

Analysis of anomalies of the epididymis and processus vaginalis in human fetuses and in patients with cryptorchidism treated and untreated with human chorionic gonadotrophin

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Accepted for publication 12 April 2006

OBJECTIVE

To analyse the incidence of epididymal anomalies and the structure of the processus vaginalis (PV) in patients with cryptorchidism treated or not with human chorionic gonadotrophin (hCG), and to compare these findings with human fetuses with testes in the scrotum.

PATIENTS, MATERIALS AND METHODS

We assessed 24 fetuses with a gestational age of 23–35 weeks, and 114 cryptorchid patients (mean age 10.3 years). The patients were divided into two groups of those who used hCG (55, 65 testes) and those who did not (59, 75 testes). The sample was divided into six

groups of possible anatomical relationships between the testis and the epididymis, according to a previous classification. Two situations were considered to analyse the PV: (a) total obliteration between the internal inguinal ring and the upper pole of the testis; and (b) total patency.

RESULTS

Epididymal anomalies were found in 35% of patients with cryptorchidism and in only 4% of normal fetuses. Of the 47 cases of epididymal anomalies in patients with cryptorchidism 23 (49%) were treated with hCG and 24 (51%) were not. The PV was patent in 58% of patients with cryptorchidism and in only 5% of fetuses. Considering the

three groups, the epididymal anomalies were more frequent when the PV was patent.

CONCLUSIONS

Patency of the PV and the incidence of epididymal anomalies were more frequent in patients with cryptorchidism. The existence of epididymal anomalies did not influence testicular migration in patients treated with hCG.

KEYWORDS

cryptorchidism, epididymis, embryo and fetal development, scrotum, chorionic gonadotrophin

INTRODUCTION

Cryptorchidism is one of the most common pathologies in boys, with an incidence of 2–5% in full-term births, reaching 30% in premature births [1–3]. Several anomalies are associated with cryptorchidism, but epididymal anomalies (EAs) and inguinal hernia are among the most frequent [3–5]; EAs are associated with cryptorchidism with an incidence of 36–79% [6,7].

Inguinal hernia results from the persistence of the processus vaginalis (PV), which is a prolongation of the peritoneum extending to the scrotum, and is usually obliterated upon the completion of testicular migration [8,9]. When the PV is patent in patients with cryptorchidism, the incidence of EAs is significantly higher than when the PV is obliterated [7].

Surgery is the best treatment for cryptorchidism [1] but there are many studies

showing good results for testicular migration after hormone therapy with hCG or with GnRH [3,10,11]. There are several studies of the incidence of EAs and the relationship with the PV [7,12] but patients with pathologies such as hydrocele or inguinal hernia were used as controls in those studies [7,13]. Reports of the analysis of EAs in patients with cryptorchidism who were treated with hCG or GnRH are scarce [14]. Thus, the objective of the present study was to assess the incidence of patency of the PV and of EAs in patients with cryptorchidism, and to assess if the presence of EAs influenced testicular migration in patients treated with hCG.

PATIENTS, MATERIALS AND METHODS

From January 2000 to October 2003, we studied 24 fetuses with a gestational age of 23–35 weeks, and 114 patients who had cryptorchidism (mean age 10.3 years, range 1–33). Patients were randomly divided into

two groups who were treated with hCG before orchidopexy (55) or not (59). The patients were randomized to receive hCG by their day of attendance at the paediatric urology clinic, with those attending on Mondays receiving hCG and those on Thursdays not so treated. The research protocol for the study was reviewed and approved by the Bioethical Committee at our Institution.

The fetuses under study had no detectable congenital malformations and their gestational ages were estimated by measuring the size of the larger foot [15,16]. Of the 24 fetuses assessed, three testes did not complete migration and 45 had completely migrated to the scrotum, and these were used as the control group.

Of the 59 patients not treated with hCG, 16 had bilateral cryptorchidism (75 testes) and of the 55 who were, 12 (22%) did not require orchidopexy, as there was complete testicular

Position of testis, n	hCG+	hCG-	Total	TABLE 1 <i>Position of testis in relation to treatment with hCG (+) or not (hCG-)</i>
Abdominal	6	10	16 (11)	
Internal inguinal ring	8	8	16 (11)	
Inguinal canal	39	32	71 (51)	
External inguinal ring	12	22	34 (24)	
Anorchia	-	3	3 (2)	
Total, n (%)	65	75	140 (100)	

hCG	Age, years (n)	PV		TABLE 2 <i>Patency of the PV in relation to age range and treatment with hCG (+) or not (hCG-); the three patients with anorchia were excluded</i>
		Patent	Occluded	
hCG+	1-4 (35)	25	10	
hCG-	1-4 (20)	12	8	
hCG+	5-8 (17)	11	6	
hCG-	5-8 (20)	6	14	
hCG+	>9 (13)	7	6	
hCG-	>9 (32)	18	14	
Total, n (%)	137 (100)	79 (58)	58 (42)	

