

Effectiveness of Hormonal Therapy for unilateral and bilateral Undescended testis

Khalil Dagher, Isaac Mhanna. Ayman Harfoush

Department of Urology, Tishreen University Hospital, Latakia, Syria.

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Abstract-

➤ Background :

The importance of our study comes from the role of conservative treatment of undescended testis in minimizing the need of invasive procedures and anesthesia. Early treatment of undescended testis reduces future complications like sterility and the increase of occurrence of malignancies.

➤ Objective :

Our study aims to evaluate the conservative treatment of undescended testis at the age of 6 months – 3 years.

➤ Patients and Methods :

Our study is prospective study. We included patients between 6 months to 3 years old with unilateral or bilateral undescended testis who visited urology clinic at Tishreen University Hospital between October 2019 and October 2021. 129 children were included and were divided according to their ages into 4 groups : Group 1: 48 children at the age of 6-18 months. Group 2: 35 children at the age of 13-18 months. Group 3: 28 children at the age of 19-24 months. Group 4: 18 children at the age of 25-36 months.

A medical history was taken and clinical examination with ultrasonography were conducted. The study of unilateral and bilateral undescended testis was conducted separately according to location, which side the testis was on, age and side effects.

➤ Results :

Ages of patients ranged between 6 and 36 months (mean 16 months). 87 patients had unilateral undescended testis (67,4%) (63 on the left side (72,4%) and 24 on the right side (27.6%)), and 42 patients had bilateral undescended testis (32.6%).

All patients were treated with B-HCG and their response to treatment was checked after 1,3,and 6 months. Response was statistically higher when age was lower than 18 months (60%) with P value of 0.011. Primary location of testis played a role in the probability of hormonal treatment success with higher partial or complete response to hormonal treatment. In case of retractile testis (92.9%) and suprascrotal testis (50%) with P value of 0.001. By comparing results after 6 months we found that success ratio in undescended testis on the right side (49.2%) were higher than the left side (29.2%) and the results were close to being statistically important P value of

0.092. By comparing results after 6 months between unilateral and bilateral groups , we found that success ratio was statistically higher in patients with bilateral undescended testis(33.3%) compared to unilateral (12.6%) with P value of 0.001.

➤ Conclusion:

Hormonal therapy of undescended testis was more effective at the age between 6 to 18 months. Partial or complete response ratio was higher in cases with retractile testis and suprascrotal testis, and minimal to zero in patients with impalpable testis. The response ratio was higher in undescended testis on the right side than the left side. As the treatment went further, there was low occurrence of side effect of hormonal treatment.

Index Terms- Undescended testis, unilateral, bilateral, hormonal therapy, infants.

I. INTRODUCTION

Normal position of the testis is inside the scrotum, where the center of the testis is at or below the border between the upper and lower half of the scrotum [1]. It descends to the scrotum usually between 25-35 weeks of gestation [2]. Testicular position is classified as intra abdominal, inguinal, supra-scrotal, high scrotal, and scrotal according to the process of testicular descent [3,4]. Undescended testis is stoppage of testis at any point of the normal tract of descending between abdominal cavity and scrotum[5]. It might be located in an abnormal extrascrotal position outside the normal tract of descending and then it's called ectopic testis[6]. Undescended testis is a congenital condition where one or both testis aren't located inside the scrotum at birth and can't be moved to normal location by manual manipulation [7]. It's found in 3% of newborn males at the end of

