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ORIGINAL ARTICLE

Adipocyte accumulation in corpus cavernosum: First clinical evidence and pathophysiological implications in erectile dysfunction☆

J. Vinay[a,*], J. Sarquella[a], J. Sanchez[a], F. Algaba[b], I. Gallegos[c], E. Ruiz-Castañe[a], C. Palma[d,e]

[a] *Departamento de Andrología, Fundación Puigvert/Universidad Autónoma de Barcelona, Barcelona, Spain*
[b] *Sección de Patología, Fundación Puigvert/Universidad Autónoma de Barcelona, Barcelona, Spain*
[c] *Departamento de Patología, Hospital Clínico, Universidad de Chile, Santiago, Chile*
[d] *Departamento de Urología, Hospital Clínico, Universidad de Chile, Santiago, Chile*
[e] *Departamento de Urología, Clínica Las Condes, Santiago, Chile*

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KEYWORDS
Erectile dysfunction;
Androgen disruption;
Adipocyte accumulation

Abstract
Objectives: Animal models have shown that erectile dysfunction is associated with adipocyte accumulation under tunica albugínea, which could be involved in venous leakage and loss of penile rigidity. In the current study, we compared the histology of the penile sub-albuginean region of drug-refractory erectile dysfunction patients undergoing penile prosthesis implantation with potent patients with Peyronie's disease undergoing curvature correction procedures.
Materials and methods: Seventeen refractory erectile dysfunction patients and fourteen potent patients with Peyronie's disease were recruited. Sub-albuginean tissue samples were taken in each surgery. An expert uropathologist analyzed each section. A bivariate analysis was performed. Multivariate logistic regression was used to calculate adjusted odds ratios; p value <0.05 was considered significant.
Results: Eleven patients (11/17) in the case group presented cavernous fat cell accumulation, while only one patient (1/14) in the control group presented this finding ($p < 0.05$). Adjusted odds ratio for erectile dysfunction was 40.72; 95% CI 2.28–727.29 ($p = 0.012$).

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* Corresponding author.
E-mail address: jose.vinay@gmail.com (J. Vinay).

Conclusions: Different studies have shown that androgen disruption could be involved in penile structural changes, leading to trabecular smooth muscle apoptosis and trans or de-differentiation into adipocytes. This is the first prospective study in humans to report an association between erectile dysfunction and sub-albuginean adipocyte accumulation. Venous leakage secondary to this phenomenon could be a factor in the pathophysiology of erectile dysfunction, especially in patients that do not respond to medical therapy.

PALABRAS CLAVE
Disfunción eréctil;
Alteración en andrógenos;
Acumulación de adipocitos

Acumulación de adipocitos en el cuerpo cavernoso: primera evidencia clínica e implicaciones fisiopatológicas en la disfunción eréctil

Resumen

Objetivo: Modelos animales han demostrado que existe una asociación entre disfunción eréctil y acumulación de grasa bajo la albugínea del pene, pudiendo provocar fuga venosa y pérdida de rigidez del pene. En este estudio se llevó a cabo una comparación de la histología de los cuerpos cavernosos bajo la albugínea de pacientes con disfunción eréctil refractarios a tratamiento médico sometidos a implante de prótesis de pene, y pacientes con enfermedad de Peyronie, sin disfunción eréctil, sometidos a corporoplastia.
Materiales y métodos: Se incluyeron 17 pacientes con disfunción eréctil y 14 pacientes potentes con enfermedad de Peyronie. Se recolectaron muestras de tejido cavernoso bajo la túnica albugínea en cada cirugía, las cuales fueron analizadas por un uropatólogo en búsqueda de adipocitos subalbugíneos. Se llevó a cabo un análisis bivariado para comparar características de ambos grupos. Se calcularon las *odds ratio* con un modelo multivariado de regresión logística. Un valor de $p < 0,05$ fue considerado significativo.
Resultados: Once pacientes (11/17) en el grupo de disfunción eréctil presentaron adipocitos en la histología, mientras solo un paciente (1/14) lo presentó en el grupo control ($p < 0,05$). El análisis multivariado mostró una *odds ratio* de 40,72; IC 95%: 2,28-727,29 ($p = 0,012$).
Conclusiones: Alteraciones en los andrógenos provocan cambios estructurales en el pene, llevando a apoptosis y desdiferenciación de músculo trabecular hacia adipocitos. Este es el primer estudio prospectivo en humanos que muestra una asociación entre grasa subalbugínea y disfunción eréctil. La fuga venosa secundaria a este fenómeno podría influir en la disfunción eréctil, especialmente en pacientes que no responden a tratamiento médico.

Background

Erectile function depends on the interaction of psychological factors and an appropriate balance between the endocrine and nervous systems, together with an adequate vascular bed.[1] Disruption of any of these elements could impair normal erections.

Several studies have been published about the role of androgens as cornerstones of this complex neurophysiological process.[2–5] Testosterone may play a pivotal role in maintaining penile nerve, smooth muscle and endothelium structure and function; maintaining tunica albuginea structural integrity and connective tissue matrix fibroelastic properties; and regulating differentiation of cavernous pluripotent cells into trabecular smooth muscle.[1]

Multiple studies have shown that patients not responding to oral phosphodiesterase 5 inhibitors (PDI5), especially those affected by metabolic syndrome, may have a quantitative or qualitative alteration in androgen metabolism.[3–6] Currently, obesity and metabolic syndrome related androgen alterations are thought to play a pivotal role in the pathophysiology of erectile dysfunction (ED).[5–7]

The role of androgens in the differentiation of pluripotent sub-albulginean cells into trabecular smooth muscle has been poorly studied. Traish et al., in an animal model, have shown that hypogonadism secondary to surgical castration produces severe ED associated with replacement of normal smooth muscle by adipocytes, in the penile sub-albuginean region.[8] Adipocyte accumulation is thought to impair penile vascular bed performance, leading to venous leakage and lack of normal tumescence.[1,6,8]

We hypothesized that penile sub-albuginean fat accumulation is associated to drug refractory ED. Venous leakage secondary to fat cell accumulation under tunica albuginea may play a pivotal role in the pathophysiology of this disorder. In the present study, we compared the histology of the penile sub-albuginean region of refractory ED patients undergoing penile implant surgery and potent patients with Peyronie's disease (PD) undergoing curvature correction procedures.

Material and methods

Subjects

This is a non-randomized, prospective trial that has been performed according to the Declaration of Helsinki and