

Patient Experiences of Hunger in POMC or LEPR Deficiency

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Summary

- Proopiomelanocortin (POMC) and leptin receptor (LEPR) deficiencies are rare genetic diseases of obesity that are associated with insatiable hunger, which places huge burdens on patients and caretakers
- We conducted in-depth interviews in a cohort of patients with POMC and LEPR deficiencies who received treatment with setmelanotide and found a decrease in the daily burdens of insatiable hunger that had meaningful impacts on the patients' quality of life (QOL)

Introduction

- Many rare genetic diseases of obesity are associated with mutations in the melanocortin-4 receptor pathway, a hypothalamic pathway that regulates hunger and energy balance^{1,3}
- Variants in key genes including POMC and LEPR can disrupt melanocortin-4 receptor signaling, resulting in hyperphagia and early-onset obesity^{1,3}
- In patients with POMC or LEPR deficiency, managing hyperphagia and obesity can be a daily struggle, and these burdens are not well characterized⁴
- In this study, we describe the experience of the daily impacts of insatiable hunger on patients with POMC or LEPR deficiency treated with setmelanotide as it relates to health-related QOL

Methods

- In-depth qualitative interviews were conducted via video conference with patients who were aged ≥15 years, had previous diagnosis of POMC or LEPR deficiency, and were participating in an ongoing open-label extension of Phase 3 clinical trials with setmelanotide (NCT03651765)
- Using a semistructured interview guide, patients were asked to describe
 - Experiences of hunger, as well as the impacts of hunger on their lives prior to setmelanotide treatment
 - Changes in hunger, weight, and functioning after initiating setmelanotide treatment, including the perceived meaningfulness of the changes
 - Treatment satisfaction and feelings if setmelanotide were to be discontinued
- Interviews were conducted in German, recorded, transcribed, and translated into English for analysis

Results




Patient Characteristics

- We interviewed 5 patients with POMC (n=3) or LEPR (n=2) deficiency
- The average age was 23.8 years (range, 15–33 years), and 4 of the 5 patients were male
- One participant was hearing impaired; the interview was facilitated by the mother, who also responded to interview questions

Patient Experience Prior to Setmelanotide Treatment

- Before setmelanotide treatment, all 5 patients described an abnormal sensation of hunger (2 described a strong psychological desire, much like addiction), with none indicating they felt full after meals (Table 1; Figure)
- All 5 patients reported insatiable hunger negatively impacted their families, emotions, and work and/or school functioning (Table 1; Figure)

Table 1. Patient-Reported Experiences of Hunger, Eating Habits, and Impact of Hyperphagia Prior to Clinical Trials With Setmelanotide




Before Setmelanotide Treatment			
Feelings of hunger 	<i>"It sometimes felt as if I were an animal that was super hungry and could only think about food, and when I wanted to eat something, I searched until I found it."</i> – Patient with POMC deficiency	<i>"What I recall very strongly is this addiction-like desire for food, and this constant preoccupation with it. It's more than the physical feeling of hunger. It also plays on a mental level."</i> – Patient with POMC deficiency	<i>"I really had to struggle with myself... sometimes I could control myself, but most of the time I couldn't."</i> – Patient with POMC deficiency
Eating habits 	<i>"When I would start eating something, I'd eat the whole thing. No matter what sort of package it was, or whatever, I'd always eat the whole thing. I also ate it at an enormous tempo...It was really terrible."</i> – Patient with LEPR deficiency	<i>"I would eat my way through everything crosswise, and very quickly, too. I would always do this in a certain feeling of stress so that my parents wouldn't see it, because they had set up certain rules about food so that I wouldn't gain weight. So, my eating was very hectic when I'd eat in secret."</i> – Patient with POMC deficiency	<i>"It was like, if there were chips somewhere, I always kept eating, kept eating, kept eating, until someone complained and said I should stop. Then I had to struggle with myself, but since everyone was there and was watching, I somehow managed it."</i> – Patient with POMC deficiency
Impacts of hyperphagia 	<i>"I was a happy child, but the emotions, particularly when it came to food, were often, well, guilt feelings, huge guilt feelings. Because you must hide everything all the time. You lie, and your mother notices it anyway. It was always a huge feeling of guilt."</i> – Patient with POMC deficiency	<i>"It was not as if I did not try to find work, but after 1 or 2 months something always occurred, so that I ended up back in the hospital, or I had to call in sick and couldn't work. Of course, I was always fired during my trial period, and I never arrived at a long-term employment situation."</i> – Patient with LEPR deficiency	<i>"They took me away when I was 4 years old, claiming that my mother was feeding me to make me fat, and they took me to some sort of psychosomatic facility, for over a year, or a year and a half, where I was supposed to lose weight. That did not work either."</i> – Patient with LEPR deficiency

LEPR, leptin receptor; POMC, proopiomelanocortin.

