



Research

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Serum Prolactin Levels in Patients with Alopecia Areata

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Abstract

Background: Alopecia areata is a chronic autoimmune disease characterized by sudden hair loss. Prolactin hormone is claimed to involve in pathogenesis of some certain autoimmune diseases. To investigate the role of prolactin in alopecia areata serum prolactin levels of patients with alopecia areata and healthy controls were compared.

Methods: Fifty patients with the diagnosis of alopecia areata and 30 healthy volunteers were compared in terms of serum prolactin levels.

Results: Hyperprolactinemia was observed in six alopecia patients and four healthy controls. There was no statistically significant difference between alopecia areata cases and healthy controls regarding serum prolactin levels.

Conclusion: Data obtained from studies investigating other lymphocyte associated or autoimmune diseases which are claimed to be associated with prolactin points that serum prolactin levels are correlated with disease severity/activity. Patient group of this study is mainly consisted of limited/mild cases as the extensive/severe forms of the disease are less common. Regarding this, a case-control study investigating serum prolactin levels of severe/extensive cases may contribute to clarify the role of prolactin in alopecia areata.

Introduction

Alopecia areata (AA) is a chronic inflammatory disorder characterised by sudden hair loss [1, 2]. As an important cosmetic problem, the disease approximately counts 2 % of first time attendances to dermatology clinics in the United States and United Kingdom [3]. Existing evidences suggest that AA is a T lymphocyte mediated, tissue specific autoimmune disease with a certain genetic background [4].

Prolactin is a polypeptide hormone produced and secreted from lactotrope cells of anterior

hypophysis [5]. Some other tissue and organs also produce prolactin, such as mononuclear blood cells (particularly T lymphocytes) and thymocytes [6, 7]. Lymphocyte originated prolactin (immunoreactive prolactin) is considered to be a cytokine acting in both paracrine and autocrine manners [5, 6, 7, 8]. In addition to its well known mammatropic and lactogenic effects, prolactin hormone plays part in stimulation of the immune system and is claimed to be related with the activities of some autoimmune based diseases such as systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), psoriatic arthritis, and

psoriasis [5]. In literature, there are case-control studies reporting higher serum prolactin levels in patients with autoimmune or lymphocyte associated diseases such as SLE, RA, psoriasis, and multiple myeloma [9, 10, 11, 12, 13].

A literature survey shows that studies assessing the role of prolactin in AA are lacking. Therefore, this study is designed to compare serum prolactin levels of patients with AA and healthy control subjects.

Materials and Methods

Participants

Fifty patients over 18 years of age with the clinical diagnosis of AA (including all clinical variants) who haven't received any medication for the treatment of AA (including topical treatments, intralesional corticosteroid injection, systemic use of corticosteroids, phototherapy, and any other immunosuppressive therapies) within a period of four weeks were included consecutively. Diagnosis of prolactinoma, thyroid disorders, renal and hepatic insufficiency were defined as exclusion criteria. For female participants, existing pregnancy and history of abortion within a period of six months were also surveyed for exclusion. 30 healthy volunteers over 18 years of age were recruited in order to form an age-sex matched control group.

Methods

The study was approved by the institutional ethical committee. Written informed consent was obtained from all subjects. Demographic data, medical history and physical examination findings of the participants were recorded. Disease severity was recorded as severity of alopecia tool (SALT) score defined by Olsen et al. [14]. Pattern and extent of alopecia was also recorded.

Participants were invited between 08:00 a.m. and 09:00 a.m. in regard to the circadian variation of prolactin secretion. Participants had rested for 30 minutes after a cannula was introduced into the antecubital vein. After the rest, venous blood samples were drawn; serum levels of prolactin, TSH, fT3, fT4, AST, ALT, urea, creatinine, and (for female participants) β -hCG were measured. The

electrochemiluminescence immunoassay "ECLIA" is used on Modular Analytics E170 (Roche, USA) for measuring serum levels of prolactin; reference range for prolactin was 86-324 mIU/L for males and 102-496 mIU/L for females.

Statistical Analysis

SPSS 16.0 programme was used for statistical analyses. The statistical significances of the results were carried out by Chi-square test and independent samples t-test. P values <0.05 were regarded as statistically significant.

Results

Alopecia patients and healthy volunteers didn't statistically differ in terms of gender and age. **Table 1** shows the demographic profiles of patient and healthy control groups.

Fourty nine patients (98 %) presented as patchy alopecia areata and one presented as ophiasic pattern alopecia areata; there were no alopecia totalis or alopecia universalis cases in the patient group. Mean SALT score of the alopecia group was $6,64 \pm 12,83$.

Hyperprolactinemia was present in six alopecia patients (four males, two females) and four control subjects (one male, three females). Serum prolactin levels of the groups didn't show statistically significant difference (**Table 2**). In regard to higher physiologic serum levels of prolactin in females, a gender based subgroup analyse was carried out and no statistically significant differences were observed between subgroups (**Table 3**).

