ranged between 63-73 kg, current weight 72.9 kg, height 1.70m, waist 88 cm, BMI 25.2

Medical problems

1. Central hypogonadism
2. Central hypothyroidism
3. Has never had growth hormone treatment
4. Hypertension - controlled
5. Past history of faecal impaction/diarrhoea - controlled with fibre supplement
6. Schizophrenia - stable on olanzepine 30 mg daily
7. "Intermittent Explosive Disorder (DSM5)" treated with carbamazepine
8. Mild hyponatremia, due to carbamazepine, so treatment now changing to propranolol
9. Osteoporosis; no fractures
10. MAIN ISSUE TO DISCUSS: severe head-drop
 - surgical management being considered
 - does GH have any role?

[Discussion following Tania Markovic's presentation](#)

CH: Growth Hormone can have impact at his age but it will not be local it will be in the body composition. The problem here seems to be with his neck so growth hormone won't contribute to this problem. How is his physical activity otherwise? Are other muscles strong?

TM: His physical activity is good. Do you understand why he's got that head drop?

CH: I think it's because of the kyphosis.

TM: Are people with PWS more prone to kyphosis?

CH: They are. It is the same mechanism as scoliosis. Weak muscles when they grow can draw in different directions and cause these problems.

TM: Is it possible that growth hormone from childhood can prevent this?

CH: No, it's not connected. Maybe he can train the neck muscles. I don't know how orthopaedics treat kyphosis. If he has chronic hyponatremia that will not make the osteoporosis better so maybe you can treat from this point of view.

Participant: We see some patients with very severe kyphosis. They are also not in bad body shape. The therapy is more complicated than for scoliosis because the special brace needed is not so well accepted. A combination of physiotherapy, growth hormone, Vitamin D is needed but past a certain point we can't do anything to improve the case.

TM: And does Intermittent Explosive Disorder exist?

Participant: It does exist but it is not the case for PWS because the criteria are that the outbursts are not connected to any other medical condition. I wouldn't not say this is something you can diagnose in a person with PWS.

TM: And is there any role for carbamazepine or propranolol for someone without PWS who has this condition?

Participant: Carbamazepine is given as a mood stabiliser sometimes but we do not have good data. We don't use them, especially in PWS because of the side effects. It is difficult to comment from the outside. There are no guidelines for treatment. For every individual you need to find the right medications.

TH: We do have a session on Behaviour and Mental Health coming up in a few weeks and we will also have a session on Orthopaedics. Tania your case presentation is a very nice example of how you actually need the skills of different disciplines in supporting people with PWS whether it's endocrinology, psychiatry, orthopaedic surgeons and so on. Also just to mention that IPWSO has a special initiative on behaviour and mental health and we're bringing together a group of people to really try and address this question that so many of the treatments, and you've illustrated this so well, Tania, that so many of the treatments used by for mental health and behaviour problems are ad hoc as the particular psychiatrist decides. We do need to get much more rigour into this.

Participant: I am a psychologist. I think it's important to build the narrative around why someone might have angry episodes and to really advocate for our PWS cohorts that it's okay to be angry but we need to work with them rather than adding a diagnosis that does actually merit being added. What can happen with that is that your patient can get lost, be seen as an angry person or if someone reads a file with intermittent explosive disorder they see a very different person than the person you see walking into your clinic. We must protect this cohort in terms of what is the mental health and psychiatric profile and really be able to outline why we don't add additional diagnosis, how we look at PWS in particular and are not confusing the matter by adding in labels that don't actually help the patient but maybe adding in strategies and management for the home that they are living in, to learn how to cope with those episodes that are distressing.

Participant: That is an important point as adding a diagnosis almost always leads to adding a new medication. We strongly try not to give a diagnosis other than PWS.

Q. Can you comment on how the remarkable weight loss was achieved.

TM: I'm sure many of you have seen this. People with PWS when they're adults, at least in Australia, get much better weight control and health outcomes if they are in a specific home set up for people with PWS, where the kitchen is locked, where their meals are very well planned, and encouraging exercise and that is how it was achieved.

Tony Holland Summary

From Charlotte's talk, we must think of people with Prader-Willi syndrome as having a disorder of hypothalamic function and therefore there is the potential for dysregulation of a number of hormonal systems. We tend to focus most specifically on Growth Hormone and Sex Hormone; Charlotte made the case for using GH in both children and then adults with PWS. There are clear benefits beyond simply that of growth which include improvements in motor skill, in body composition, and in cognition and behaviour. There are comparatively few disadvantages or side effects to the use of GH.

So, the case has been made, undoubtedly for children. The case is also made for adults but interestingly in the breakout discussions questions were raised about whether GH is available to adults.

There was a lot of discussion around sex hormone replacement, particularly in boys the relationship between testosterone use, and a deterioration in general behaviour, with a general conclusion that if done at an appropriate dose this is not a serious issue.

Tania's Case Presentation illustrated the complexity and the challenge of proving good support and the need to bring in people of different disciplines and the dangers around excess medication use. The particular problem of head drop which was described was dramatically shown on x-rays and clearly must affect this person greatly. The general conclusion was that if he had had growth hormone it would not have prevented this orthopaedic condition. Interestingly only now are we beginning to see people with PWS in this age group (52) and it's likely we will begin to see more new issues. IPWSO for example has been interested in learning if dementia becomes a problem in later life for people with PWS. These issues will become of greater concern, but for a very good reason, which is that people with PWS are living longer.

Upcoming Health ECHO sessions

Tue 18 th May	<i>Understanding Hyperphagia</i> Tony Goldstone, Endocrinologist, Clinical Researcher.
Tue 15 th June	<i>Behaviour and Mental Health</i> Tony Holland, Clinical and Academic Psychiatrist, IPWSO President.
Tue 13 th July	<i>Sleep Disorders</i> Brendon Yee, Associate Professor, Respiratory and Sleep Physician.

Thank you very much to everyone who attended the session and participated. We look forward to seeing you on Session 4 in May.

Ends.