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Fertility potential in a cohort of 65 men with previously acquired undescended testes ☆,☆☆,★

Jocelyn van Brakel [a,*], Ries Kranse [a], Sabine M.P.F. de Muinck Keizer-Schrama [b], A. Emile J. Hendriks [b], Frank H. de Jong [c], Wilfried W.M. Hack [d], Laszla M. van der Voort-Doedens [d], Chris H. Bangma [a], Frans W. Hazebroek [e], Gert R. Dohle [a]

[a] Department of Urology, Erasmus University Medical Center, 3000 CA Rotterdam, the Netherlands
[b] Departments of Pediatrics, Endocrinology, Erasmus University Medical Center–Sophia Children's Hospital, 3000 CA Rotterdam, the Netherlands
[c] Departments of Internal Medicine, Endocrinology, Erasmus University Medical Center, 3000 CA Rotterdam, the Netherlands
[d] Department of Pediatrics, Medical Center Alkmaar, 1800AM Alkmaar, the Netherlands
[e] Department of Pediatric Surgery, Erasmus University Medical Center–Sophia Children's Hospital, 3000 CA Rotterdam, the Netherlands

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ABSTRACT

Purpose: To evaluate testicular function in men with previously acquired undescended testes (AUDT) in whom spontaneous descent was awaited until puberty followed by orchiopexy in case of nondescent.
Methods: Andrological evaluation including paternity, scrotal ultrasound, reproductive hormones, and semen analysis was performed in three groups: men with AUDT, healthy controls, and men with previously congenital undescended testes (CUDT).
Results: In comparison with controls, men with AUDT more often had significantly abnormal testicular consistency, smaller testes, lower sperm concentration, and less motile sperm. Except for more often a normal testicular consistency in men with AUDT, no differences were found between men with AUDT and men with CUDT. Also, no differences were found between men with AUDT which had spontaneously descended and men who underwent orchiopexy.
Conclusions: Fertility potential in men with AUDT is compromised in comparison with healthy controls, but comparable with men with CUDT. This suggests that congenital and acquired UDT share the same etiology. No significant difference was found between men who had spontaneous descent and men needing orchiopexy. However, fertility potential is unknown for men after immediate surgery at diagnosis, and this should be a subject for future studies.

Undescended testis (UDT) is a frequent urogenital abnormality in boys with an incidence around 1% at 1 year of age [1]. The abnormality may be of congenital or acquired origin [2,3]. In the congenital type a stable scrotal position was never reached. Acquired UDT is defined as a palpable UDT that previously had a normal scrotal position, as documented by a physician. Acquired UDT is seen in 1%–3% of boys during childhood [4,5] and its etiology, natural course, and treatment are still debated. Two studies on the proportion of (pre) pubertal spontaneous descent in boys with acquired UDT found a prevalence of 57% and 71.4% spontaneous descended testes [6,7]. Congenital UDT is associated with infertility [8,9]. However, little is known about fertility in men with previously acquired UDT (AUDT) and the effect of a "wait-and-see until puberty" policy [6]. The aim of our study was to evaluate the impact of AUDT on fertility parameters in comparison with controls and men with previously congenital UDT (CUDT). Furthermore, we evaluated testicular function in men with AUDT after spontaneous descent or orchiopexy.

1. Materials and methods

1.1. Acquired UDT group

Between 1982 and 2004, boys with acquired UDT referred to Erasmus Medical Center–Sophia Children's Hospital, Rotterdam, and

Abbreviations: ART, assisted reproductive treatment; AUDT, previously acquired undescended testes; BMI, body mass index; CI, confidence interval; CUDT, previously congenital undescended testes; FSH, follicle-stimulating hormone; LH, luteinizing hormone; OR, odds ratio; TTP, time to first pregnancy; UDT, undescended testes.

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* Corresponding author. Department of Urology, Erasmus University Medical Center, 3000 CA Rotterdam, the Netherlands. Tel.: +31 10 7032254, +31 6 14997281; fax: +31 10 7034749.
E-mail addresses: j.vanbrakel@erasmusmc.nl (J. van Brakel), ries.kranse@gmail.com (R. Kranse), s.demuinckkeizer-schrama@erasmusmc.nl (S.M.P.F. de Muinck Keizer-Schrama), a.e.j.hendriks@erasmusmc.nl (A.E.J. Hendriks), f.h.dejong@erasmusmc.nl (F.H. de Jong), w.hack@mca.nl (W.W.M. Hack), l.vander.voort@mca.nl (L.M. van der Voort-Doedens), h.j.vanalphen@erasmusmc.nl (C.H. Bangma), f.hazebroek@erasmusmc.nl (F.W. Hazebroek), g.r.dohle@erasmusmc.nl (G.R. Dohle).

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the Medical Center, Alkmaar, were followed by three experienced physicians (S.de.M.K.-S., F.W.H., or W.H.) annually until puberty. Acquired UDT implied that a previous normal stable scrotal position was documented at least once either by the Regional Youth Health Care Institution, general practitioner, or hospital. Furthermore, the testis had to be palpable without ipsilateral, inguinal, clinically present pathological findings or previous ipsilateral, inguinal surgery, and the most caudal testicular position after manipulation had to be nonscrotal or unstable scrotal position. Spontaneous descent was awaited until at least Tanner stage P2G2, after which orchiopexy was performed in case of nondescent. Findings at physical examination were registered on a standardized form. Retractile testes were excluded. Orchiopexy was performed by pediatric surgeons with years of experience performing orchiopexies.