Changes With Setmelanotide Treatment Experienced by Patients




- After setmelanotide treatment, all 5 patients reported profound reductions in hunger and eating and substantial improvements in QOL (Table 2; Figure)
- Patients with POMC deficiency reported weight loss ranging from 40 to 97 kg following setmelanotide treatment, and those with LEPR deficiency reported weight loss ranging from 25 to 35 kg
- All 5 patients indicated they were very satisfied with the impact of setmelanotide treatment and would be upset if they had to discontinue (Table 3; Figure)

Table 2. Patient-Reported Experiences of Hunger, Eating Habits, and Impact of Hyperphagia During and After Clinical Trials With Setmelanotide

After Setmelanotide Treatment			
Feelings of hunger 	<i>"A lot has changed, and when I look at the hunger today, I'm assuming it's on the same level as other people. I don't have anything to compare it by, but I'm just assuming that."</i> – Patient with POMC deficiency	<i>"Now, I do not feel huge hunger, but sometimes it's difficult to say. It's still like... You want to eat; you feel the urge. But the hunger itself is not that great."</i> – Patient with POMC deficiency	<i>"Now, I really feel it. My stomach growls and I notice that I am hungry. It's a feeling I never had before. It is funny."</i> – Patient with LEPR deficiency
Eating habits 	<i>"I no longer eat as much. For example, if we make spaghetti Bolognese for supper in the evening, I'll only eat one and a half plate [portion], but usually just one and that will be it."</i> – Patient with POMC deficiency	<i>"I still give thought to food, and maybe I feel like eating this or that. But I can choose to eat something, and I can also set it aside, and in no way does it still hold this status."</i> – Patient with POMC deficiency	<i>"[Now, if] I am hungry, I eat something, I am full right away and I stop, very simple. Previously, I wasn't able to manage that. It just didn't work."</i> – Patient with LEPR deficiency
Impacts of decreased hyperphagia 	<i>"Emotionally—it was a burden before because you were insecure the whole time because you were always the fat one, and whenever you had trouble, you were always afraid, they would ignore you or insult you. And now you do not ever have these problems."</i> – Patient with POMC deficiency	<i>"For me, not being able to work was the worst thing, to be honest. I simply could not, and this has changed with the study and with the weight loss...I've been working steadily for 2 years now, without interruptions and I'm doing well in my job. It's fun, no problems at all. It is really unbelievable."</i> – Patient with LEPR deficiency	<i>"Before, I tried for a long time to study, but I failed due to my physical and mental state. But now that I've been receiving the medication, I got into it very fast, and I'm beginning my final [undergraduate] semester, and it's working really super, I have to say. There's no comparison. Before, it just wouldn't have been possible, and now it's working wonderfully. That's also a big change."</i> – Patient with POMC deficiency

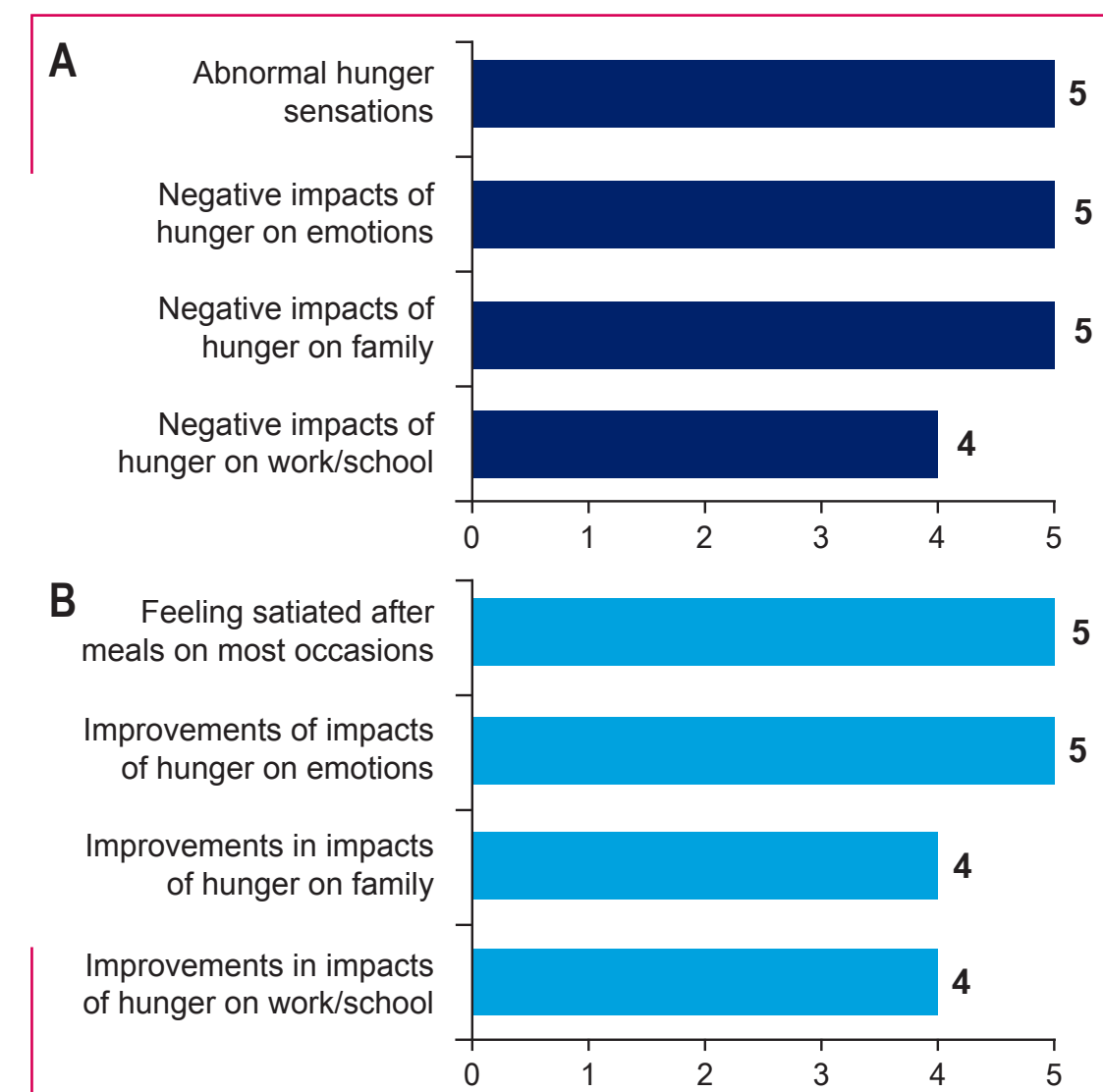
LEPR, leptin receptor; POMC, proopiomelanocortin.

