

**EFFICACY OF OCTREOTIDE ACETATE ON ACROMEGALIC PATIENTS**

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**ABSTRACT**

Sandostatin® (octreotide acetate) exerts pharmacologic actions similar to the natural hormone, somatostatin. It is an even more potent inhibitor of growth hormone, glucagon, and insulin than somatostatin. This study was directed to monitor the impact of long acting Octreotide (Sandostatin LAR) after multiple injections on growth hormone levels of acromegalic patients. Ten acromegalic patients aged (30-35) years, (8 males, 2 females) admitted to clinic of endocrinology in Al yarmook hospital were enrolled in this study. IM Sandostatin LAR monthly for 3 months intervals were used. measurement of growth hormone level were performed at the baseline(before treatment), after the initiation and at the end of the study. The results of this study showed that Growth hormone level was dropped from 20.5 µg/L (±8.2) before treatment to 15.4 µg/L (±7.3) after 24 hours treatment and to 5.6 µg/L (±3.2) after 3 months treatment with Sandostatin LAR injection. On conclusion, measuring of growth hormone level after multiple injections of Sandostatin LAR is a useful method for prediction of patients response to the drug.

**KEYWORDS:** Sandostatin LAR, Growth hormone, acromegaly.**1. INTRODUCTION**

Octreotide (brand name Sandostatin, Novartis Pharmaceuticals) is an octapeptide that mimics natural somatostatin pharmacologically, though it is a more potent inhibitor of growth hormone(GH), glucagon and insulin than the natural hormone.<sup>[7,11]</sup>

Octreotide acetate is a synthetic, octapeptide analogue of the natural hormone, somatostatin. Octreotide is absorbed quickly and completely after subcutaneous application. Maximal plasma concentration is reached after 30 minutes. The elimination half-life is 100 minutes (1.7 hours) on average when applied subcutaneously; after intravenous injection, the substance is eliminated in two phases with half-lives of 10 and 90 minutes, respectively.<sup>[1]</sup>

The Food and Drug Administration (FDA) has approved the usage of a salt form of this peptide, octreotide acetate, as an injectable depot formulation for the treatment of acromegaly, gigantism, thyrotropinoma, flushing episodes associated with carcinoid syndrome and diarrhea in patients with vasoactive intestinal peptide-secreting tumors.<sup>[2,12]</sup>

**1.1 PATIENTS AND METHODS**

Ten acromegalic patients aged (30-35) years, (8 males, 2 females) were recruited from clinic of endocrinology in Al yarmook hospital. The diagnosis of acromegaly was made upon the finding of absence of growth hormone suppression to less than 2 µg/L following the intake of 75

mg glucose and the higher level of Insulin like growth factor -1 (IGF1) than normal. The dose of Sandostatin LAR was 20 mg monthly throughout the treatment period lasting 3 months. The study protocol was approved by the institutional ethics committee and all patients were informed about the study protocol and their consent was obtained.

Measurement of growth hormone level was done with radio immunoassay (RIA) method at the baseline (before treatment), after the initiation and at the end of the study intervals. Results are shown as mean ± SD with 95% confidence interval (CI) and *P* values of 0<0.05 were regarded to be statistical significant. All statistical analyses were performed using series SPSS version 18.

**1.1.1 RESULT**

As shown in table -1 and figure -1, a significant suppression in growth hormone level was noted after 24 hour treatment with Sandostatin LAR compared to prior treatment (15.4±7.3 vs. 20.5±8.2), whereas a high significant suppression in growth hormone level was clarified after 3 months treatment with Sandostatin LAR in relation to prior treatment (5.6±3.2 vs. 20.5± 8.2).

Additionally, the percentage of suppression of growth hormone level after one day was (-24.88%) and after 3 months was (-72.68%) regarding to basal value as illustrated in figure-2.

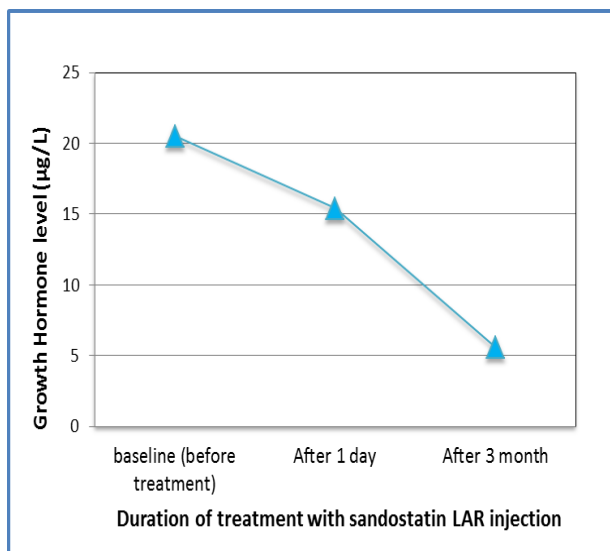
Power analysis for the minimum detectable effect of Sandostatin LAR injection on growth hormone levels

after one day and after three months treatments are illustrated in figure -3.