pregnancy and more than 30% of premature newborns which makes it the most common genital congenital condition of males at birth [8,9]. Its prevalence is 5.9% at birth, 2.4% at 3 months old, 6.7% at one year old [10]. Unilateral undescended testis is more common than bilateral undescended testis [6]. 70% of undescended testis move to their normal location within the first year (mostly during the first 3 months), the number of boys whose condition persists remains constant at 1% [7]. Expectancy of full spontaneous descending during the first 3 months of life depends on: Low birth weight, bilateral undescended testis, normal scrotal anatomy, low point of location along the normal descending tract [6]. Long term complications of undescended testis include torsion of the testis, malignancies, infertility and sterility [11,12]. There is evidence to support that undescended testis is associated with decreased testicular hormone production later in life. It has been shown that undescended testis impairs long-term Sertoli cell function, but may also affect Leydig cells [13]. When diagnosed, therapeutic options include monitoring, hormonal or surgical treatment [6]. With clinical approach, choosing the primary treatment depends on age and location of undescended testis [6]. Children at one year old with a testis at a lower location with a high probability of spontaneous descending can be monitored [5]. Hormonal and surgical treatments depend primarily on the location and the appearance of undescended testis [14]. Hormonal therapy with Luteinizing Hormone Releasing Hormone agonists (LHRH agonists) and/or Human Chorionic Gonadotropin (HCG) increases free Androgen levels which induces testis descending by activating thalamic-pituitary-gonadal axis. B-HCG induces Leydig cells production of testosterone while Gonadotropin-Releasing Hormone (GNRH) induces pituitary production of Luteinizing Hormone (LH) [6]. The dosage of HCG is 50 IU/kg body weight intramuscularly twice a week for 3-5 weeks (total dosage of 6000-9000 IU)[15]. The treatment success rates of hormonal therapy are higher in retractile testis, testis under the superficial inguinal ring, bilateral undescended testis, and low androgen levels [6]. However, HCG therapy can cause germ cells apoptosis, penile growth, pubic hair, frequent erection, behavior problems, and injection site pain up to 75% of patients [16]. Hormonal therapy is contraindicated in patients with previous surgical intervention history on the testis [6]. Surgical options include numerous techniques of orchidopexy or orchiectomy [5].

Objectives:

Our main aim is to assess the results of conservative treatment of undescended testis at age between 6 months old and 3 years old.

The minor aims include assessment of the effect of hormonal dosage in some children and assessment of side effects of conservative treatment.

Patients and Methods:

Our study is prospective study. We included patients between 6 months to 3 years old with unilateral or bilateral undescended testis who visited urology clinic at Tishreen University Hospital in Latakia between October 2019 and October 2021. 129 children were included and were divided according to their ages into 4 groups :

Group 1: 48 children at the age of 6-18 months. Group 2: 35 children at the age of 13-18 months. Group 3: 28 children at the age of 19-24 months. Group 4: 18 children at the age of 25-36 months.

A medical history was taken and clinical examination with sonography were conducted. The study of unilateral and bilateral undescended testis was conducted separately according to location, which side the testis was on, age and side effects. All included patients took 1500 IU of B-HCG per week for 3 weeks, and were monitored to assess response after 1, 3 and 6 months.

Inclusion criteria:

Children with undescended testis at age of 6 months old - 3 years old

Exclusion criteria:

1- Existence of hormonal therapy contraindications. 2- Undescended testis with inguinal hernia.

- 3- Abdominal testis.
- 4- Atrophic testis.
- 5- Ectopic testis.
- 6- Previous surgical intervention.

Statistical Analysis

Descriptive Statistics:

Quantitative variables: By central tendency measure and dispersion.

Qualitative variables: By frequencies and percentages.

Inferential Statistics:

Chi-Square test was used to find the relationship between the qualitative variables.

Independent T Student test was used to determine any statistically significant difference between the means in two unrelated groups.

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For all the tests conducted in the study, p -value < 0.05 was considered to indicate statistical significance. The data was analyzed using IBM® SPSS® (version 20)

Results:

A total of 129 cases were studied. Patients had either unilateral or bilateral undescended testis. Their ages ranged between 6 - 36 months (The mean of age was 16 months old). In table 1 we present the distribution of the sample's ages across 4 groups. The highest percentage (37.2% , 48 cases) was for patients between 6-12 months old , 2nd group included patients at age of 13-18 months old (35 cases, 27.1%), 3rd one included patients at age of 19-24 months old (28 cases, 21.7%), and the last one was for patients between 25-36 months old (18 cases, 14%).

87 (67.4%) patients had unilateral undescended testis and 42 (32.6%) patients had bilateral undescended testis.

