

The effect of octreotide treatment on somatic and psychological symptoms of acromegaly

Marek RUCHALA, Izabela STANGIERSKA, Edyta GURGUL, Adam STANGIERSKI, Jolanta FAJFER, Jerzy SOWINSKI

Department of Endocrinology, Metabolism and Internal Medicine, University of Medical Sciences, Poznan, Poland

Correspondence to: Assoc. Prof. Marek Ruchala, MD.
Department of Endocrinology, Metabolism and Internal Medicine,
University of Medical Sciences,
60-355 Poznań, Przybyszewskiego Str. 49, Poland
TEL: +48 61 867-55-14 (869-13-30); FAX: +48 61 869-1682;
E-MAIL: mruchala@ump.edu.pl

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Abstract

OBJECTIVES: Acromegaly is a chronic disease caused by excessive growth hormone secretion resulting in bone and soft tissue overgrowth. Body image changes as well as systemic complications may considerably influence patients' psychological health and disturb everyday activities. The aim of this study was to determine the effect of octreotide treatment on somatic and psychological symptoms of acromegaly, and thus on patients' quality of life.

MATERIALS AND METHODS: The study was conducted on 15 patients with acromegaly. The average duration of octreotide therapy was 5.6 years (1–10 years). The respondents created a list of subjective signs and symptoms of acromegaly before treatment and reported changes observed during therapy. The psychological examination was performed with appropriate test scales assessed patients' self-efficacy, emotional control, psychological gender and their life satisfaction.

RESULTS: The most important changes observed during octreotide therapy were associated with head and joint pain relief and reduction of physical limitations. The patients also noticed the improvement of cognitive functions and interpersonal relations. The study revealed average life satisfaction in the group. The patients on the one hand demonstrated high self-efficacy and on the other hand – intensive repression of emotions. The undifferentiated sex-role schema dominated in group.

CONCLUSIONS: The study proved a significance of octreotide therapy in acromegalic patients' life. In spite of chronic disease, all the respondents reported good quality of life (average life satisfaction). Additionally, their high self-efficacy helps to cope with the disease. Nevertheless, undifferentiated sex role schema in the study group suggests lack of behavioral flexibility and high emotional repression predicts negative somatic consequences.

Abbreviations :

hGH	- human growth hormone	IGF-1	- insulin-like growth factor 1,
GHRH	- growth hormone releasing hormone	GSES	- Generalized Self-efficacy Scale
SST	- somatostatin receptor	CECS	- Courtauld Emotional Control Scale
LAR	- long acting release	IPP scale	- sex-role inventory scale
		SWLS	- Satisfaction with Life Scale

INTRODUCTION

Acromegaly is a chronic disease caused by excessive growth hormone (hGH) secretion. In most cases (98%) it results from pituitary adenoma (somatotropinoma), rarely from ectopic GHRH or hGH secretion (Gola *et al.* 2006; Scacchi & Cavagnini 2006). The term 'acromegaly' meaning extremity enlargement, speaks for the manifestations. Bone and soft tissue overgrowth resulting from hGH excess is not only disabling, but also disfiguring. However, the prognosis in acromegaly is determined by visceral organs enlargement and systemic consequences including cardiovascular and pulmonary abnormalities, diabetes mellitus and bone degenerative disorders (Clayton 2003; Colao *et al.* 2000; Grunstein 1994; Liote & Orcel 2000; Sze *et al.* 2007). Furthermore, acromegaly is associated with higher risk of malignancies, such as colon, prostate, breast and thyroid cancer (Chan *et al.* 1998; Cullen *et al.* 2000; Jenkins & Besser 2001; Matyja *et al.* 2006; Popovic *et al.* 1998; Ruchala *et al.* 2009). The most often complaints reported by patients include head and joint pain, hyperhidrosis and symptoms resulting from hypopituitarism due to pituitary tumor mass.