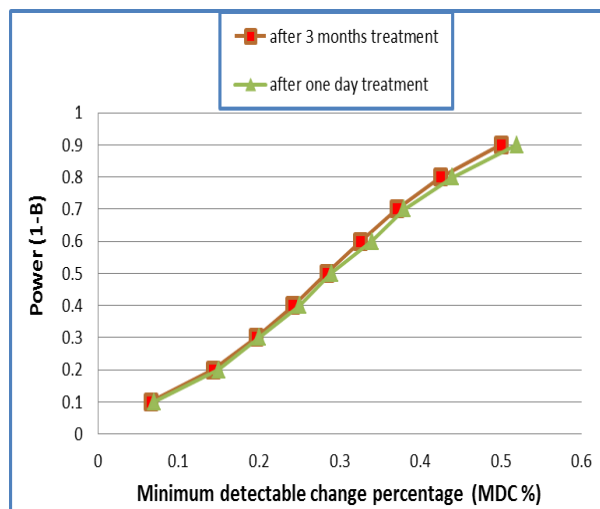
**Table 1- Alteration of growth hormone levels before the initiation and after treatment with Sandostatin LAR injection in acromegalic patients.**

	Baseline (before treatment)	After 1 day treatment	After 3 months treatment
-Growth hormone level (µg/L)	20.5 ±8.2	15.4 ±7.3 *	5.6 ±3.2 **
- Percentage of growth hormone suppression	----	-24.88 %	-72.68%

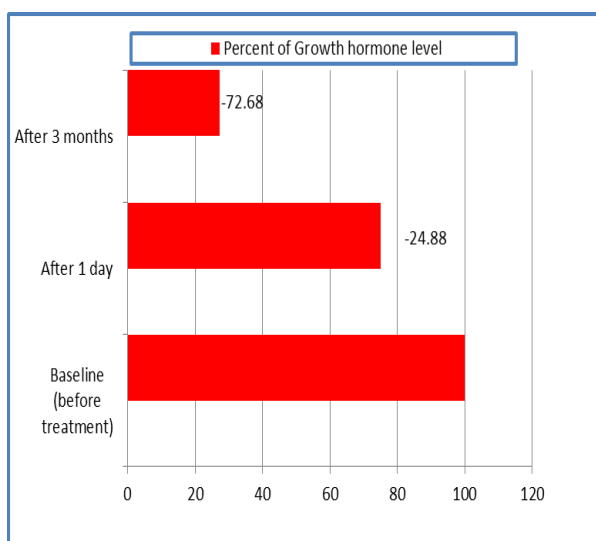
(\*)= Significant differences ( $P < 0.05$ );(\*\*)= High significant differences ( $P < 0.001$ ).



**Figure-1: Line chart demonstrates the effects of treatment with Sandostatin LAR injection on the mean levels of growth hormone (µg/L) over three months intervals in patients with acromegaly.**



**Figure -3: Power analysis for the minimum detectable effect of Sandostatin LAR injection on growth hormone levels after one day and after three months treatments**



**Figure-2: Prominent percentage of suppression of growth hormone level over three months treatment with Sandostatin LAR injection as compared with baseline (before treatment) in patients with acromegaly.**

**1.1.2 DISCUSSION**

In the current study there were 24.88% reduction in the growth hormone level occur after 24 hours treatment and 72.68% reduction achieved after 3 months treatment with Sandostatin LAR injection in acromegalic patients.

It was reported that octreotide usage lead to growth hormone reduction in 90% of patients and in 40-50% lead to reduction of growth hormone to less than 10 µg/L.<sup>[14]</sup> Other study denoted that therapeutic effect of Sandostatin LAR injection was equal in 4 weeks and 6 weeks intervals.<sup>[15]</sup>

Like somatostatin, Octreotide exerts inhibitory effects on the release of pituitary and gastroenteropancreatic hormones (i.e. GH, TSH, insulin, glucagon, CCK, VIP and gastrin) inhibits gastric acid, pancreatic enzyme secretion and bile flow; prolongs intestinal transit time and decreases gallbladder contractility.<sup>[9,13]</sup>

Growth hormone and insulin growth factor -1 (IGF1) normalization after sandostatin LAR leads to a decrease in joint thickness because IGF1 suppression decreases tissue hypertrophy in acromegaly patients joints.<sup>[8]</sup>

Compared to native somatostatin, Octreotide is 45 times more potent in inhibition of growth hormone secretion, 11 times more potent in inhibition of glucagon, but only 1.3 times as active in inhibition of insulin secretion.<sup>[6]</sup>

A reduction in daily insulin dose was found in many Octreotide-treated insulin-dependent diabetics<sup>[3,4]</sup> which may be attributed to its inhibitory action on growth hormone and glucagons.<sup>[10]</sup> Therefore, hypoglycemic episodes may occur 10-14 days after the initial Sandostatin LAR injection if insulin dose is not reduced especially in patients with desirable glycemia.<sup>[5]</sup>

### 1.1.3 CONCLUSION

Monitoring of growth hormone level after multiple dose of Sandostatin LAR is important for expectation of patients response and individual duration of the treatment.

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