IPWSO Health ECHO abstract
July 13, 2021: Sleep disorders in PWS

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) Tony Holland (TH)

Presenters: Brendon Yee (BY) and Zsófia Gács (ZG)

Video link

Brendon Yee: Sleep and respiratory manifestations of PWS: an adult perspective

PDF available here.

Q&A Following Brendon Yee's Presentation

Q: My question is about the idea of needing to check for sleep apnoea before they start growth hormone. When we see people as adults they're already been on GH for some time as a child. In Australia we're lucky that it's subsidised to receive the GH as an adult if they've received it as a child so we're not stopping and starting, it's continuous use of GH. Does that mean we should be doing periodic sleep studies along the way, or only if we're concerned?

BY: Looking at the literature it's not that clear cut that GH worsens sleep disordered breathing. What I was worried about, is when the initially started GH these post mortem studies suggested these kids might have underlying sickness or disordered breathing. If they are assessed at the start when they in the paediatric population that is probably more important than as an adult. The evidence that GH worsens sleep disordered breathing – if they don't have it, it won't bring it on. But if you've got it in the first place, it may make it worse.

Q: My understanding is they start GH when they are really, really little now. Is it even practical to test for sleep apnoea in a tiny little person?

Q: I work in a UK PWS clinic. We have children within the first year of life starting on GHT. We follow the pathway that in the first year of life they have a sleep study and then six months afterward, and then we do yearly follow ups. The follow up studies can depend on clinical history taking, if there is any noticeable snoring, disrupted sleep or excessive daytime sleepiness they may have another TOSCA. If everything is reported to be fine they just have another pulse oximetry and the community nurses do it. My son is an adult with PWS. He has a (Sentec), that's not the level 1 Brendon described, it's Level 2. Or is it level 3?

BY: It's a Level 3 or 4 – it's a system measuring O2 and TCO2, is that right?

Q: Also, it monitors abdominal movement so he has a strap round his tummy, strap round his chest, nasal cannula and oximeter on his finger.

BY: That's Level 3. Level 2 is like a full sleep study, but you do that at home with no one monitoring you. Level 3 is what you've described.

Q: So in the UK they are doing respiratory function tests within adult services but I think its likely to depend on the consultant you're with whether you're in a specialist service or not.

ZG: I'm seeing a teenage boy, presentation is when he has to present in school or read a long passage aloud (times of anxiety) he falls asleep in the middle of the school day. It's practically impossible to wake him up. He was admitted to hospital 2 or 3 times already. To emergency, he's seen neurologists, had EG monitoring, it seems it's a normal very deep sleep. It's a problem for the family because the school calls them away because of these problems. What should I advise them?

BY: How old is the child? Could they do a Multiple Sleep Latency Test (MSLT)? Because it would be nice to get a diagnosis. But if you can't then sometimes you may just empirically give them a trial of modafinil. So if there are no contraindications I would start with 50mg, to make sure they tolerate it. Usually with narcolepsy they go up to 200-400mg, but I think if there are no contraindications, warn them about side effects, you could give them a dose of modafinil. It can be good in children with narcolepsy as well. If you can't do a MSLT, you want to treat them empirically, I would be comfortable with you giving a trail of modafinil. Take it in the morning, sometimes they need divided doses, so morning and lunchtime, has a half life of about 8 hours. There's a longer acting form of modafinil called armodafinil you could consider. This is maybe something you can do. It doesn't cure the daytime sleepiness but it definitely improves the daytime sleepiness such that they can function a bit better. It would be nice to do an MSLT to confirm the diagnosis, to confirm they've got pathological objective daytime sleepiness, but with the history you've given me, they fall asleep at school, they fall asleep in active situations, they've got severe daytime sleepiness. The pragmatic part of me would say if you can't do an MSLT, empirically try the modafinil and see how you go.

Q: I am a psychiatrist in Germany and I see a lot of adult patients. Most of my older patients, after the age of 30 very often report daytime sleepiness. What would you recommend for making a diagnosis of obstructive sleeping disorder or apnoea or is it just and effect of growing older?

