Potential Factors Related to Treatment Changes in Acromegaly Patients: Analysis of a US Prospective Registry

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BACKGROUND

- Acromegaly results in considerable comorbidity, decreased quality of life, and increased mortality. [1-3]
- Initial treatment is usually surgery, followed by pharmacotherapy if biochemical values (growth hormone [GH], insulin-like growth factor [IGF-I]) are uncontrolled.[4, 5]
- Changes in treatment may be provoked by lack of biochemical control, intolerance, cost or other factors, but little is known about reason for these treatment changes in real-world practice.

OBJECTIVE

- To identify factors related to treatment changes in acromegaly patients.

METHODS

Study Design and Setting

- Retrospective cohort study from acromegaly registry at the Pituitary Center at Cedars-Sinai Medical Center (CSMC-PC), which has been recruiting patients since 1985.

Ethics and Safety

- The CSMC-PC registry contains only observational data and the study was approved by the CSMC-PC institutional review board.

Study Population and Study Cohorts

- Biochemical-control status cohorts based on patients' final IGF-I or GH value:
  - Controlled: IGF-I ≤100% of upper limit of normal; *or* GH nadir <1.0 µg/L within 2 hours following OGTT; *or* random GH level <1 µg/L; *or* mean integrated 24-hour GH <2.5 µg/L.
  - Uncontrolled: GH *and/or* IGF above levels noted.
  - Discordant: 2 tests within 7 days, and only 1 met definition of "controlled."

Study Measures

- Baseline measures were determined in the period from first lab test to 6 months from that date.
- Prevalence of comorbidities was determined across the entire period of enrollment in the registry.
- The following treatment changes were excluded from analysis:
  - Medications used briefly prior to surgery;
  - Octreotide SA use ≤30 days before octreotide LAR or lanreotide.
- Combination treatment meant simultaneous multiple medication use for >90 days.

Data Analysis

- All analyses were performed using SAS® version 9.4 (SAS Institute, Cary, NC).

RESULTS

Baseline Characteristics

- 121 patients were followed for mean 8.8 years or 1,065 patient years.
- Mean age was 55.4 years; 55.4% were female; and, 72.7% were Caucasian.

Baseline Characteristic	Biochemical Status			
	Controlled N = 70; 57.9%	Discordant N = 16; 13.2%	Uncontrolled N = 35; 28.9%	All N = 121
Age, mean (SD)	55.0 (15.9)	52.6 (16.6)	57.6 (18.4)	55.4 (16.7)
Age at diagnosis,[a] mean (SD)	43.9 (14.7)	37.8 (14.4)	41.8 (15.8)	42.4 (15.0)
Female, n (%)	39 (55.7)	8 (50.0)	20 (57.1)	67 (55.4)
Race/ethnicity, n (%)				
Caucasian	51 (72.9)	11 (68.8)	26 (74.3)	88 (72.7)
Asian	8 (11.4)	0 (0.0)	8 (22.9)	16 (13.2)
Hispanic	9 (12.9)	3 (18.8)	0 (0.0)	12 (9.9)
Other	9 (12.9)	3 (18.8)	0 (0.0)	12 (9.9)
Macroadenoma, n (%)	59 (84.3)	9 (56.3)	25 (71.4)	93 (76.9)
Adrenal insufficiency, n (%)	10 (14.3)	3 (18.8)	5 (14.3)	18 (14.9)
Gonadal insufficiency, n (%)	16 (22.9)	0 (0.0)	4 (11.4)	20 (16.5)
Hypothyroidism, n (%)	10 (14.3)	2 (12.5)	7 (20.0)	19 (15.7)
Years of follow-up[b], mean (SD)	8.5 (6.7)	10.9 (9.5)	8.5 (7.1)	8.8 (7.2)

[a] 109 patients had information about age at diagnosis; [b] The period between the first and the last IGF-I/GH date; Prolactin elevation was observed in 1 (6.3%) patient in the discordant group. But not all patients had data on prolactin elevation recorded at presentation at CSMC-PC because presentation may have occurred prior to care at CSMC-PC and prolactin elevation information was not available on all patients.

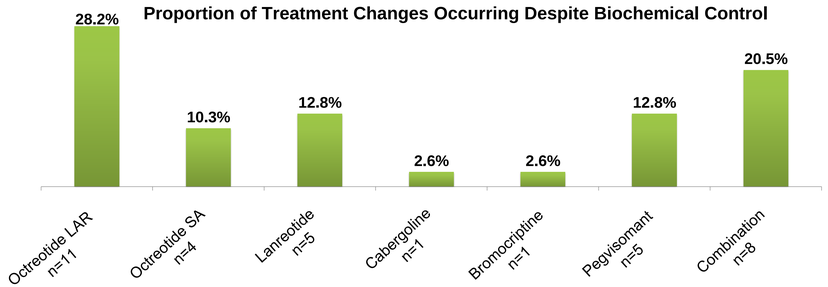
Clinical Outcomes

- Hypertension (HTN) (47.9%) and diabetes mellitus (DM) (31.4%) were the most common comorbidities, and were more common in uncontrolled patients than in controlled patients.
- The prevalence rates for HTN, DM, and sleep apnea were higher in this registry than in European registries: 39.4%, 25.3%, and 17.1%, respectively, in the Belgian registry[6]; and 39.1%, 37.6%, and 13.2%, respectively, in the Spanish registry.[7]

Outcome, n (%)	Controlled N = 70; 57.9%	Discordant N = 16; 13.2%	Uncontrolled N = 35; 28.9%	All N = 121
Hypertension	30 (42.9)	7 (43.8)	21 (60.0)	58 (47.9)
Diabetes mellitus	18 (25.7)	5 (31.3)	15 (42.9)	38 (31.4)
Sleep apnea	17 (24.3)	1 (6.3)	10 (28.6)	28 (23.1)
Colonic polyps or colon cancer	15 (21.4)	1 (6.3)	8 (22.9)	24 (19.8)
Visual field defects	12 (17.1)	2 (12.5)	6 (17.1)	20 (16.5)
Left ventricular hypertrophy	9 (12.9)	0 (0.0)	4 (11.4)	13 (10.7)
Cardiomyopathy or heart failure	3 (4.3)	0 (0.0)	3 (8.6)	6 (5.0)

Treatment Changes

- Over more than 1,065 patient-years, there were 240 evaluable treatment changes in 73 patients.
- 39 (16.3%) changes occurred in patients with biochemical control prior to the change, 24 (10%) in discordant patients, and 177 (73.8%) in biochemically uncontrolled patients.



- Each bar represents patients treated with a different agent. The height of the bar indicates the proportion of those patients who left that treatment for another, despite having adequate biochemical control on treatment.

LIMITATIONS

- Care outside of CSMC-PC may have been incompletely documented.
- Institutional variation may limit the generalizability of these findings.
- This study was descriptive only; no statistical comparisons were attempted due to the small sample size

CONCLUSIONS

- Biochemically uncontrolled patients had higher rates of DM and HTN than those who were controlled.
- Most treatment changes were preceded by abnormal lab parameters, suggesting that physician recognition of the long-term importance of biochemical control is associated with adjustment of treatment.
- Potential reasons for changing therapy in controlled patients may include intolerance, persistent or new symptoms, or cost (e.g. changes in insurance).
- Multiple therapeutic options are required since biochemical control is not the only determinant of drug choice.

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