Research Brief

Multi-Institutional Survey of Medical Treatment for Late-Onset Hypogonadism in Japan

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Abstract

The adequate criteria for late-onset hypogonadism (LOH) diagnosis, including serum testosterone levels, type (total or free testosterone) and duration of androgen replacement therapy, and evaluations of treatment effectiveness remain controversial. To evaluate the current status of medical treatment for LOH in Japan, the first nationwide survey were performed. A total of 35 questionnaires answered by urologists in high-volume facilities were analyzed. The median numbers of patients with hypogonadism-related symptoms per month were 10. Aging Male Symptom Score, International Index of Erectile Function, and International Prostate Symptom Score questionnaires were widely used for questionnaires. The diagnostic criteria for LOH varied. Among the patients who presented with hypogonadism-related symptoms, the mean proportion of patients undergoing treatment for LOH was 62.3%. In Japan, LOH was treated not only with testosterone enanthate injections or testosterone ointment but also with Kampo medicine. In many facilities, LOH treatment effectiveness was assessed after a 3-month period. Efficacy was assessed in different ways. Treatment effectiveness rate ranged from 30% to 80%. The duration of LOH treatment was not fixed and was established individually by both the patient and treating physician. This study showed that the real clinical practices for LOH are very diverse, and a general consensus is needed.

Keywords

late-onset hypogonadism, androgen replacement therapy, Aging Male Symptom Score

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Introduction

Late-onset hypogonadism (LOH), a clinical and biochemical syndrome, is characterized by typical symptoms and serum testosterone deficiency in aging men. It may result in significant detriment to the quality of life and adversely affect the function of multiple organs according to the International Society of Andrology, International Society for the Study of Aging Male, European Association of Urology, European Academy of Andrology, and American Society of Andrology (Wang et al., 2008). LOH is the presence of symptoms associated with hypogonadism, such as low libido, decline in general well-being, and fatigue. The widely accepted laboratory parameter for diagnosis is the measurement of serum total testosterone level (Wang et al., 2008). The main objective of androgen replacement therapy (ART) for LOH is to prevent decreased organ function secondary to decreased androgen levels and maintain a satisfactory quality of life. In Japan, the clinical practice manual for LOH was published in 2007 by the Japanese Urological Association and the Japanese Society for the Study of the Aging Male. Rather than the value of total testosterone, free testosterone is recommended as the first diagnostic parameter for LOH. The reason is that the decrease in the normal level of free testosterone is more marked with aging than that of total testosterone (Namiki et al., 2008). Reportedly, improvement of depression, erectile function, and metabolic syndrome achieved by ART occurs gradually (Yassin, Doros, Hammerer, & Yassin, 2014). Nevertheless, adequate criteria for LOH diagnosis, including serum testosterone levels, type (total or free testosterone) and duration of ART, and evaluations

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of treatment effectiveness remain controversial. Although the Aging Male Symptom Score (AMS) is a widely used questionnaire; however, given its low specificity, AMS should not be used for diagnosis, rather for monitoring of ART (Wang et al., 2008). To evaluate the current status of medical treatment for LOH in Japan and establish future goals to improve LOH management, a questionnaire survey was performed among some urologists in Japan.
Method

From 15 to 30 March 2016, 45 urologists in 45 facilities were identified by searching for the keywords “male menopause and LOH” in a Japanese database (Ichushi ver. 5; http://search.jamas.or.jp/). These 45 urologists received the original questionnaire by mail. The questionnaire evaluated the following aspects: number of patients, practice style, blood sampling panel, diagnostic methods for LOH, proportion of patients undergoing LOH treatment, duration of LOH treatment, cutoff for evaluations of LOH treatment effectiveness, and treatment effectiveness rate. This study was approved by the ethical committee of Kansai Medical University Hirakata Hospital (#H150393).