TABLE 3 *EAs and patency of the PV according to treatment with hCG (+) or not (hCG-); the morphological relations of types I and II are considered normal, and types III-VI as anomalies. There were no cases type VI EAs*

	PV	Epididymis	
		I and II	III-V
hCG+	Patent, 43	23	20
hCG-	Patent, 36	21	15
hCG+	Occluded, 22	19	03
hCG-	Occluded, 36	27	09
Total, n (%)	137 (100)	90 (66)	47 (34)

migration after treatment. These patients were followed for ≥ 12 months. Of the 43 patients treated with hCG and surgery, 22 had bilateral cryptorchidism (65 testes) for analysis. The sample thus comprised 102 patients with cryptorchidism (140 testes presumably), but later we found that three patients had anorchia and the final sample analysed comprised 137 testes.

The hCG doses were administered i.m. twice weekly for 5 weeks, according to the following regimen [3,11]: children aged ≤ 2 years received injections with 250 IU (total 2500 IU), children aged >2 years and ≤ 6 years received 500 IU (total 5000 IU) and children aged >6 years received 1000 IU of hCG (total 10 000 IU).

The relationship between the testis and the epididymis was analysed during surgery, according to a previous classification [17,18] in which there are six types of anatomical relationships: type I, epididymis united to the testis by head and tail; type II, epididymis totally united to the testis; type III, epididymis united to the testis by its head only; type IV, epididymis united to the testis by its tail only; type V, total disjunction between testis and epididymis; type VI, epididymal atresia.

While analysing the structure of the PV we considered two situations: (a) total obliteration of the PV between the internal inguinal ring and the upper pole of the testis; and (b) total patency of the PV. For contingency analysis of the populations studied, we used Fisher's exact test, with significance indicated at $P < 0.05$.

RESULTS

The positions of the cryptorchid testes are shown in Table 1. Of the 137 cases of cryptorchidism, the PV was patent in 79 (58%) and occluded in 58 (42%). Of the 79 cases where the PV was patent, 43 patients (54%) were treated with hCG and 36 (46%) were not. Of the 58 cases where the PV was occluded, 22 (38%) had hCG and 36 (62%) did not. There was no statistically significant difference between patency of the PV in boys who did or did not receive hCG ($P = 0.059$).

The relationship between treatment with hCG, patient age and patency or occlusion of the PV is shown in Table 2, and that between hCG, patency of the PV and presence or absence of EAs in Table 3. In the 79 cases where the PV was patent there were EAs in 35 (44%). Of the 58 cases where the PV was occluded, there were EAs in 12 (21%), and the difference between the groups was statistically significant ($P < 0.01$).

The relationship between the structure of the PV and the relationship between testis and epididymis in the three groups (fetuses, patients treated with hCG or not) is shown in Table 4. In fetuses with testes already in the scrotum there were two cases of EAs (both type III) and four of a patent PV. The two cases with EAs had a patent PV. When we compared the fetuses with those patients treated with hCG there was a higher prevalence (statistically significant) of both the incidence of EAs ($P = 0.002$) and of a patent PV ($P < 0.001$) in patients treated with hCG.

When comparing the 133 cases of normal anatomy of epididymis with the 49 with an anomaly, the PV was patent in 46 and 37, respectively ($P = 0.007$). Comparing the fetuses with those patients not treated with hCG, there was a higher prevalence of both the incidence of EAs, and of a patent PV (both $P = 0.002$).

DISCUSSION

The medical treatment of cryptorchidism has a variable reported success rate, at 25-55% [3,19]. In the present study, 22% of patients treated with hCG had testicular migration and did not require surgery. The testicular position is relevant when considering the clinical treatment of cryptorchidism. Abdominal testes respond poorly to clinical treatment, whereas true retractile testes tend to attach in the scrotum in all cases [19,20].

The precise moment of closure of the PV remains unknown. Studies suggest that at birth there would be a patent PV in up to 80% of boys, with progressively lower rates throughout the first year of life [7,9,21]. In significantly many adult men the PV never obliterates, but in most of these cases there is no development of an inguinal hernia [7,9,21].

In the present study, the PV was patent in 58% of patients with cryptorchidism and in 5% of fetuses. Regardless of treatment with

hCG, the incidence of a patent PV was significantly higher in patients with cryptorchidism than in fetuses that had their testes in the scrotum. Interestingly, we did not identify a greater incidence of a closed PV with a normal epididymis in the hCG-treated group, as reported previously [10]. Although fetuses are not an ideal control group, they were the only 'normal' individuals that we were able to assess; it is very difficult to obtain a normal group of living individuals to assess the patency or not of the PV.