Table 3. Patient-Reported Meaningfulness of Improvements in Hunger, Overall Satisfaction of Treatment, and Feelings if Treatment Were Discontinued

Meaningfulness 	<i>"I'd never have reached the point I'm at now, and I never would have experienced and achieved what I've got. This medication has really fundamentally transformed my life."</i> – Patient with POMC deficiency	<i>"I think it's certainly very important for my life. That I no longer have the feeling that I must eat everything, like an animal. I don't have that anymore. But the secondary aspects are more important than the hunger since I've lost so much weight. My blood values are good. It's had hugely positive effects on my life, for which I am very grateful."</i> – Patient with POMC deficiency	<i>"Extremely. I have absolutely no illnesses at all. I have not been in the hospital even once, or anything else like that. I am top fit. I cannot complain at all. I've got nothing at all. It's unbelievable.... This study came, and everything changed immediately. It was absolutely unbelievable."</i> – Patient with LEPR deficiency
Overall satisfaction 	<i>"I am very satisfied. Really. I am very, very satisfied. I cannot say any more about it. It is a blessing that I am permitted to take this medication."</i> – Patient with LEPR deficiency	<i>"I'm very satisfied...I've lost a lot of weight, and I have a lot more energy. The doctors are very nice, and it's nice to see that someone is paying attention to this, and there's a medication for this, that they're deploying people to deal with this problem, when people used to have to go without care."</i> – Patient with POMC deficiency	<i>"It has totally transformed my life. It was huge, good fortune for me. I would definitely recommend it to everybody in my situation, or who has lived with this illness for a long time. It causes a great external change but also a great internal change."</i> – Patient with POMC deficiency
Discontinuing setmelanotide 	<i>"Oh God. Well, that would be a catastrophe. I can simply say that. It would really be a catastrophe. Yes, it would be the end, somehow."</i> – Mother of patient with LEPR deficiency	<i>"I would say I would fall into a very extreme hole, and I do not know what would happen. I'm very honest. I know that the medication has changed everything for me. I have already talked to someone about that, and I said I think I would jump off a tall building if I no longer had the medication. I am saying that very honestly, because if I would imagine it would be the way it was before, I would not be able to stand it. I would not be able to bear it."</i> – Patient with LEPR deficiency	<i>"I have thought about it, and I think that for me it would mean the end of the world, because I would probably gain weight again, and when you gain weight your life expectancy is not all that long, since, like I said, I had very poor blood values. It would be really terrible."</i> – Patient with POMC deficiency

LEPR, leptin receptor; POMC, proopiomelanocortin.

Figure. Number of patients with POMC (n=3) or LEPR (n=2) deficiency who experienced hyperphagia and related impacts on QOL (A) before and (B) after treatment with setmelanotide.



LEPR, leptin receptor; POMC, proopiomelanocortin; QOL, quality of life.

Conclusions

- Hyperphagia and the constant inability to feel satiety negatively impact QOL in patients with POMC or LEPR deficiency
- Reduced hunger and improved satiety resulting from setmelanotide treatment substantially and meaningfully change these patients' lives
- Results from this qualitative study are consistent with those reported in Phase 3 trials of setmelanotide and suggest that the impacts of setmelanotide treatment also include QOL improvements

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