Currently, there are several therapeutic methods for acromegaly, that usually are combined. Transsphenoidal resection of tumor is often the first-line treatment. Patients who fail to have clinical and biochemical remission after surgery continue the therapy with dopamine agonists, somatostatin analogs (octreotide, lanreotide), somatostatin antagonist (pegvisomant) and/or radiotherapy.

Somatostatin analogs exert their antisecretory and antitumoral effects by acting on somatostatin receptors (SSTR) type 2 and 5 (Chanson & Salenave 2008). Octreotide was the first somatostatin analog introduced in acromegaly treatment as a drug injected subcutaneously on average 2–3 times a day. Slow release form of octreotide – octreotide LAR, permitting once-monthly intramuscular injections, improved patients' compliance. Several studies revealed, that octreotide LAR potently decreases GH and IGF-1 level, achieving normalization in 50–70% of acromegalic patients (Colao *et al.* 2001; Freda 2002; Lancranjan & Atkinson 1999; Turner *et al.* 1999) and reduces tumor volume in 20–80% of patients (Colao *et al.* 2001). The subjective signs and symptoms of acromegaly improve in 64–74% of patients treated with somatostatin analogs (Freda 2003).

The efficacy of therapy encloses biochemical (GH and IGF-1) remission, tumor removal preserving appropriate pituitary function and the reduction of comorbidities and mortality. The last, but not the least aspect of the treatment is associated with psychological disorders. Acromegaly is a chronic disease, what means, that its outcomes and symptoms can not be completely eliminated with treatment. Untreated may disturb everyday activities, impair day-and-night rhythm, limit

social life. It may also interfere with occupational activities and reduce financial status. Several studies revealed, that in comparison with healthy controls acromegalic patients had reduced quality of life, that usually remains relatively low even after treatment (Biermasz *et al.* 2004; Kauppinen-Mäkelin 2006; Rowles *et al.* 2005). However, appropriate therapy ameliorating physical and psychological symptoms of the disease may considerably improve their quality of every-day life.

The aim of the study was to determine the effect of octreotide therapy on somatic and psychological features of acromegaly. In the first part of the research we evaluated subjective improvement in patients' condition, due to introduced treatment. Since personality mechanisms play important role in therapeutic process, the study included also the evaluation of individual parameters of pro-health activities among acromegalic patients, that contribute in therapeutic process. Therefore, the second part consisted of psychological examination assessing patients emotional control, self-efficacy and life satisfaction.

MATERIAL AND METHODS

The study group consisted of 15 patients with diagnosed acromegaly (11 women and 4 men, aged 38–58) treated in Clinical Department of Endocrinology, Metabolism and Internal Medicine of University of Medical Sciences in Poznan. The respondents were treated with octreotide LAR in intramuscular injections performed every 4 weeks. The average duration of octreotide therapy in the study group was 5.6 years (1–10 years). 11 of the patients were treated with transsphenoidal resection of pituitary tumor followed by octreotide therapy, three underwent surgery, radiotherapy and received octreotide injections and one was treated with radiotherapy and somatostatin analog. The study was approved by a medical ethics committee and all the patients gave their informed consent to participate.

The respondents were asked to create retrospectively a list of subjective signs and symptoms of acromegaly before octreotide treatment and then to report the changes observed during the therapy.

The psychological examination was performed with following methods:

Generalized Self-efficacy Scale GSES (by Schwarzer 1993) assessing a general sense of perceived self-efficacy – a self-administered scale with comprehensive questionnaire consisting of 10 items mixed at random into a larger pool of items, that have the same response format. It predicts coping with difficult life demands as well as adaptation after various stressful events.

The Courtauld Emotional Control Scale CECS (by Watson 1983) measuring emotional control by the extent of the suppression and control of (1) anger, (2) depression, (3) anxiety, and total negative emotion in daily life. It is a 21 item self report questionnaire divided

into 3 subscales with each item scoring from 1 (“not at all”) to 4 (“very much so”). The higher CECS score, the more intense emotional repression.