Discussion

SLE has the most powerful evidences which point a possible relationship between autoimmune diseases and prolactin.

The prevalence of hyperprolactinemia in patients with SLE ranges from 12-35 %. Kaercher Kramer et al. reported higher serum

Table 1. Demographic Characteristics of Alopecia Areata Group and Control Subjects

	Alopecia Group		Control Group		p
	n	%	n	%	
Female	33	66	17	56,7	
Male	17	34	13	43,3	0,477
	Mean	sd	Mean	sd	
Age (years)	33,1	12,78	31,2	7,44	0,403

Table 2. Serum Prolactin Levels of Alopecia Areata Group and Control Subjects

	Alopecia group	Control group	P
Prolactin, mIU/L (mean±sd)	276,35± 196,65	248,42± 116,23	0,909

Table 3. Serum Prolactin Levels of Gender Based Subgroups of Subjects

	Alopecia group	Control group	P
Prolactin, mIU/L (mean±sd)	Male	234,62± 158,77	198,81± 73,96
	Female	357,34± 239,69	313,29± 131,56

prolactin levels of 26 patients with SLE in comparison to 28 healthy controls and 48 patients with other certain autoimmune diseases ($p=0,006$) [9]. Higher prolactin levels in SLE correlates with clinical disease activity and auto antibody titers. Conventional immunosuppressive therapy both reduces prolactin levels and suppresses disease activity [5]. Peripheral blood mononuclear cells, mainly B lymphocytes, from patients with active SLE have increased production rates of a prolactin isoform which has a different molecular weight. These data suggest that active SLE lymphocytes may be the source of hyperprolactinemia observed in patients with SLE and lymphocytes may alter serum prolactin levels by producing immunoreactive prolactin [8, 15].

Bromocriptine is an ergot alkaloid that inhibits pituitary prolactin synthesis and release. It also suppresses immune responses mediated by T and B lymphocytes directly through dopamine receptors but the immunosuppressive activity of bromocriptine is claimed to be mainly associated with suppression of serum prolactin levels. Although its effect on immunoreactive prolactin synthesis and release remains to be elucidated, bromocriptine is considered to be a candidate for the treatment of SLE and some other autoimmune diseases [16, 17].

Multiple myeloma is a monoclonal malignancy of B lymphocytes. Gadó et al. reported higher serum prolactin levels in both male and female patients with advanced multiple myeloma compared with healthy controls

($p<0,001$ and $p<0,01$ respectively). Elevated prolactin levels are shown to be associated with disease progression and partial remission achieved by chemotherapy led to a decrease in serum prolactin levels [11].

T lymphocytes infiltrating the synovium of patients with RA has shown to produce prolactin and elevated prolactin levels are found to be correlated with disease activity [5]. Seriolo et al. reported higher serum prolactin levels of 29 male patients with RA compared with 30 male patients with mild osteoarthritis ($p=0,001$). There was no association between serum prolactin levels of patients with RA and clinical disease activity, but a positive correlation with erythrocyte sedimentation rate, CRP, and rheumatoid factor was reported [12]. Similarly, Ram et al. reported higher serum prolactin levels of 60 female patients with RA compared with 31 female patients with osteoarthritis ($p<0,05$) [13].

Khandpur and Reddy reported a female patient with pemphigus vulgaris and idiopathic hyperprolactinemia. Re-epithelialization of pre-existing skin lesions and dramatic regression of new blister formation was achieved with bromocriptine monotherapy. Although no statistical comparison was reported, circulating auto-antibody levels were stated as in correlation with serum prolactin levels. The clinical signs were exacerbated and serum prolactin and auto-antibody levels were elevated after bromocriptine therapy was stopped. These data supports a causal relationship between pemphigus vulgaris and hyperprolactinemia [18].

Sánchez Regaña and Umbert Millet reported three female patients with psoriasis vulgaris and prolactinoma. Psoriasis severity was found to be related with elevated serum prolactin levels and treatment with bromocriptine led to improvement in psoriasis area and severity index [19]. Giasuddin et al. reported higher serum prolactin levels of 12 patients with psoriasis vulgaris compared to nine patients with atopic dermatitis and 20 healthy control subjects ($p=0,0008$). Prolactin has both direct effect on keratinocyte proliferation and modulates T lymphocyte functions, thus may have a role in the pathogenesis of psoriasis [10].

All these data supporting a possible relation between prolactin and certain autoimmune or

lymphocyte associated diseases suggest that prolactin may also play part in progression of the autoimmune process which causes follicular damage in alopecia areata. As mentioned above, it is claimed that lymphocytes may produce sufficient amounts of immunoreactive prolactin to alter serum prolactin levels and prolactin levels are closely related with disease severity.