In 2009, a total of 231 men with 287 AUDT were screened for eligibility for this study, of whom 99 men had undergone orchiopexy. Seven men were excluded mostly because of chromosomal abnormalities and dysmorphic syndromes besides UDT. For 17 no current address was available, thus 207 were invited to participate.

1.2. Control group and congenital UDT group

Fifty-three healthy men without a history of UDT served as controls. These men previously participated in a study evaluating fatherhood after use or nonuse of sex steroids treatment during adolescence to reduce final height. Men, who were not treated, were used as our control group. Furthermore, we created a CUDT group ($N = 62$, 69 testes) of men who participated in a study evaluating fertility potential after treatment of congenital UDT during childhood. Both groups were previously described in detail [10,11]. These men had the same evaluation as men with AUDT, except for morphological evaluation of semen, which was not performed in the controls.

1.3. Methods

The methods for recruitment and andrological evaluation were published previously [11]. In short, all 207 men were invited to participate by post. Those who refused were invited to fill out a questionnaire on fertility and risk factors for subfertility or infertility. Participation involved a single hospital visit including medical history taking, physical examination, scrotal ultrasound, venous puncture, and semen sample delivery. Special attention was paid to attempting fatherhood, duration of child-wish, and the time to first pregnancy (TTP).

Testicular volume and presence of testicular and epididymal abnormalities and varicocele were assessed by physical examination and confirmed by scrotal ultrasound.

The following endocrinological values were evaluated: luteinizing hormone (LH) and follicle-stimulating hormone (FSH), testosterone, and inhibin B.

Semen parameters that were evaluated were analyzed according to the WHO manual of 2010 [12], which included volume, concentration, total sperm count, progressive motility, and morphology.

1.4. Statistical analysis

Continuous variables were tested with the Mann–Whitney *U* test; categorical variables were tested with the Fisher's exact test. The Kaplan–Meier survival method was used for time-to-event analyses, Wilcoxon's test was used to test between group differences in such cases. Multivariate logistic regression analyses were used to test the relationship between bivariate categories and their predictors. For example, we have studied the relationship between fertility parameters (bivariate classes: being below or above the reference value) and the predictor “type of UDT” controlling for known confounders: smoking, varicocele, and body mass index (BMI) and unilateral–bilateral UDT. A two-sided p-value of less than 0.05 was considered statistically significant.

1.5. Ethics

The study was reviewed and approved by the Medical Ethical Review Committee at Erasmus University Medical Center in Rotterdam (MEC number 2004-206). Written informed consent was obtained from all participants.

2. Results

2.1. Inclusion of men with AUDT

Sixty-five (31%) of the 207 eligible men participated (Fig. 1). Most of the 49 nonparticipants who nevertheless returned the questionnaire (35%) mentioned time constraints and bothersomeness of the investigations as reasons for refusal. Only two men reported that having fathered children was also a reason to decline participation. Table 1 shows the characteristics of study participants and nonparticipants. No significant differences were found between participants and men returning the questionnaire in terms of the proportion of men attempting fatherhood, number of pregnancies, TTP, and proportions of men having an active child-wish. One nonparticipant with bilateral acquired UDT with spontaneous descent replied that he had azoospermia.

Fifty of the 65 men with AUDT had unilateral AUDT. Spontaneous descent had occurred in 32 participants (24 unilateral and 8 bilateral). Median age at orchiopexy ($N = 33$; 26 unilateral and 7 bilateral) was 13.2 years (range 4.75 to 17.8 years). The most important criteria for prepubertal orchiopexy were inguinal complaints or ipsilateral inguinal hernia.

2.2. Comparisons of fertility parameters

2.2.1. Men with unilateral AUDT vs. controls (Table 2)

Testicular volume, both of the previously undescended one and the contralateral testis was significantly smaller than that of controls. Testicular consistency was normal in all controls; 13 men with AUDT (26%) had unilateral or bilateral soft testicular consistency (p-value < 0.001).

Endocrinological data were obtained from 49 men with AUDT: 1 of them refused blood sampling. Endocrine function did not differ significantly between men with AUDT and controls.

One man with AUDT was unable to produce semen. Semen of five controls who had undergone vasectomy was not analyzed. Concentration and progressive motility in men with AUDT were significantly lower than those in controls. Azoospermia was noted in four men with AUDT (three spontaneous descent and one orchiopexy).

Controls, who were significantly older than men with AUDT, significantly more often attempted fatherhood. However fatherhood, TTP, cumulative probability of conception, and duration of child-wish did not statistically significantly differ between men with AUDT and controls.

Two partners of controls had undergone intrauterine insemination. The reason was unknown for one couple and for the other couple it was caused by a female problem. The partner of one man with AUDT who had had orchiopexy, needed assisted reproductive treatment (ART) because she had a fertility problem.

2.2.2. Men with unilateral AUDT vs. men with unilateral CUDT (Table 2)

Normal testicular consistency was significantly more often found in men with AUDT than in men with CUDT (74% versus 53%; p-value $= 0.03$).