Results

A total of 35 questionnaires answered by 35 urologists were analyzed. Eighteen (51.4%) of the urologists worked at university hospitals, 11 (31.4%) at community hospitals, and 6 at clinics. The mean and median numbers of patients with hypogonadism-related symptoms per month were 25.4 and 10, respectively. Nineteen of 35 (54%) urologists treated less than 10 patients with LOH per month. Seventeen of 35 (48.6%) urologists performed LOH examination at special clinics. At first examination, AMS (Heinemann, Zimmermann, Vermeulen, & Thiel, 1999), International Index of Erectile Function (Rosen, Cappelleri, Smith, Lipsky, & Pena, 1999), and International Prostate Symptom Score (Barry et al., 1992) questionnaires were widely used. Conversely, questionnaires related to depression diagnosis were used infrequently (Figure 1a). The diagnostic criteria for LOH varied. Though 16 of 35 (45.7%) urologists diagnosed LOH by combining serum testosterone level with symptoms, 9 (25.7%) urologists diagnosed this condition only by testosterone levels and 8 (22.9%) urologists diagnosed this condition by combining testosterone levels and questionnaires (Figure 1b). Twenty-five of 33 (75.8%) urologists used free testosterone levels for LOH diagnosis and only 4 of 33 (12.1%) urologists used total testosterone levels for LOH diagnosis. Among the patients who presented with hypogonadism-related symptoms, the proportion of patients undergoing treatment for LOH ranged from 20% to 98% (mean 62.3%). In Japan, LOH was treated not only with testosterone enanthate injections but also with testosterone ointment and Kampo medicine (traditional Japanese medicine; Komiya, Watanabe, & Fuse, 2011; Tsujimura et al., 2008; Figure 1c). Many urologists assessed the effectiveness of LOH treatment after a 3-month period. Efficacy was assessed in different ways. Eleven of 34 (32.4%) urologists assessed treatment efficacy only by doctor’s inquiry, 9 of 34 (26.5%) only by questionnaires, and 8 of 34 (23.5%) by combining doctor’s inquiry and questionnaires (Figure 1d). Treatment effectiveness rate ranged from 30% to 80% (mean 63.8%). The duration of LOH treatment was not fixed and was established individually by both the patient and treating physician (Figure 1e).

Discussion

The present study is the first nationwide survey of medical treatment for LOH in Japan. However, this survey was only targeted to urologists. This is a study limitation, because this may have introduced selection bias as LOH can also be treated by internal medicine specialists. This study identified that the real clinical practices for LOH are very diverse, and a general consensus is needed. It is necessary to increase the awareness of LOH in the general population, examine the evaluation of LOH by worldwide standards (e.g., measurement of total testosterone levels), create disease-specific questionnaires, evaluate the effectiveness of treatment using testosterone ointment and Kampo medicine, and arrive at a general consensus regarding the ideal treatment duration based on objective findings.

Declaration of Conflicting Interests

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References

Barry, M. J., Fowler, F. J., Jr., O’Leary, M. P., Bruskewitz, R. C., Holtgrewe, H. L., Mebust, W. K., & Cockett, A. T. (1992). The American Urological Association symptom index for benign prostatic hyperplasia. Journal of Urology, 148, 1549-1557.

Heinemann, L. A., Zimmermann, T., Vermeulen, A., & Thiel, C. (1999). A new “aging males” symptoms’ rating scale. Aging Male, 2, 105-114.

Komiya, A., Watanabe, A., & Fuse, H. (2011). Herbal medicine in Japan. Journal of Men’s Health, 8, S15-S18.

Namiki, M., Akaza, H., Shimazu, T., Ito, N., Iwamoto, T., Baba, K., . . . Kumamoto, Y. (2008). Clinical practice manual for late-onset hypogonadism syndrome. International Journal of Urology, 15, 377-388.

Rosen, R. C., Cappelleri, J. C., Smith, M. D., Lipsky, J., & Pena, B. M. (1999). Development and evaluation of an abridged,
5-item version of the International Index of Erectile Function (IIEF-5) as a diagnostic tool for erectile dysfunction. *International Journal of Impotence Research, 11*, 319-326.

Tsujimura, A., Takada, S., Matsuoka, Y., Nakayama, J., Takao, T., Miyagawa, Y., . . . Okuyama, A. (2008). Clinical trial of treatment with saikokaryokotsuboreito for eugonadal patients with late-inset hypogonadism-related symptoms. *Aging Male, 11*, 95-99.

Wang, C., Nieschlag, E., Swerdloff, R., Behre, H. M., Hellstrom, W. J., Gooren, L. J., . . . Wu, F. C. (2008). Investigation, treatment and monitoring of late-onset hypogonadism in males: ISA, ISSAM, EAU, EAA and ASA recommendations. *European Journal of Endocrinology, 159*, 507-514.

Yassin, D. J., Doros, G., Hammerer, P. G., & Yassin, A. A. (2014). Long-term testosterone treatment in elderly men with hypogonadism and erectile dysfunction reduces obesity parameters and improves metabolic syndrome and health-related quality of life. *Journal of Sexual Medicine, 11*, 1567-1576.