Concomitant medication in growth hormone (GH)-treated patients with adult GH deficiency (AGHD): an analysis from NordiNet® International Outcome Study (IOS)

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Disclosures
C Höybye is a NordiNet® IOS investigator and member of NordiNet® IOS International Study Committee (ISC). E Pournara and BT Pedersen are employees of Novo Nordisk. JO Jørgensen is a NordiNet® IOS investigator and NordiNet® IOS ISC member; he has received consulting fees from Novo Nordisk, and lecture fees, consulting fees and unrestricted research grants from Pfizer Inc.

Introduction

- Patients with adult growth hormone deficiency (AGHD) have an impaired metabolic profile and other characteristic clinical features that negatively affect health (Carroll PV *et al. J Clin Endocrinol Metab* 1998;83:382–95) and quality of life (Giovannini L *et al. Endocr J* 2015;62:1037–48).
- The aim of growth hormone (GH) therapy in AGHD is to improve the metabolic profile and quality of life of patients who are GH deficient (Ho KKY *et al. Eur J Endocrinol* 2007;157:695–700).
- Patients with AGHD often have comorbidities and may be prescribed concomitant treatment to decrease the burden of associated medical conditions.

Aims and Objectives

- The aim of this study was to evaluate the patterns of first prescription for concomitant medication in connection with GH therapy initiation in patients with AGHD.

Methods

- Patients with AGHD and recorded data on concomitant medication enrolled in NordiNet® International Outcome Study (IOS) (NCT00960128), an international, non-interventional study evaluating effectiveness and safety of treatment with Norditropin® (somatropin [recombinant GH], Novo Nordisk A/S, Denmark), were included in the analysis.
- Fifty different types of concomitant medication were identified. Each type was allocated to one of nine treatment clusters based on their main therapeutic properties and/or their target body system.
  - Medications that did not fit into one of the nine defined treatment clusters were grouped under miscellaneous.
- Patients were stratified into one of three subgroups by first prescription for concomitant medication relative to GH therapy initiation:
  - before
  - at (±2 months)
  - after.
- The association between first prescription for concomitant medication and GH therapy initiation (before versus after) was analysed using the chi-square test.

Results

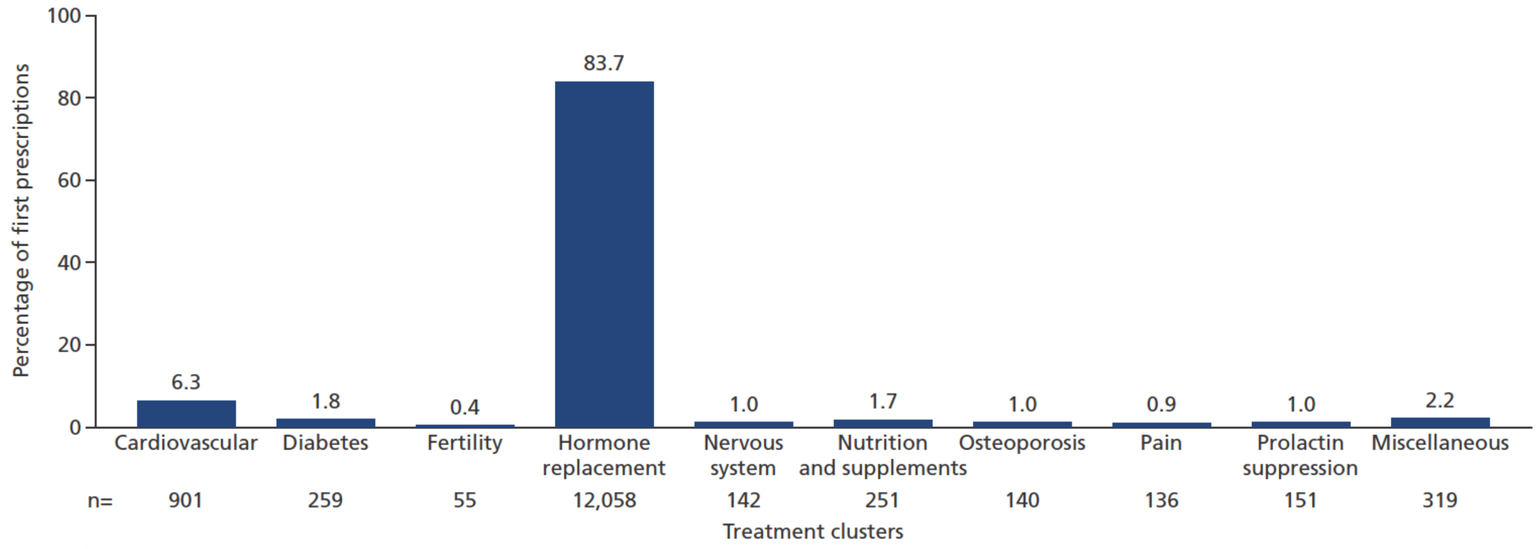
- Data on concomitant medication were recorded for 986 patients (57.6% males), representing 42.4% of patients with AGHD enrolled in NordiNet® IOS. The majority of patients had adult-onset AGHD (88.4% adult-onset vs. 11.6% childhood-onset) (Table 1).
  - Proportionally more patients received a first prescription of concomitant medication before (60.8%) compared with at (20.2%) or after GH therapy initiation (19.0%).
  - More men than women received concomitant medication before, at and after GH therapy initiation (56.4%, 54.8% and 64.4%, respectively).
  - Patients who started on a first prescription for concomitant medication after GH therapy initiation were, on average, younger at GH therapy initiation than those who started on concomitant medication before GH therapy initiation (mean [standard deviation]; 38.1 [22.5] vs. 44.9 [16.2] years).
- Overall, 14,412 prescriptions of concomitant medication were recorded. On average, each patient received 14.6 prescriptions for concomitant medication. The distribution of prescriptions by treatment cluster is shown in Figure 1.

