DEUTSCHES AKROMEGALIE REGISTER

Primary Medical Therapy of Acromegaly with Dopamine Agonists: Analysis of the German Acromegaly Register

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for the Participants of the German Acromegaly Register

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Introduction:

Dopamine agonists (DA) represent an orally effective and comparably cheap therapy for acromegaly. To evaluate this treatment option, we screened the newly established German Acromegaly Register for patients treated primarily with DA. The German Acromegaly Register is an initiative of the Pituitary Working Group of the German Endocrine Society. The aim of the German Acromegaly Register is to collect data on patients suffering from acromegaly in Germany, both retrospectively and prospectively.

Methods:

The Register uses the UK electronic database to assure comparison between these two countries with different health care systems. All German health care providers are invited to participate. To assure correct and uniform data entry, two trained nurses visit all centers for data acquisition. GH and IGF-1 levels are those reported by case notes. Due to variations in assays and reference ranges, normalization of IGF-1 is assessed using local criteria. Sponsorship is provided by an unrestricted grant from Novartis Oncology, Germany.

Results are expressed as mean±SEM. GraphPad Prism 4.0 (GraphPad Software Inc., San Diego, USA) was used for statistical analyses. The Mann Whitney test and the Kruskal-Wallis test, followed by Dunn's multiple comparison test, were performed where appropriate.

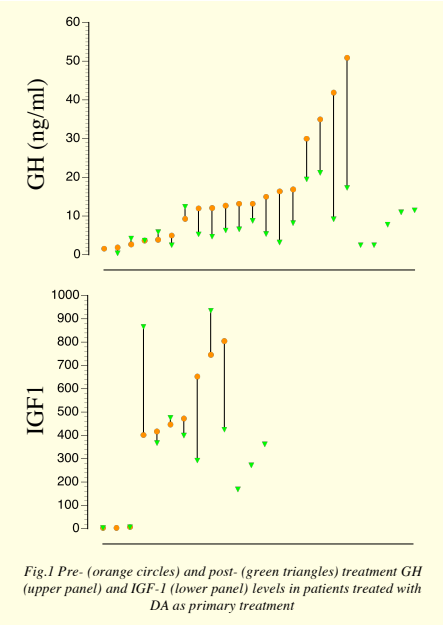

Fig.1 Pre- (orange circles) and post- (green triangles) treatment GH (upper panel) and IGF-1 (lower panel) levels in patients treated with DA as primary treatment

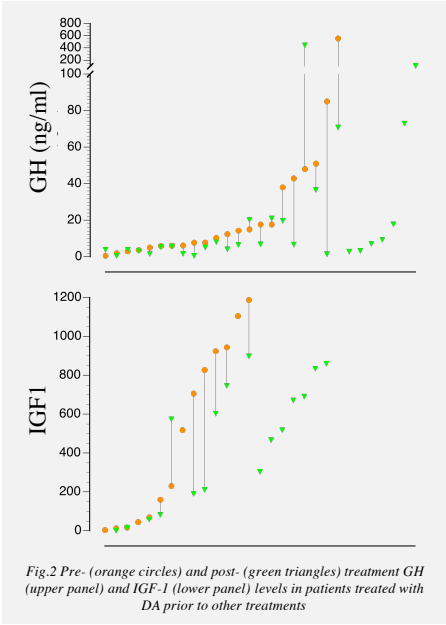

Fig.2 Pre- (orange circles) and post- (green triangles) treatment GH (upper panel) and IGF-1 (lower panel) levels in patients treated with DA prior to other treatments

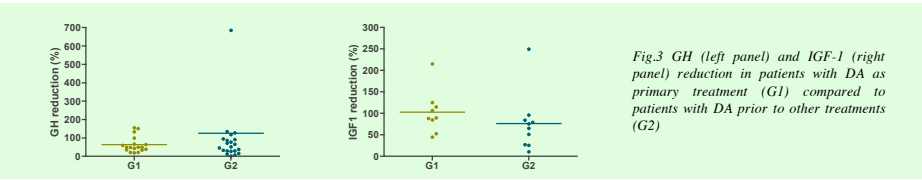

Fig.3 GH (left panel) and IGF-1 (right panel) reduction in patients with DA as primary treatment (G1) compared to patients with DA prior to other treatments (G2)