BY: If they have a history of snoring or apnoea, stopping breathing or unrefreshing sleep and they've got PWS I would have a low threshold for doing a simple sleep study on them. Because sleep disordered breathing, particularly OSA is very common in adult PWS patients – maybe 60-70%. If they've got sleep apnoea I would aim to treat it. If it's severe enough I would try then on CPAP and the reassess them, because their sleepiness may improve. But if the sleepiness persists despite using a CPAP machine, despite being compliant with therapy, then I would consider doing a MSLT test, if they can comply with instructions, to confirm they've got daytime sleepiness, or empirically give them a trial of modafinil or pitolisant, which you have available there. It's generally well tolerated, modafinil, and I think pitolisant's well tolerated as well, and it's not a stimulant, not an amphetamine. In Australia we don't have pitolisant so we only use modafinil or amphetamines which is quite scary. So I would exclude sleep disordered breathing. If there's no sleep disordered breathing and subjective sleepiness is a concern, if you can't get access to a MSLT you could just treat empirically with modafinil or pitolisant.

Poll question

1. What sleep disorders do you commonly see in your clients/patients with PWS? (Choose as many as apply).

a) Obstructive sleep apnoea (6 responses)
b) Central sleep apnoea (1 response)
c) Narcolepsy (1 response)
d) Daytime Sleepiness (6 responses)
e) Other (use chat box) (1 response)

Case presentation (Abridged)

GL: Zsófia Gács works as a pediatric endocrinologist at 2nd Department of Pediatrics, Semmelweis University, Budapest, Hungary. She has been seeing patients with PWS for 2,5 years: she says, "Although I try to find their best possible endocrinological treatment (hypothalamus-pituitary dysfunction, glucose homeostatis disturbances, hypertension), I realize that their multidisciplinary approach needs more help to 'come true', so I try to find specialists in other departments to work together with. Together with an enthusiastic medical student we're working on a survey on everyday life's problems of PWS families in Hungary."

Case presented:

Zsófia Gács Case Presentation

Age and gender: 16-yr-old girl

Diagnosis and date of diagnosis: Genetic diagnosis of PWS in 2010 (5-yrs)

Treatment and significant information to date:

-GH (2017)

-antihypertensive (2016)

-metformin (2019)

Physical:

Lack of orthopedic investigations - severe scoliosis found

Lack of sleep apnoe check-ups - ?

Problems with (close) psychiatrist - psychological help still needed

Psychosocial:

The family seems unable to change a thing, as everything were just 'over the borders' - many inner and external factors explain, but still... (eg more and more serious tantrums, respiratory infections)

Availability of school, of psychologist?

Please provide some key questions for the participants to consider with regards to this case.

-Should I discontinue GH?

-Should I insist on starting estrogen replacement?

-Should I insist on going to all specialists, starting psychotherapy, measuring blood pressure more often, losing weight, etc - on doing things which are really uncomfortable for the patient and the family as well on short time - but would be beneficial on the longer term

Discussion following Zsófia Gács' case presentation

Comment: I think estrogen replacement can wait. I would only deal with one thing at a time. I'm not an orthopedic (expert) at all but that scoliosis looks dreadful. That is what I would be most worried about and would try and intervene with now. I'm sure she'll cope with the surgery; she's young. Her weight is a problem too. I would also focus on that. I don't know what services (are available). It sounds like the mother is having a difficult time. Is she on her own, is there a partner?

ZG: The father and brother and uncle also provide a working small circle of relatives for support.

Comment: So, if it was me, I would be focusing on her weight and her scoliosis for the moment.

Comment: This is an interesting case and reminds me of some cases I know of. The questions refer to each other because the temper outbursts, the family problems, the difficulty in bringing her to surgery – you don't really know where to start and I think that is one of the problems. By now I could call it a hobby of min to prescribe serotonin reuptake inhibitors for patients like this. I would try this.

But my main comment was on how can you help the family as a whole? A lot of parents I see don't want to see a psychiatrist or psychologist. They say the problem is not with me it’s with my son or my daughter. As a psychotherapist I don’t talk to my patients for most of the time when I see them, I talk to the parents, and they receive psychotherapy to cope with the situation. Perhaps that might be an approach to the problem that they mother doesn’t want to see anyone to help her. I am pretty sure she will open up about her problems when the daughter sees a psychotherapist or psychiatrist.

Comment: This case is typical of many PWS cases. I assure you, you are not alone this is happening the world over. If the family can cope, weight loss is the most important. You can continue the growth hormone, I agree with not starting estrogen now. Helping the family so that the girl loses weight demands a very clear cooperation about food. I would start there. If she loses weight she can help her diabetes. The x-ray is awful but you see that not so rarely in adults with PWS and if breathing is not disturbed by it I would concentrate on the weight loss, get her out walking and give them a system to follow at home.

Comment: This is a very challenging and difficult case. Certainly, one of the ways in which it is challenging is where would you start? One of the things for me certainly would be concentrating on the weight. I wonder if there might be potential for a period of hospitalisation which would support the family but also where you could have more intensive input to manage that.