In boys with cryptorchidism, the highest frequency of a patent PV was in those aged 1–4 years (67%) but there was no statistically significant difference in the other groups. Of the 45 patients who were >9 years old, in 25 (56%) the PV was patent. Such findings did not confirm the tendency towards closure of the PV with increasing age. Although there were relatively few patients in the different age groups there were enough for a significant statistical analysis.

Other relevant published data suggest that the highest incidence of EAs is associated with the patency of the PV [18]. Patients with cryptorchidism and an obliterated PV have significantly fewer EAs [7,14]. In the present study the PV was occluded in 58 cases, of which 12 (21%) had EAs; of these 12, nine had been treated with hCG.

The index of patency of the PV and its relation to EAs is well documented; Barthold and Redman [7], during 58 orchidopexies, reported 80% EAs in patients with a patent PV. Bica and Hadziselimovic [14] reported an association of EAs and patency of the PV in 88.7% of the 64 patients they treated surgically. Elder [13], in a study of 90 cases of cryptorchidism, found that half the patients with a patent PV had EAs.

When analysing only those testes with EAs in the present study (49), in 37 (75%) the PV was patent. Of the 23 patients treated with hCG, only three (13%) had EAs with an occluded PV. The two fetal testes that had EAs had a patent PV. Of the 24 patients not treated with hCG and with EAs, nine (38%) had an occluded PV. However, in the 133 cases with a normal anatomy of the epididymis (patients with cryptorchidism, and fetuses), the PV was patent in 46 (35%). Bica and Hadziselimovic [14] reported 88.7% patency of the PV in cases with an EA, and 45.5% patency in those with an epididymis of

TABLE 4 The incidence, *n* (%), of anatomical relations regarded as normal between the testis and the epididymis (types I and II) or as anomalous (types III–V), and the patency or occlusion of the PV, among the three groups; fetuses, and patients with cryptorchidism treated with hCG (+) or not (hCG–)

Groups	Types		PV	
	I and II	III–V	Patent	Occluded
Fetuses	43 (32)	2 (4)	4 (5)	41 (42)
hCG+	42 (32)	23 (47)	43 (52)	22 (22)
hCG–	48 (36)	24 (49)	36 (43)	36 (37)
Total	133 (100)	49 (100)	83 (100)	99 (100)

normal appearance, results very similar to the present findings.

Turek *et al.* [17] questioned the reported high incidence of EAs associated with cryptorchidism [4,13]; they regarded it as a consequence of the lack of definition of the normal anatomical pattern of the epididymis. Even with care when interpreting the normal pattern of the epididymal anatomy, we found EAs in 47 (35%) patients with cryptorchidism and in only two (4%) of the fetal testes (the control group), an incidence almost nine times higher. In previous similar studies the control groups comprised patients with congenital anomalies, e.g. inguinal hernia or hydrocele [7,14], with no study reported in fetuses with testes positioned in the scrotum as a control group. Although this control group is not ideal, it is probably the best to date.

In cases of cryptorchidism where the testis was in the internal inguinal ring or in the abdomen, there were EAs in 34%. Of the 105 cases of testes in the inguinal canal or in the region of the external inguinal ring, there were EAs in 34%, with no statistically significant difference between these groups. In the present sample of testes with cryptorchidism, the testicular location was not a factor that correlated with the occurrence of EAs.

Also, from Table 1 it can be inferred that there appears to be no bias towards treating boys with hCG who had more inferiorly positioned testes, because the patients were randomly assigned for treatment or not. It was reported that lower testes might be more likely to be associated with a closed PV and/or a normal epididymis [3,4,19,20]. Nevertheless, our data provide no evidence that hormone treatment causes closure of the PV and 'normalization' of the epididymis.

The main conclusions from the present study are: (i) in the three groups (fetuses, patients with cryptorchidism treated with hCG, or not) EAs were more frequent when the PV was patent; (ii) the patency of the PV and the incidence of EAs was more frequent in patients with cryptorchidism than in fetuses (control); (iii) the existence of EAs did not influence testicular migration in patients treated with hCG.

ACKNOWLEDGEMENTS

Supported by grants from the National Council of Scientific and Technological Development (CNPq) and Foundation for Research Support of Rio de Janeiro (FAPERJ), Brazil.

CONFLICT OF INTEREST

None declared. Source of funding: Governmental.

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Abbreviations: PV, processus vaginalis; EA, epididymal anomaly.