Table 2 shows the distribution of patients with unilateral undescended testis according to their ages. 30 patients (34.55%) were between 6-12 months old, 23 patients (26.4%) were between 13-18 months old ,18 patients (20.7%) were between 19-24 months old ,and 16 patients (18.4%) were between 25-36 months old.

Unilateral undescended testis was found more in right side (63 cases, 72.4%) than the left one (24 cases, 27.6%).

Table 3 shows the distribution of patients with unilateral undescended testis according to the testis location. Suprascrotal testis was found in (28 cases, 32.2%), Retractable testis was found in (25 cases, 28.7%), Testis in inguinal duct was in (18 cases, 20.7%) ,and testis at a high location was found in (16 cases, 18.4%).

By clinical examination on the studied sample , 67 cases of unilateral undescended testis were palpable (77%) and 20 ones were impalpable (23%).

All patients underwent hormonal therapy with 1500 IU. of B- HCG per week for 3 weeks, and then were monitored to assess response after 1, 3 and 6 months.

Table 4 shows that response to treatment is higher at 6 months after therapy than at the beginning of the therapy.

Table 5 shows higher response ratio to treatment in patients at age 18 months or less with statistically significant importance (P -value = 0.032).

In Table 6 we present that the primary location of testis had a role in probability of hormonal treatment success. It shows higher response ratio to treatment in patients with retractile testis and suprascrotal testis (P value = 0.001).

Table 7 shows higher response ratio in undescended testis on the right side than the left one , and the results were close to being statistically important P value of 0.092.

As for bilateral undescended testis, Table 8 shows the distribution of patients with bilateral undescended testis according to their ages. 18 patients (42.9%) were between 6-12 months old ,12 patients (26.6%) were between 13-18 months old, 10 patients (23.8%) were between 19-24 months old , and 2 patients (4.8%) were between 25-36 months old.

Table 9 explains the distribution of patients with bilateral undescended testis according to the testes locations. suprascrotal testes were the most common (35.8%, 15 cases) followed by patients with retractile testes (21.4% , 9 cases), then the patients with one suprascrotal testis and the other in inguinal duct (19%, 8 cases), after that the patients with one testis in high location and the other one in the inguinal duct (14.3% , 6 cases), finally both of the testes are intra inguinal duct (9.5% , 4 cases) .

Table 10 shows that response to hormonal treatment in patients with bilateral undescended testes was higher after 6 months than at the beginning of the treatment.

Table 11 shows that response to treatment was higher in patients at age less than 18 months with statistically significant importance (P value = 0.011).

Table 12 shows that the primary location of the testes had a role in the probability of the success of hormonal treatment with higher response ratio in patients with retractile testes and suprascrotal testes (p value = 0.001).

Table 13 shows that success ratio was higher in bilateral undescended testes than in unilateral undescended testis with statistically significant importance (P value = 0.001).

Table 14 shows that partial response ratio in impalpable unilateral or bilateral undescended testis was too low and there was no full response (descending to the scrotum).

Table 15 shows that side effects of hormonal therapy happened at the beginning of the treatment and decreased by the time of treatment, until they disappeared after 6 months of treatment.

Discussion:

All patients were treated with B-HCG and monitored after 1, 3 and 6 months of treatment.

Response to treatment was higher with statistically significant importance when age was less than 18 months.

The primary location of the testis had a role in the probability of the success of hormonal treatment with higher partial or full response to treatment in retractile and suprascrotal testis.

According to the side of the undescended testis ,we found higher success ratio in patients with right undescended testis than others with left undescended one after 6 months of treatment.

Partial response ratio to treatment in impalpable unilateral or bilateral undescended testis was too low and there was no full response to treatment.

As for side effects, we found penile enlargement in 18.6% of cases, an increase in hair distribution and scrotal wrinkles in 38% of cases ,and both of them were found in 24.8% . While no side effects were found in 18.6% of cases.

By comparing our study to the international studies :

Our study included 129 patients aged between 6-36 months old, 87 patients were with unilateral undescended testis and 42 ones were with bilateral undescended ones, which was a close number to Biers et al [17] study (145 cases; 99 ones were unilateral

undescended testis and 46 cases were bilateral undescended ones) ,and to Ležakov et al [18] study sample (101 cases; 56 cases were unilateral undescended testis and 45 cases were bilateral ones).