The GH question in challenging and relates to the diabetes. So if the diabetes is well controlled continuing the GH would be an ideal thing to do. All these things would be a process towards getting her to a better place if you did want to pursue spinal surgery because as you say the anaesthetic challenges would be significant.

TH: Can I ask whether the family are attempting to restrict access to food? Do they lock cupboards? My suspicion is they have never really done that. For them to try and do it now, while it is the priority, will be very, very difficult. Almost certainly she would escalate behaviours and so very quickly the situation would break down. Are the family trying to manage her weight at all?

ZG: I think they are trying, or at least they think they are trying. But I am not sure if they are really trying or making every attempt. Whenever I ask them they say the diet is okay. But I don’t consider it okay because her weight is extreme now.

TH: I think I would try and develop a programme of reward, obviously nothing to do with food but reward for weight loss. I might look to plotting her weight over time to make it visual and actually setting targets. If there were things she really enjoyed, trips out, clothes, try and build more positive reinforcement. At the moment, partly due to exhaustion on the side of the parents, generally the atmosphere feels one of failure and despair rather than one of trying to seek positive reward for achievement of losing weight. Trying to change the whole atmosphere in the family seems crucial.

ZG: I think also not the patient, but the family will be rewarded when she is able to lose some weight.

Comment: Often when you talk about food with families, they say they try but they have too little knowledge about calories. If it is possible, a nurse coming into the home and looking at what is in the cupboard helps. People might think things are low calorie when they are not. When she is so heavy and not moving her calorie needs are very low. Sometimes they are prescribed a diet from a dietician which is too high calorie because they are not aware how little they more. Get the family support about the food. Then give them successes.

Tony Holland Summary

Brendon started his talk by highlighting the importance of sleep disorders, because sleep disordered breathing, daytime sleepiness, all this may contribute to the shorter life expectancy that we observe in people with PWS.

He then described the different forms of disordered breathing, from central sleep apnoea, obstructed sleep apnoea, sleep related hyperventilation and a combination of these.

When talking about central sleep apnoea he said he thought this largely a maturational issue so present in infants and young children with Prader-Willi syndrome, generally that would improve over time. He went into some detail about how you separate out what is central sleep apnoea from obstructed sleep apnoea in terms of whether there is evidence on the assessment of whether the patient is making any effort to breathe or not.

He then went on to discuss obstructive sleep apnoea, the importance of tonsillectomy, or adenotonsillectomy, the relevance to obesity, and then went on to describe some of the assessments, polysomnography that needs to be done. The different levels, Level 1 being the gold standard and Level 4 being the most limited of assessment.

The most serious form of sleep disorder he described was nocturnal hyperventilation which is generally associated with severe and long-term obesity.

In terms of the treatments CPAP remains one of the key forms of treatment but also things like weight loss, adenotonsillectomy, and he also went on to discuss novel therapies such as mandibular advancements (MAD) that might eventually become more standard in people with PWS.

He also discussed the issue of narcolepsy in PWS and made the point that is it best to think of it as a narcolepsy-like state rather than true narcolepsy. That's primarily because the hypocretin levels are not so low as you would expect in someone with true narcolepsy.

For daytime sleepiness he talked about the potential use of modafinil or pitolisant. There was discussion after the talk about whether or not sleep investigations were necessary when you start GH. The conclusion was it was necessary early in life but if someone is starting GH later in life and there'd been no indication of problems throughout their life it may not be so necessary.

The case that Zsófia discussed, all of us who've worked in the field recognise that scenario and we've all seen people with this combination of challenges and families that are exhausted and feel paralysed and unable to move forward. She raised 4 really important issues; behaviour and family support, the use of GH, the issues of puberty and the scoliosis. (December Health ECHO will focus on orthopaedics.)

How do you prioritise where your interventions might be? I think the conclusion was a combination of weight loss, and support to the family. Some of these other issues can wait until the person loses weight and you can help the family to respond to their needs.

Upcoming Health ECHO sessions

Tues 14th Sept	*Diet and Exercise and the Prevention of Obesity* Dr Constanze Lämmer, Children's Hospital, St. Bernward Hospital, Hildesheim, Germany and Georgina Loughnan, Royal Prince Alfred Hospital, Camperdown, NSW, Australia
Tues 12th Oct	*Caring and Living with PWS in Italy* Dr Maria Giulia Marini, Fondazione ISTUD, Milan, Italy

Thank you very much to everyone who attended the session and participated. We look forward to seeing you on Session 7 in September.

Ends.