Consensus statement of the Polish Society for Endocrinology

Presurgical somatostatin analogs therapy in acromegaly

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Abstract62

Consensus statement of the Polish Society for Endocrinology, regarding presurgical somatostatin analogs in acromegaly has been presented. It is suggested to administer depot somatostatin analog (Octreotide LAR at the dose 20 mg and then 30 mg or equivalent doses of Lanreotide Autogel 90/120 mg every 4 weeks) in order to normalize or suppress to a maximal extent GH and IGF-1 concentrations. The period of therapy in case of microadenoma would be at least 3 months (targets: biochemical improvement, reduced risk of disease's complications, perioperative risk reduction, inhibition of tumor growth). The period of therapy in case of macroadenoma would be at least 6 months, until maximal possible reduction of GH and IGF-1 concentrations (targets: tumor shrinkage, biochemical improvement, reduced risk of disease's complications, perioperative risk reduction). Using an uniform approach in a group, as numerous as possible, of treated patients would allow objective evaluation of long-term efficacy of the treatment.

LETTER

Abbreviations:

ECG	– electrocardiogram
fT4	– free thyroxine
GH	– growth hormone
IGF-1	– insulin-like growth factor-1
LAR	– long acting repeatable
MR	– magnetic resonance
OGTT	– oral glucose tolerance test
PRL	– prolactin
TSH	– thyroid stimulating hormone

Acromegaly is a rare disease caused by growth hormone (GH) secreting pituitary adenoma. Typical clinical symptoms are accompanied by metabolic disorders such as impairment of carbohydrate tolerance, diabetes mellitus, hypertension, arrhythmias, myocardial dysfunctions, changes in the locomotor system. Such morbidities result in increased mortality among patients with acromegaly [1–6]. The goal of treatment is normalization of GH secretion which restores a normal life expectancy, decreases incidence of complications, compensates metabolic disturbances and improves patient's quality of life. A radical method of treatment for acromegaly is a selective transsphenoidal resection of the tumor, if possible with pituitary hormonal function preserved [7–10]. Efficacy of a neurosurgical procedure depends on the tumor size and its location, as well as on baseline GH levels. The efficacy of treatment in case of microadenomas reaches 61–91% whereas for macroadenomas the value is 23–53% [11–14]. Taking into account that 70% of subjects with acromegaly have macroadenomas, neurosurgical treatment is not effective in the majority of patients.

Depot somatostatin analogs play a significant role in treatment of acromegaly before surgical procedures, in case a surgical procedure failed or when surgical procedure is not an option (contraindications, no patient's consent for the surgery). The treatment with somatostatin analog in acromegaly results in normalization of GH secretion in 50–60%, IGF-1 secretion in 60–70%, decrease in tumor size in 20–80% of treated subjects, decrease in the intensification of metabolic disorders and a reduction in death risk [15–21]. A decrease in tumor size is difficult to predict and is not always accompanied by decreased levels of GH and IGF-1 [22]. IGF-1 level after administration of somatostatin analog is the best index to evaluate predicted tumor shrinkage [23]. During the treatment with somatostatin analog an increase in tumor size can be observed in less than 5% of cases [23, 24]. Moreover, it should be pointed out that surgical tumor size reduction (incomplete resection) improves the efficacy of the subsequent treatment with somatostatin analog [25].

There is some controversy whether presurgical treatment with somatostatin analog in acromegaly is appropriate [22–31]. Arguments in favor of such a regimen are the following: decreased secretion of GH and IGF-1 resulting in reduced escalation of metabolic disorders the presence of which increases the incidence of complications and surgical risk; tumor size reduction and liquidation of its structure what facilitates neurosurgical procedures; decrease in soft tissue oedema and decreased predisposition to sleep apnoea what is significant for intubation in patients and for perioperative care [30–36]. For the above reasons, pre-surgical treatment with somatostatin analog is important in patients with congestive heart failure, cardiomyopathy, severe apnoea, intubation or respiratory problems [26, 36].

It is suggested to administer depot somatostatin analog at the dose 20 or 30 mg (Octreotide LAR, or equivalent doses of Lanreotide Autogel – 90/120 mg) which normalizes (or maximally reduces) GH and IGF-1 levels, every 4 weeks prior to a surgical procedure.

The period of treatment in case of microadenomas would be at least 3 months (targets: biochemical improvement, reduced risk of developing complications, perioperative risk reduction, inhibition of tumor growth).

The period of treatment in case of macroadenomas would be at least 6 months until maximal possible GH and IGF-1 levels reduction (targets: tumor shrinkage, biochemical improvement, reduced risk of developing complications, perioperative risk reduction).

Using an uniform approach in a group, as large as possible, of treated patients would allow objective evaluation of long-term efficacy of the treatment.

ANNEX: DIAGNOSTIC-THERAPEUTIC APPROACH

1. Initial diagnostics

1.1. Necessary tests

- Medical examination
- GH, glucose estimated by an oral glucose tolerance test (OGTT)
- IGF-1
- PRL
- Pituitary-thyroid, -adrenal, and -gonadal axes assessment
- Urine general analysis (specific gravity)
- Pituitary MR imaging (with contrast enhancement)
- Visual field examination
- Abdominal ultrasound
- ECG

1.2. Additional tests

- Echocardiography
- Colonoscopy
- Test with short-acting somatostatin analog
- Thyroid ultrasound
- Pelvis ultrasound

2. Presurgical treatment with depot somatostatin analogs

2.1. Microadenoma:
Octreotide LAR 20–30 mg (or Lanreotide Autogel 90–120 mg) every 4 weeks for 3–6 months
- Targets: biochemical improvement, reduction of the risk of developing complications, perioperative risk reduction, inhibition of tumor growth.

2.2. Macroadenoma:
Octreotide LAR 20 and then 30 mg (or Lanreotide Autogel 90–120 mg) every 4 weeks for 6–12 months
- Targets: tumor shrinkage, biochemical improvement, reduction of thr risk of developing complications, perioperative risk reduction.

2.3. Evaluation of efficacy of the analog in order to adjust (increase to maximum) the dose (every 3 months)
- GH
- IGF-1

3. Diagnostic tests directly prior to a surgical procedure

3.1. Necessary tests
- Medical examination
- GH estimated by OGTT
- IGF-1
- TSH
- Pituitary MR imaging (with contrast enhancement)
- Visual field examination

3.2. Additional tests
- PRL
- fT4
- Pituitary-thyroid, -adrenal, and -gonadal axes assessment
- Urine general analysis (specific gravity)
- Echocardiography
- ECG
- Abdominal ultrasound

4. Diagnostic tests directly following a surgical procedure

4.1. Necessary tests
- Medical examination
- GH
- Pituitary-thyroid, -adrenal, and -gonadal axes assessment
- Urine general analysis (specific gravity)
- Visual field examination

5. Diagnostic tests 3 months following a surgical procedure

5.1. Necessary tests
- Medical examination
- GH
- IGF-1
- PRL
- Pituitary-thyroid, -adrenal, and -gonadal axes assessment

5.2. Additional tests
- Visual field examination
- Urine general analysis (specific gravity)
- Pituitary MR imaging (with contrast enhancement)

6. Diagnostic tests every 12 months following a surgical procedure

6.1. Necessary tests
- Medical examination
- GH
- IGF-1
- PRL
- Pituitary-thyroid, -adrenal, and -gonadal axes assessment
- Pituitary MR imaging (with contrast enhancement)

6.2. Additional tests
- Urine general analysis (specific gravity)
- Visual field examination
- Echocardiography
- ECG
- Colonoscopy

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