Treatment of Cryptorchidism With Pulsatile Luteinizing Hormone-Releasing Hormone (LH-RH)

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● **This preliminary report describes a new method of treating bilateral cryptorchidism that may modify the need for surgical intervention. Four of five boys (3½, 3½, 7, 11 and 12½ years of age) given hourly subcutaneous pulses of luteinizing hormone-releasing hormone (LH-RH, 10 to 100 μg/day, given in a 3-min pulse every hour) showed evidence of testicular descent after 3 to 19 weeks. The battery-operated, programmable syringe driver was well tolerated by the boys, and the daily insertion of the scalp-vein needles was managed at home by their parents.**

INDEX WORDS: Cryptorchidism; luteinizing hormone-releasing hormone (LH-RH).

TESTICULAR DESCENT is androgen mediated and under pituitary control. Dihydrotestosterone in high local concentration around the testis induces thickening of the gubernaculum, which permits testicular descent.[1] Attempts to mimic this normal process in cryptorchid boys have included human chorionic gonadotrophin (HCG)[2] therapy and luteinizing hormone-releasing hormone (LH-RH)[3,4,5] therapy. Both have been successful. In this preliminary report, however, we describe a different mode of LH-RH administration in which small dosages are given in a manner that simulates the physiologic release of this hormone from the hypothalamus. The efficacy of this method is demonstrated by satisfactory testicular descent in four out of five boys with both testes arrested in the line of descent. They were not retractile and were to be operated upon.

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MATERIALS AND METHODS

We used a portable syringe driver designed for insulin administration (Graseby-Dynamics MS-16; Graseby-Dynamics, Watford U.K.), which was fitted with an integrated circuit that activated the motor for 3 min each hour. It was worn in a vest pocket and fitted with a 2.5 mL syringe that delivered 0.1 mL/hr. The LH-RH solution (5 to 50 μg/mL) was delivered to a subcutaneous site on the anterior abdominal wall via a 25-gauge scalp-vein needle. After brief instruction, the daily changing of the syringe and scalp-vein needle was easily undertaken by the boys' parents. Testes were measured with a Prader orchidometer.

CASE REPORTS

Case 1

A boy aged 3 years and 2 months presented with both testes (1.5 mL each) in the inguinal pounches just outside the superficial rings. The boy weighed 18 kg. Treatment with LH-RH (100 μg/day) was given initially for three weeks, then for another four weeks. At this stage treatment was stopped because both testes were located in the scrotum and were 3.5 mL in volume.

Case 2

A 12½-year-old boy presented with his testes in the superficial inguinal pouch; both testes were 2 mL in volume. The boy weighed 35 kg and showed no sign of puberty. He received LH-RH therapy at 100 μg/day for three weeks. Treatment was terminated when the testes were located in the scrotum and had enlarged to 4 and 6 mL.

Case 3

A boy 11-years-old presented with a 2 mL testis at the right inguinal ring and a 2 mL testis in the left superficial inguinal pouch just outside the ring. He weighed 38 kg and was 151.5 cm tall; his bone age was 10½ years. Treatment with LH-RH at 45 μg/day was given for 19 weeks. After 7 weeks the right testis had descended to the superficial pouch and the left testis reached the top of the scrotum. By 19 weeks both testes were 4.5 mL and were in the scrotum. At follow-up 6 months later, both testes were located in the scrotum (4 mL each) and there was no clinical evidence of precocious puberty. This was supported by an estimation of the boy's bone age, which was 10½ years.

Case 4

A 3½-year-old boy presented with both testes (1.5 mL each) in the superficial inguinal pouch and on the left side there was a clinically significant hernia. In view of his weight (17½ kg) he received only 10 μg of LH-RH/d. Since no

change was observed after 3 weeks, 20 μg/d was administered for a further 2 weeks. Again in the absence of a clinical response, the dose was increased to 67 μg/d for 13 weeks. At the conclusion of this period, there was no obvious descent, therefore orchidopexy was performed. Bone age estimation after treatment was 3 years.

Case 5

A 7-year-old boy was referred due to bilateral cryptorchidism with the left testis at the superficial inguinal ring. The right testis was impalpable. He received 100 μg of LH-RH/d for 4 weeks after which both testes were in the scrotum (3 mL each).

DISCUSSION

The conventional approach to the treatment of bilateral cryptorchidism is with human chorionic gonadotrophin (HCG) for 8 to 12 weeks[2] and, if this is not successful, with orchidopexy. The eventual location of the testes in the scrotum, by either of these procedures, does not guarantee normal testicular function, particularly normal spermatogenesis.[6,7] There is general agreement that the testes should assume a scrotal position as soon as is practicable to prevent damage to the germinal epithelium. However, one of the problems of operating on children of less than three years of age is the delicate blood supply and small size of the testes. A problem with medical therapy is that commercial batches of HCG may contain impurities.[8]

LH-RH has been used as an alternative medical therapy. Spona and colleagues[5] reported successful descent of the testes in 23 of 88 boys having intranasal administration of 1 to 2 mg of LH-RH each day. The pulsatile administration technique we describe has the advantage of using much smaller and more precise doses (100 μg/d) delivered in a more physiological manner. This method has the advantage of avoiding the desensitization of pituitary gonadotrophes as may occur when using larger doses. We have found no evidence of inadvertent induction of precocious puberty.

Another advantage of the method we have described is that in the event of failure of testicular descent, the testes become larger and the surgical difficulties of handling small testes are reduced. If LH-RH therapy is not successful or if there is a significant hernia, orchidopexy should be carried out as soon as possible since there is a regression of testicular size once LH-RH therapy is stopped. It is not possible at present to know whether this form of therapy will lessen the incidence of infertility in patients with cryptorchidism.

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