Results:

At the time of this analysis, retrospective data from 1000 patients had been entered into the database. Initial random GH levels of patients with biochemical data available were 29.7+/-2.1 ng/ml, with 92.3% of GH levels >2.5 ng/ml and 96.1% of IGF-1 levels elevated. Radiological evaluation revealed micro- and macroadenomas in 21.2% and 63.6% of patients, respectively.

Sixty-seven patients received DA with the intention of primary treatment (Group 1). Biochemical data after 6-18 months were considered for re-evaluation, which was available for 24 patients (Bromocriptine 87.5%, Cabergoline 12.5%) (Fig.1). Random GH<2.5 ng/ml were found in 17.4% of patients, and normal IGF-1 in 30.8%. GH and IGF-1 were reduced to 63.7+/-10.1% and 102.5+/-16.6% of initial values, respectively.

Another 36 patients received DA prior to other forms of therapy (Group 2), with biochemical data available for re-evaluation in 29 patients treated for 11.9+/-2.1 months (Bromocriptine 69.0%, Cabergoline 24.1%) (Fig.2). In this subgroup, random GH<2.5 ng/ml was obtained in 17.2% of patients, and normal IGF-1 in 16.7%. GH and IGF-1 were reduced to 126.0+/-48.2% and 76.5+/-21.1% of initial values, respectively.

Discussion:

- In a total of 53 patients available for analysis, random GH<2.5 ng/ml was found in 17.3% of patients treated by DA, and normal IGF-1 in 22.6%.
- Separate analysis depending on the treatment intention did not reveal any significant differences between the two groups investigated. Compared with patients in Group 2, patients in Group 1 had similar response rates regarding GH reduction (Fig.3, p=0.97), IGF-1 reduction (Fig.3, p=0.08), and IGF-1 normalization (p=0.5).
- Due to the retrospective nature, the reasons for patient's assignment to either treatment group are difficult to elucidate. Pre-treatment random GH did not differ significantly between both groups (15.7+/-3.2 ng/ml compared with 43.5+/-24.8 ng/ml, p=0.69).
- The better response rate in Group 1 may be explained by the lower rate of macroadenomas (41.7% compared with 58.6%, p<0.05). However, biochemical response parameters did not differ between micro- and macroadenomas in separate analysis for each group (G1: %GH p=0.42, %IGF-1 p=0.14, G2: %GH p=0.77, %IGF-1 p=0.96).

Summary:

- Primary medical treatment with DA is effective only in a small subgroup of patients with acromegaly. However, a treatment trial may still be cost-effective to identify patients, who specifically benefit from this orally available treatment.
- Prospective studies are necessary to identify criteria for patient selection and to evaluate a larger number of patients treated with second generation DA.

Participants of the German Acromegaly Register:

Biering H, Blossey HC, Blum H, Bogner U, Buchfelder M, Caspar-Bell G, Demtröder F, Diederich S, Droste M, Faust M, Finke R, Gräf KJ, Gerbert B, Grußendorf M, Hampel R, Heckmann C, Hehrmann R, Herrmann BL, Höffken K, Hüfner M, Jacobeit J, Jaursch-Hancke C, Jockenhövel F, Knippert A, Koch C, Kornely E, Krone W, Lehnert H, Levasseur S, Lößner C, Mann K, Meuser J, Meyer A, Minnemann T, Mönig HI, Müller UA, Paschke R, Petersenn S, Pfeiffer A, Plöckinger U, Raue F, Reincke M, Reschke K, Rudorff KH, Rühle H, Schopohl J, Schories M, Schröder H, Schröder HE, Schröder U, Schulte HM, Stamm B, Steinmetz M, Strasburger CJ, Tharandt L, Tuschy U, von Werder K, Weber MM, Würl K