Although we did not define any limitation for disease severity as an inclusion criteria, patient group of this study is mainly consisted of mild cases as the extensive/severe cases are less common. Extent of hair loss is reported to be more than 40 % in only 11 % of alopecia areata cases [20]. With this limitation to be kept in mind, investigating serum prolactin levels of severe/extensive cases may help to elucidate the role of prolactin in alopecia areata.

References

- Gilhar A, Kalish RS. Alopecia areata: A tissue specific autoimmune disease of the hair follicle. *Autoimmun Rev* 2006; 5: 64-69. PMID: 16338213
- McDonagh AJG, Messenger AG. Alopecia areata. *Clin Dermatol* 2001; 19: 141-147. PMID: 11397592
- Wasserman D, Guzman-Sanchez DA, Scott K, McMichael A. Alopecia areata. *Int J Dermatol* 2007; 46: 121-131. PMID: 17269961
- Blaumeiser B, van der Goot I, Fimmers R, Hanneken S, Ritzmann S, Seymons K, Betz RC, Ruzicka T, Wienerker TF, Weert JD, Lambert J, Kruse R, Nöthen MM. Familial aggregation of alopecia areata. *J Am Acad Dermatol* 2006; 54: 627-632. PMID: 16546583
- Chuang E, Molitch ME. Prolactin and autoimmune diseases in humans. *Acta Biomed* 2007; 78: 255-261. PMID: 17465339
- Drača S. Prolactin as an immunoreactive agent. *Immunol Cell Biol* 1995; 73: 481-483. PMID: 8713468
- Orbach H, Shoenfeld Y. Hyperprolactinemia and autoimmune diseases. *Autoimmun Rev* 2007; 6: 537-542. PMID: 17854745
- Jara LJ, Navarro C, Medina G, Vera-Lastra O, Blanco F. Immune-neuroendocrine interactions and autoimmune diseases. *Clin Dev Immunol* 2006; 13: 109-123. PMID: 17162354
- Kaercher Kramer C, Tourinho TF, Pedro de Castro W, Oliveira M da C. Association between systemic lupus erythematosus, rheumatoid arthritis, hyperprolactinemia and thyroid autoantibodies. *Arch Med Res* 2005; 36: 54-58. PMID: 15777996
- Giasuddin ASM, El-Sherif AI, El-Ojali SI. Prolactin: Does it have a role in the pathogenesis of psoriasis? *Dermatology* 1998; 197: 119-122. PMID: 9732158
- Gadó K, Rimanóczki É, Hasitz Á, Gigler G, Tóth BE, Nagy GM, Pálóczi K, Domján G. Elevated levels of serum prolactin in patients with advanced multiple myeloma. *Neuroimmunomodulation* 2001; 9: 231-236. PMID: 11847486
- Seriolo B, Ferretti V, Sulli A, Fasciolo D, Cutolo M. Serum prolactin concentrations in male patients with rheumatoid arthritis. *Ann NY Acad Sci* 2002; 966: 258-262. PMID: 12114281
- Ram S, Blumberg D, Newton P, Anderson NR, Gama R. Raised serum prolactin in rheumatoid arthritis: Genuine or laboratory artefact? *Rheumatology* 2004; 43: 1272-1274. PMID: 15266060
- Olsen EA, Hordinsky MK, Price VH, Roberts JL, Shapiro J, Canfield D, Duvic M, King Jr LE, McMichael AJ, Randall VA, Turner ML, Sperling L, Whiting DA, Norris D. Alopecia areata investigational assessment guidelines-part II. *J Am Acad Dermatol* 2004; 51: 440-447. PMID: 15337988
- Chikanza IC. Prolactin and neuroimmunomodulation: In vitro and in vivo observations. *Ann NY Acad Sci* 1999; 876: 119-130. PMID: 10415600
- McMurray RW. Bromocriptine in rheumatic and autoimmune diseases. *Semin Arthritis Rheum* 2001; 31: 21-32. PMID: 11503136
- Neidhart M. Bromocriptine has little direct effect on murine lymphocytes, the immunomodulatory effect being mediated by the suppression of prolactin secretion. *Biomed Pharmacother* 1997; 51: 118-125. PMID: 9181047
- Khandpur S, Reddy BS. An unusual association of pemphigus vulgaris with hyperprolactinemia. *Int J Dermatol* 2002; 41: 696-699. PMID: 12390198
- Sánchez Regaña M, Umbert Millet P. Psoriasis in association with prolactinoma: Three cases. *Br J Dermatol* 2000; 143: 864-867. PMID: 11069474
- Bolduc C, Lui H, Shapiro J. Alopecia areata (overview). 2010. Available at: <http://emedicine.medscape.com/article/1069931-overview>