Table 1. Demographic data.

	First prescription for concomitant medication (N=986)		
	Before n=599	At n=199	After n=188
Male, n (%)	338 (34.3)	109 (11.1)	121 (12.3)
Adult-onset AGHD, n (%)	561 (56.9)	177 (18.0)	134 (13.6)
Childhood-onset AGHD, n (%)	38 (3.9)	22 (2.2)	54 (5.5)
Mean age at GH therapy initiation, years (SD)	44.9 (16.2)	43.1 (19.0)	38.1 (22.5)
Mean age at concomitant medication start, years (SD)	38.1 (17.3)	43.1 (19.0)	42.7 (20.9)

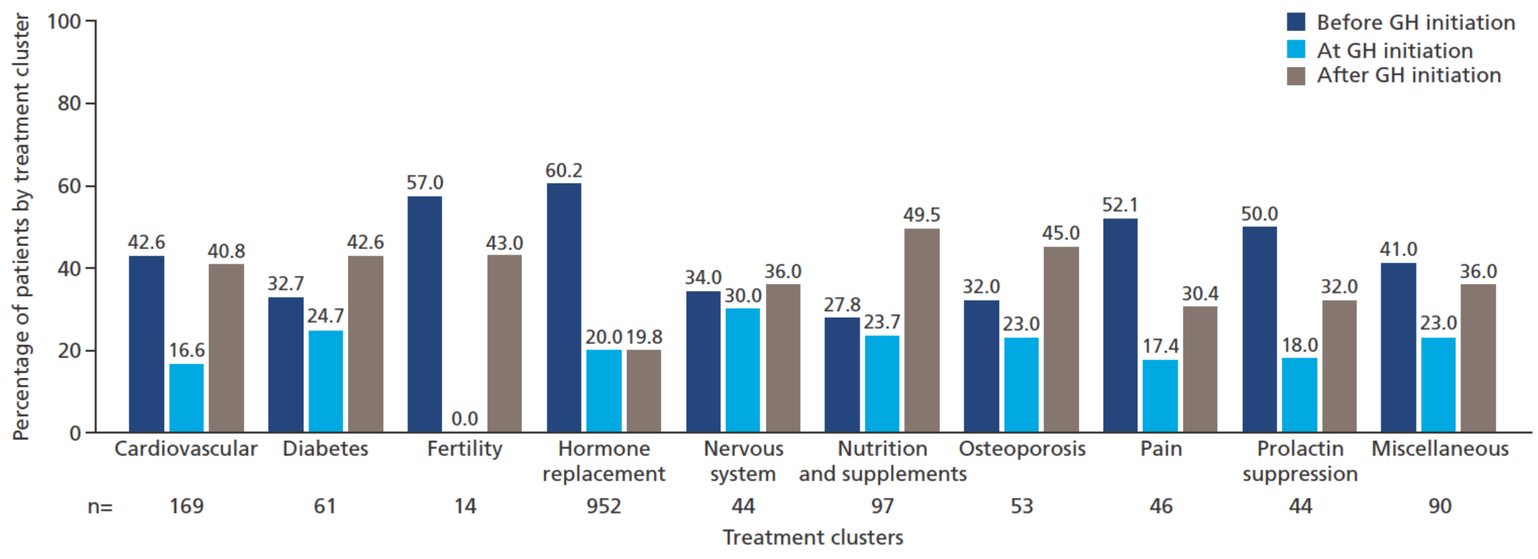
AGHD, adult growth hormone deficiency; GH, growth hormone; SD, standard deviation.

