Reproductive dysfunction as a result of physical training: “exercise-hypogonadal male condition”

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Summary

The objective of this short review is to discuss how exercise training in men can result in changes in the reproductive system similar to those observed in women who develop athletic amenorrhea or suffer the Female Athlete Triad. Men chronically exposed to training for endurance sports exhibit persistently reduced basal free and total testosterone concentrations without concurrent luteinizing hormone elevations. These men are deemed to have the “Exercise-Hypogonadal Male Condition” (EHMC). Broadly, dysfunction in the hypothalamic-pituitary-gonadal regulatory axis is associated with either of these states. In women this effect on the axis is linked to the existence of a low energy availability (LEA) state, research in men relative to LEA is ongoing. The exact physiological mechanism inducing the reduction of testosterone in these men is currently unclear but is postulated to be a dysfunction within the hypothalamic-pituitary-gonadal regulatory axis. The potential exists for the reduced testosterone concentrations within EHMC men to be disruptive and detrimental to some anabolic-androgenic testosterone-dependent physiological processes. Findings, while limited, suggest spermatogenesis problems may exist in some cases; thus, infertility risk in such men is a critical concern. Present evidence suggests the EHMC condition is limited to men who have been persistently involved in chronic endurance exercise training for an extended period of time, and thus is not a highly prevalent occurrence. Nevertheless, it is critical that endocrinologist and fertility clinicians become more aware of the existence of EHMC as a potential problem-diagnosis in their male patients who exercise.

Key words: Exercise-Hypogonadal male condition. Reproductive system dysfunction. Endurance training. Fertility. Bone Health.

Disfunción reproductiva por entrenamiento físico: el “hipogonadismo masculino producto del ejercicio”

Resumen

El objetivo de esta breve revisión es describir cómo el entrenamiento físico en hombres puede provocar cambios en el sistema reproductivo similares a los observados en mujeres que desarrollan amenorrea atlética o sufren la tríada de la mujer atleta. Hombres expuestos sistemáticamente a entrenamientos para deportes de resistencia exhiben concentraciones reducidas de testosterona libre y basal sin manifestar un aumento simultáneo de la hormona luteinizante. Estos hombres son considerados como portadores del “hipogonadismo masculino producto del ejercicio” (EHMC). En general, la disfunción en el eje hipotalámico-hipofisario-gonadal es asociada a uno de estos estados. En las mujeres, la alteración del eje se vincula a la existencia de un bajo estado de energía (LEA) en estado de baja disponibilidad energética (BDE); en los hombres, la investigación relacionada con la BDE está en curso. El mecanismo fisiológico exacto que induce la disminución de testosterona en estos hombres aún no está claro, pero se postula que es una disfunción dentro del eje regulador hipotalámico-hipofisario-gonadal. Existe la posibilidad de que las bajas concentraciones de testosterona en los hombres con EHMC sean disruptivas y perjudiciales para algunos procesos fisiológicos anabólico-androgénicos dependientes de testosterona. Los hallazgos, aunque limitados, sugieren que en algunos casos pueden existir problemas de espermatogénesis; por lo tanto, el riesgo de infertilidad en tales hombres es una preocupación crucial. La evidencia actual sugiere que el EHMC se limita a hombres que han estado involucrados en entrenamiento de resistencia de manera persistente y durante tiempo prolongado, por lo que el EHMC no es una condición prevalente. De todos modos, es fundamental que médicos endocrinólogos y especialistas en fertilidad estén atentos a la existencia del EHMC como potencial problema – y diagnóstico – que pueden padecer sus pacientes deportistas varones.


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Introduction

For almost 40 years it has been known that women who do a lot of physical training, particularly when insufficiently nourished, are at greater risk of developing reproductive dysfunction\textsuperscript{1-4}; specifically, oligomenorrhea or secondary amenorrhea (athletic amenorrhea)\textsuperscript{1-3}. These conditions are associated with varying degrees of reproductive hormone abnormalities (hypoestrogenism), the risk of infertility, decreased bone mineral density and eating disorders, typically known as the female athlete triad (FAT)\textsuperscript{1-3}. Until recently it was thought that such reproductive disorders related to exercise were specific to females. In the last two decades, however, evidence has built up to suggest that men can also suffer from similar reproductive disorders; that is, they are likely to develop what is called exercise-hypogonadal male condition (EHMC)\textsuperscript{1,6-10}. The purpose of this brief review is to provide an overview of EHMC and the physiopathogenic mechanisms which are probably involved, drawing parallels with what is already known about FAT.

Foregoing research

Retrospective and cross-sectional studies show that baseline testosterone levels are lower in male athletes who train systematically, specifically on those who do long-term endurance sports such as the marathon, long-distance triathlon and Olympic-style race walking\textsuperscript{1,9}. The subjects of these studies are typically athletes who have trained consistently for several years (≥5-15)\textsuperscript{10-15}. They report that the levels of testosterone (free and total concentration) in these athletes barely reach 50-85% of the levels found in male controls of the same age who do not do exercise\textsuperscript{10-17}. Prospective studies in which blood samples have been collected at rest over periods of days, weeks and months while participants follow strenuous endurance training regimes have also found their testosterone levels are reduced. However, the findings of these prospective studies are less convincing than those reported by the retrospective studies\textsuperscript{1,13,14}. The differences in the state of initial training of the participants or the specifics of the training programmes used in the different prospective studies could be behind these discrepancies\textsuperscript{1,15}. For a definitive explanation of the origin of such inconsistencies, more comprehensive and longer-lasting prospective studies would be needed; such studies, however, are often difficult to implement.