The Sex-Role Inventory – IPP scale (by Kuczynska 1992) estimating the psychological gender: (1) sex-typed with psychological features reflecting biological gender (feminine woman, masculine man), (2) cross-sex-typed – psychological gender opposite to the biological one (feminine man, masculine woman) (3) androgynic possessing feminine and masculine characteristics regardless of their biological gender, (4) undifferentiated with feminine or masculine features of little intense

The Satisfaction with Life Scale SWLS (by Diener 1985) evaluating life satisfaction. It consists of five items scored 1 to 7 points, reaching 5–35 points in total. Subsequently, the results are converted and presented in sten. Outcome from 1–4 sten means low life satisfaction, 5–6 means medium life satisfaction and 7–10 means high life satisfaction (Juczynski 2001)

RESULTS

The list of subjective signs and symptoms of acromegaly observed at the disease onset compared to the list of improvements after treatment allowed to estimate somatic and psychological changes in patients' condition (Table 1).

Tab. 1. Signs and symptoms of acromegaly on disease onset and improvements after treatment.

Signs and symptoms before treatment	Improvements after treatment
bone tissue overgrowth, bone & joint pain	reduced pain
joint edema, numbness	
headache, eye ball pain, impaired vision	
polydypsia, xerostomia	
reduced muscle strength	
reduced psychomotor drive	improved psychomotor drive
impaired day-and-night rhythm, insomnia	good night rest
amenorrhoea (women)	eumenorrhoea (women),
impotency	increased libido
hyperhidrosis, constipation	reduced hyperhidrosis
reduced immunity	
lability, impaired emotional control	balanced mood
subdepression, irritability, absent-mind	improved emotional control
retention defect	improved cognitive functions
social isolation	improved social activity

Tab. 2. The results of CECS scale.

	CECS (points)			
	general	anger	depression	anxiety
average score	55.5	17.5	19.3	18.7

The list of improvements includes only these declared by all of the patients. The most important changes were associated with the reduction of pain and physical limitations, what significantly influenced quality of life. The respondents also marked enhancement of cognitive functions, such as attention, memory and verbal fluency. Their emotional functions became more stable and controllable, what resulted in better interpersonal relations in family, including recurrence of sexual activity and increased activity in social life. Many of them started to organize or returned to professional engagement.

The CECS revealed high level of total emotional control (55.5 points in scale ranging from 21 to 84) resulted from high indicators of anger, anxiety and depression suppression [scale 7–28 points]. The patients also estimated high their general self-efficacy (6.9 sten). In GSES scale score 1–4 sten reflects low and 7–10 sten indicates high self efficacy.

Life satisfaction of acromegalic patients was assessed as average (5 sten) in SWLS scale.

The evaluation of psychological gender showed, that undifferentiated sex role schema dominated in the study group. The most adaptive androgynic schema was noted sporadically (Figure 1)

DISCUSSION

Many of disfiguring acromegalic features are irreversible. The most stigmatizing symptoms of acromegaly are body image changes. These visible features denounce the disease, bring out comments and fear. Since external appearance and physical fitness are important determinants of everyday comfort and self-confidence, body image distortion leads to disruption in interpersonal relations and social anxiety. Decreased

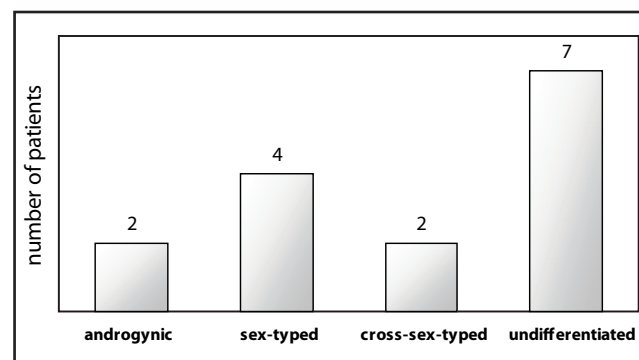


Fig. 1. Results of sex role inventory.

self-esteem leads to poor psychological immunity and disorganizes in endangerment. Patients demonstrate mood swings liability, loss of initiative and spontaneity and their quality of life becomes worse. Thus, considering the efficacy of treatment, psychological and sociological aspects of the disease should be discussed.