Figure 1. Distribution of prescriptions for concomitant medications by treatment cluster.



n=number of prescriptions.

Figure 2. Distribution of patients by treatment cluster relative to GH therapy initiation.



Patients may have received more than one concomitant medication, but are only represented once within a cluster based on the first prescribed drug.
GH, growth hormone; n=number of patients.

- The most frequently prescribed clusters of concomitant medication were hormone replacement therapies (antidiuretic hormone [ADH], thyroxine, hydrocortisone and sex hormones) and cardiovascular therapies (anti-arrhythmics, anticoagulants, antihypertensive, lipid-lowering and angina pectoris treatments).
- Among clusters, the five most frequently prescribed types of concomitant medication were thyroxine replacement therapy (31.8% of prescriptions in 82.6% of patients), hydrocortisone replacement (25.0% of prescriptions in 70.8% of patients), androgens (13.9% of prescriptions in 42.7% of patients), ADH replacement (6.7% of prescriptions in 21.8% of patients) and sex steroid replacement (6.4% of prescriptions in 22.0% of patients).
- Similar proportions of men and women received prescriptions for thyroxine replacement therapy (81.2% and 84.4%, respectively), hydrocortisone (72.0% and 69.1%, respectively) and ADH (22.0% and 21.8%, respectively).
  - 46.7% of women and 72.0% of men received first prescriptions for oestrogen and androgen replacement therapy, respectively.
- The distribution of patients by treatment cluster relative to GH therapy initiation is shown in Figure 2.
- 96.5% of the total group of patients received hormone replacement therapies.
- A significantly higher proportion of patients received a first prescription for hormone replacement therapies before versus after GH therapy initiation (60.2% vs. 19.9%, respectively; $p<0.0001$).
- Conversely, more patients received a first prescription for nutrition and supplement treatment after versus before GH therapy initiation (49.5% vs. 27.8%, respectively; $p=0.0153$).
- Within the other clusters, notably the cardiovascular, diabetes and osteoporosis treatment clusters, no significant difference was observed in the proportion of patients receiving their first prescription after versus before GH therapy initiation.

Conclusions

- More than half of the patients in this report were already receiving concomitant medication before initiating GH therapy.
- The medication cluster most frequently prescribed concomitantly with GH was hormone replacement therapies, with the second most frequently prescribed cluster being treatment pertinent to the cardiovascular system.
  - Hormone replacement therapies were initiated in a significantly higher proportion of patients before versus after GH treatment initiation, suggesting that GH might be the last pituitary hormone to be replaced.
- Significantly more prescriptions for nutrition and supplements were recorded after versus before GH therapy initiation, suggesting that further efforts might have been made to optimise patients' health after initiating GH therapy.
- The proportions of first prescriptions for concomitant medication for the cardiovascular system, diabetes or osteoporosis treatments were similar after versus before GH therapy initiation.
- Further analyses are required to assess whether the effect of GH therapy on cardiovascular risk factors, metabolism and bone health also impacts on the proportions of cardiovascular system, diabetes or osteoporosis treatments before versus after GH therapy initiation.

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This study was sponsored by Novo Nordisk Health Care AG. NordiNet® IOS is registered at ClinicalTrials.gov NCT00960128.
The authors take full responsibility for the content of the poster but are grateful to Watermeadow Medical, an Ashfield Company (supported by Novo Nordisk), for writing assistance.
Presented at the 18th European Congress of Endocrinology (ECE), 28–31 May 2016, Munich, Germany.