Male endurance athletes with low testosterone levels usually present other reproductive hormone abnormalities. The most common are abnormalities in basal prolactin levels and baseline concentrations of luteinizing hormone (LH) and/or its pulsatile characteristics\textsuperscript{6,12,23}. These alterations in LH suggest the existence of a disruption in the hypothalamic secretion of gonadotropin-releasing hormone (GnRH)\textsuperscript{13}, as is the case with many women with reproductive dysfunction related to exercise\textsuperscript{1,2}. These alterations in LH and GnRH are indicative of a dysfunction in the hypothalamic–pituitary–gonadal axis (HPG; testicular in man, ovarian in women), which controls the reproductive system\textsuperscript{6,14}.

Taking into consideration the specifics of the reproductive endocrine system according to sex, decreased testosterone levels at rest in male athletes is analogous to lower levels of oestrogen-progesterone found in female athletes with reproductive dysfunctions related to exercise\textsuperscript{21-30}. The studies aimed at elucidating the physiological mechanism underlying the dysfunction of the HPG axis in men with EHMC have focused on whether the origin of the disorder is central (hypothalamic-pituitary) or peripheral (testicular). The former have examined the glandular secretion of LH and/or prolactin (PRL), while the latter have examined the secretion of testosterone. Since alterations in the release of LH-PRL had previously been studied in female athletes with reproductive disorders\textsuperscript{1,13,14}, the studies with male athletes took those conducted with women as a model.

Regarding the central mechanisms, the studies show that men with EHMC display extreme PRL release from the pituitary gland in response to endogenous or exogenous stimuli\textsuperscript{3,32}. Attenuated release of LH can also be seen in response to analogous endogenous or exogenous stimuli\textsuperscript{8,13}. Similar findings had previously been reported in female athletes with reproductive dysfunction (oligomenorrhea or athletic amenorrhea)\textsuperscript{1,12}. It should be pointed out that due to sex-specific aspects of the HPG axis, not all changes in reproductive hormones observed in male and female athletes fully coincide. Furthermore, the type and nature of the research protocols and demographic differences between the male and female athletes studied have given rise to some variability in the findings.

With respect to peripheral mechanisms, the studies have demonstrated that men with EHMC show lower secretion of testosterone from the testes in response to an exogenous stimulus\textsuperscript{1,13}. When compared with sedentary controls, there is a reduction of 15-40% in testicular testosterone secretion in response to the same stimulus dose. It is still unclear whether this attenuated secretion is due to a decrease in the sensitivity of the glandular receptor or to alterations in some subsequent event of the steroidogenic process for the synthesis of testosterone\textsuperscript{6}.

Loucks’ work clearly shows that a state of low energy availability (LEA) is a key trigger for female athletes to develop FAT and related reproductive disorders\textsuperscript{1}. LEA occurs when energy intake is insufficient to maintain the necessary functions of the body and those involved in physical training; this usually happens when caloric intake is <30 kcal/kg\textsuperscript{-1} FFM/day\textsuperscript{-1}. Evidence that LEA in men is a causal factor in the development of EHMC is less definitive. However, Hooper et al. recently published convincing findings supporting this possibility; although it should be borne in mind that the number of subjects in the study was relatively small\textsuperscript{17}. Therefore, it is unclear to date whether LEA is the chief cause of the development of either FAT or EHMC; that is to say, more studies are needed, particularly involving men.
Physoiological impact of low testosterone in men

The low basal testosterone level that men with EHMC present with could affect physiological processes which depend on testosterone. There is evidence, for example, of a decrease in spermatogenesis and oligozoospermia conditions in athletes with EHMC. It is likely that a disturbance in sperm production increases the risk of infertility in men with EHMC; in the case of women, several studies have shown a strong relationship between athletic amenorrhea and fertility problems.

Study of the effects that the low testosterone levels of men with EHMC produce on other androgenic-anabolic processes -such as protein synthesis and the development of muscle mass- is limited. In all events, we put forward the hypothesis that the lower testosterone levels that these athletes exhibit could bring the benefit of a lower total muscle mass, something which could be advantageous in endurance sports (a lower body mass results in a lower oxygen requirement and, therefore, lower energy expenditure).

One matter which calls for further research is the relationship between low testosterone, reduced bone mineral density and osteopaenia in athletes with EHMC. In the clinical field, there is evidence indicating that men with hypogonadism and hypotestosteronaemia may suffer severe bone mineral loss. To date, the data on changes in bone mineral content in athletes with EHMC are somewhat contradictory, although convincing case studies have been published.

It should be noted that the prevalence of EHMC would appear to be lower considering the population of male endurance athletes (15–25% according to existing estimates). This could be due to the fact that only a small percentage of these athletes train intensely and consistently long enough to display symptoms.

Conclusion

Persistent physical training, specifically that associated with endurance sports, negatively affects the principal male hormone (testosterone) and other reproductive hormones (LH and PRL). This reproductive endocrine status has been named exercise-hypogonadal male condition. The mechanism involved in this hormonal diminishment is still unclear, but would seem to be related to a dysfunction of the HPG axis caused by years of continuous exposure to significant amounts of exercise training and could affect physiological processes which depend on testosterone. There is evidence, for example, of a decrease in spermatogenesis and oligozoospermia conditions in athletes with EHMC. It is likely that a disturbance in sperm production increases the risk of infertility in men with EHMC; in the case of women, several studies have shown a strong relationship between athletic amenorrhea and fertility problems.

Although the prevalence of EHMC is relatively low, it is recommended that sports doctors and particularly endocrinologists and fertility specialists be mindful of the existence of EHMC. The evidence indicates that doctors may need to incorporate strategies within their procedures to assess and perhaps treat EHMC, especially given concerns about the potential problem of infertility.

Conflict of interest

The authors declare that they are not subject to any type of conflict of interest.

Bibliography