Patients' self-estimation of life quality plays important role in therapeutic process. In spite of long disease duration and many irreversible symptoms, well-being and good quality of life were noticed in all respondents (average life satisfaction). Rational psychological management of the disease concentrates firstly at reversible symptoms, such as patient's frame of mind, not necessarily at external appearance. Examined patients seemed aware of this. Listing the symptoms, none of the respondents concentrated on visible features of the disease, probably being conscious of their irreversibility. All of them mainly paid attention to handicapping symptoms of psychological impairment. They admitted, that intellectual functions, such as recent memory and concentration improved during octreotide treatment. Social activities elicited less anxiety. The patients also noticed the enhancement of psychomotor and sexual drive. Although, they associated these changes with the reduction of certain symptoms (better sleep, pain relief, edema regression), it remains unclear what was the primary factor – psychological functions improvement or physical symptoms reduction.

The study group demonstrated high self-efficacy revealed in GSES scale. Self-efficacy defined as belief of being capable of performing in a certain manner to attain certain goals can play a major role in approaching various tasks and life challenges (Gapinska *et al.* 2008). The results of our study demonstrate therefore, that acromegalic patients treated with octreotide are more likely to view difficult tasks as something to be mastered rather than something to be avoided. Thus, since illness is understood as a specific and difficult task, they seem to cope better with the disease.

High scores obtained in CECS correspond with intensive repression of emotions and indicate a tendency to suppress negative emotions. This tendency labeled as 'repressive coping style' is known to distort the assessment of patient's distress. In the long term, it may have negative somatic consequences. This is an important topic in behavioral medicine, since studies have shown that repression is a potential risk factor of chronic pain and cancer (Beutler *et al.* 1986; Garsen 2007; Jensen 1987; Weihs *et al.* 2000).

The sex-role concept was found useful in explaining the differential importance of various domains of life as well as the relative contribution of those domains to the individual's general life satisfaction. Four sex type described in gender schema theory (sex-typed, cross sex-typed, androgynic and undifferentiated) indicate respondents' behavior, intelligence and stress reaction.

Sex-typed and cross-sex typed subjects cope easily only with tasks consistent with their psychological sex role. Since behavioral flexibility was shown to derive from strong identifications with both masculine and feminine roles (androgyny), androgynic subjects exhibit the greatest adaptability, performing well on both masculine and feminine tasks (Bem 1981).

The undifferentiated and sex-typed sex-role schema dominating in the study group suggests lack of behavioral flexibility and low adaptive predispositions of respondents. Undifferentiated subjects did not performed well neither on masculine nor on feminine, particularly sex-reversed tasks.

Dealing with stress of disease, personal equipment or so-called own resources seem very important. These include relatively constant personality features, such as disposable optimism, self-control and self-efficacy. Human do not react to direct external stimuli, but rather to thoughts, convictions and emotions induced by the stimuli. High self-esteem improves stress management, generates stamina and improves self-efficacy, whereas low self-esteem may lead to anxiety, helplessness and depression (John & Gross 2004). The study group revealed some features facilitating the therapeutic process, such as high self-esteem and average life satisfaction. However, on the other hand they demonstrated tendency to repressive emotional hypercontrol and behavioral rigidity, that worsen stress management. Thus, the positive reaction to introduced treatment cannot be associated strictly with their psychological equipment. Conversely, improvement probably was induced by external factor (octreotide), what confirms the efficacy of the treatment. Indeed, patients themselves underlined the positive influence of therapy on their quality of life.

CONCLUSIONS

The study revealed a significance of octreotide therapy in acromegalic patients' life. Examined group declared considerable reduction of burdensome symptoms and improvement of mood and social relations during and after treatment. These changes cannot be explained only by respondents' individual predispositions to deal with disease, as their basic psychological equipment was not completely favorable. On the one hand average life satisfaction and high self-efficacy are useful in management with a chronic disease. On the other hand undifferentiated sex role schema dominating in the group, suggests lack of behavioral flexibility and high emotional repression predicts negative somatic consequences.

The study showed that octreotide therapy may motivate patients to everyday activities and to constructive forms of coping with life disturbances. What is more, it also improves their compliance and cooperation in therapeutic process.

REFERENCES

- 1 Bem SL. (1981). Gender schema theory. A cognitive account of sex typing *Psychological Review*. **88**(4): 354–364.
- 2 Beutler, LE, Engle D, Oro-Beutler ME, Daldrup, R, Meredith K. (1986). Inability to express intense affect: A common link between depression and pain? *Journal of Consulting Clinical Psychology*. **54**: 752–759.
- 3 Biermasz NR, van Thiel SW, Pereira AM, Hoftijzer HC, van Hemert AM, Smit JWA *et al.* (2004). Decreased Quality of Life in Patients with Acromegaly Despite Long-Term Cure of Growth Hormone Excess. *J Clin Endocrinol Metab*. **89**(11): 5369–5376.
- 4 Chan JM, Stampfer MJ, Giovanucci E, Gann PH, Ma J, Wilkinon P *et al.* (1998). Plasma insulin-like growth factor I and prostate cancer risk: a prospective study. *Science*. **279**: 563–566;
- 5 Chanson P, Salenave S. (2008) Acromegaly. Review. *Orphanet J Rare Dis*. **3**: 1–17.
- 6 Clayton RN, 2003. Cardiovascular function in acromegaly. *Endocr Rev*. **24**: 272–7.
- 7 Colao A, Baldelli R, Marzullo P, Ferretti E, Ferone D, Gargiulo P, *et al.* (2000). Systemic hypertension and impaired glucose tolerance are independently correlated to the severity of the acromegalic cardiomyopathy. *J Clin Endocrinol Metab*. **85**: 193–9.
- 8 Colao A, Ferone D, Marzullo P *et al.* (2001). Long-term effects of depot long-acting somatostatin analog octreotide on hormone levels and tumor mass in acromegaly. *J Clin Endocrinol Metab*. **86**: 2779–2786.
- 9 Cullen KJ, Yee D, Sly WS, Perdue J, Hampton B, Lippman ME *et al.* (1990). Insulin-like growth factor receptor expression and function in human breast cancer. *Cancer Res*. **50**: 48–53.
- 10 Freda PU. (2002). Somatostatin analogs in acromegaly. *J Clin Endocrinol Metab*. **87**: 3013–8.
- 11 Freda PU. (2003). How effective are current therapies for acromegaly? *Growth hormone & IGF research* **13**: 144–151.
- 12 Gapinska B, Tartas M, Walkiewicz M, Majkovic M., (2008). Self-efficacy and anxiety and depression in patients with colostomy. *Wspolczesna Onkologia* **12**(2): 84–89.
- 13 Garsen B. (2007). Repression: Finding Our Way in the Maze of Concepts. *J Behav Med*. **30**(6): 471–481.
- 14 Gola M, Doga M, Bonadonna S, Mazziotti G, Vescovi PP, Giustina A. (2006). Neuroendocrine tumors secreting growth hormone-releasing hormone: pathophysiological and clinical aspects. *Pituitary*. **9**: 221–9.
- 15 Grunstein RR, Ho KK, Sullivan CE. (1994). Effect of octreotide, a somatostatin analog, on sleep apnea in patients with acromegaly. *Ann Intern Med*. **121**: 478–83.
- 16 JenkinsPJ, Besser M. (2001). Clinical perspective: acromegaly and cancer: a problem. *J Clin Endocrinol Metab*. **86**: 2935–41.
- 17 Jensen MR. (1987). Psychobiological factors predicting the course of breast cancer. *Journal Personality* **55**: 317–342.
- 18 John OP, Gross JJ. (2004). Healthy and unhealthy emotion regulation: Personality processes, individual differences, and life span development. *Journal of Personality*. **72**: 1301–1333
- 19 Juczynski Z. (2001). Narzędzia pomiaru w promocji i psychologii zdrowia [Tools for Health Assessment in Health Promotion and Psychology] (in Polish), Warszawa, Pracownia Testów Psychologicznych Polskiego Towarzystwa Psychologicznego.
- 20 Kauppinen-Mäkelin R, Sane T, Sintonen H, Markkanen H, Välimäki MJ, Löyttyniemi E *et al.* (2006). Quality of Life in Treated Patients with Acromegaly. *J Clin Endocrinol Metab*. **91**(10): 3891–3896.
- 21 Lancranjan I, Atkinson AB. (1999). Results of a European multicentre study with Sandostatin LAR in acromegaly patients. *Pituitary* **1**: 105–114.
- 22 Liote F, Orcel P. (2000). Osteoarticular disorders of endocrine origin. *Baillieres Best Pract Res Clin Rheumatol*. **14**: 251–76.
- 23 Matyja V, Kos-Kudła B, Foltyn W, Strzelczyk J, Latos W, Marek B *et al.* (2006). Detection of colorectal lesions by using autofluorescence colonoscopy in acromegalics and their relation to serum growth hormone and insulin-like growth factor-1 levels. *Neuroendocrinol Lett*. **27**(5): 639–643.
- 24 Popovic V, Damjanovic S, Micic D, Nesovic M, Djurovic M, Petakov M *et al.* (1998). Increased incidence of neoplasia in patients with pituitary adenomas. *Clin Endocrinol*. **49** (4): 441–445.
- 25 Rowles SV, Prieto L, Badia X, Shalet SM, Webb SM and Rainer PJ. (2005). Quality of Life (QOL) in Patients with Acromegaly Is Severely Impaired: Use of a Novel Measure of QOL: Acromegaly Quality of Life Questionnaire. *J Clin Endocrinol Metab* **90**(6): 3337–3341.
- 26 Ruchala M, Skiba A, Gurgul E, Uruski P, Wasko R, Sowinski J. (2009). The occurrence of thyroid focal lesions and a need for fine needle aspiration biopsy in patients with acromegaly due to an increased risk of thyroid cancer. *Neuroendocrinol Lett*. **30**(3): 382–386.
- 27 Scacchi M, Cavagnini F. (2006). Acromegaly. *Pituitary*. **9**: 297–303.
- 28 Sze L, Schmid C, Bloch KE *et al.* (2007) Effect of transsphenoidal surgery on sleep apnoea in acromegaly. *Eur J Endocrinol*. **156**: 321–9.
- 29 Turner HE, Vadivale A, Keenan J, Wass JA. (1999). A comparison of lanreotide and octreotide LAR for treatment of acromegaly. *Clin Endocrinol (Oxf)*. **51**: 275–280.
- 30 Weihs KL, Enright TM, Simmens SJ, Reiss D. (2000). Negative affectivity, restriction of emotions, and site of metastases predict mortality in recurrent breast cancer. *Journal of Psychosomatic Research*. **49**: 59–68.
- 31 Foltyn W, Kos-Kudła B, Strzelczyk J, Matyja V, Karpe J, Rudnik A *et al.* (2008). Is there any relation between hyperinsulinemia, insulin resistance and colorectal lesions in patients with acromegaly? *Neuroendocrinol Lett*. **29**(1): 107–12.
- 32 Lancranjan I, Bruns C, Grass P, Jaquet P, Jervell J, Kendall-Taylor P *et al.* (1996). Sandostatin LAR: a promising therapeutic tool in the management of acromegalic patients. *Metabolism*. **45**: 67–71.
- 33 Pawlikowski MG, Melen-Mucha. (2003). Perspectives of new potential therapeutic applications of somatostatin analogs. *Neuroendocrinol Lett* **24**: 21–27