Success ratio of conservative treatment of bilateral undescended testis was 33% in our study , which corresponds with Biers et al study ratio (30% , ages were between 1-11 years old), Bakker et al [19] study ratio (23% , ages were between 1-4 years old), Abacı et al [20] study ratio (23% , ages were between 1-2 years old) and Ležakov et al [18] study ratio (36% , ages were between 6months – 8 years).

We found that success ratio of conservative treatment of unilateral undescended testis was 12.6% in our study , 32.3% in Biers et al study [17], 17.6% in Ležakov et al study [18], 17.4% in Bakker et al study [19], and 19% in Abacı et al study [20]. In our study we found that that response to treatment was higher in patients at age less than 18 months with statistically significant importance (P value = 0.011), while Ležakov et al found in their study that response to hormonal therapy treatment was highest amongst oldest group, this difference may be related to the difference in the studied age groups between these two studies (6 months to 3 years old in our study vs 6 months to 8 years old in Ležakov et al study).

Conclusions:

Hormonal therapy of undescended was more effective at age between 6-18 months old.

Full or partial response ratio was higher in retractile and suprascrotal testis and rare to nonexistent in impalpable testis.

Success ratio in right undescended testis was higher (most common location was inside the inguinal duct) than the left undescended testis (most common location was in a high location.)

The side effects of hormonal therapy decrease by the time of treatment.

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AUTHORS

First Author – Khalil Dagher, Department of Urology, Tishreen University Hospital, Latakia, Syria.

Second Author – Isaac Mhanna, Department of Urology, Tishreen University Hospital, Latakia, Syria.

Third Author – Ayman Harfoush, Department of Urology, Tishreen University Hospital, Latakia, Syria.

Correspondence Author – kh.dagher@hotmail.com

Table 1: Distribution of the patients in those groups according to their ages.

Age group (months)	Number of cases	Percentage
6-12	48	37.2%
13-18	35	27.1%
19-24	28	21.7%
25-36	18	14%
Total	129	100%

Table 2: Distribution of patients with unilateral undescended testis according to their ages.

Age group (months)	Number of cases	Percentage
6-12	30	34.5%
13-18	23	26.4%
19-24	18	20.7%
25-36	16	18.4%
Total	87	100%

Table 3: Distribution of patients with unilateral undescended testis according to the testis location.

Location	Number of cases	Percentage
Retractile	25	28.7%
Suprascrotal	28	32.2%
Inside inguinal duct	18	20.7%
High location	16	18.4%
Total	87	100%

Table 4: Response to treatment in patients with unilateral undescended testis after 1, 3 and 6 months of therapy.

		Full response	Partial response	Failure of therapy
After 1 month	No.	6	15	66
	%	6.9%	17.2%	75.9%
After 3 month	No.	9	23	55
	%	10.3%	26.4%	63.2%
After 6 month	No.	11	27	49
	%	12.6%	31%	56.3%

Table 5: A comparison of hormonal therapy results between the two age- groups.

		Any kind of response	Failure of therapy	P Value
6-18 months old	No.	28	25	0.032
	%	52.8%	48.2%	
19-36 months old	No.	10	24	
	%	29.4%	70.6%	

Table 6: A comparison of hormonal therapy results according to the primary position of the testis.

		Any kind of response	Failure of therapy	P Value
Retractile	No.	16	9	0.001
	%	64%	36%	
Suprascrotal	No.	16	12	
	%	57.1%	42.9%	
Inside inguinal duct	No.	4	14	
	%	22.2%	77.8%	
High location	No.	2	14	
	%	12.5%	87.5%	

Table 7: A comparison of hormonal therapy results in unilateral undescended testis according to which side the testis was on.

		Any kind of response	Failure of therapy	P Value
Right	No.	31	32	0.092
	%	49.2%	50.8%	
Left	No.	7	17	
	%	29.2%	70.8%	

Table 8: Distribution of patients with bilateral undescended testis according to their ages.

Age group (months)	Number of cases	Percentage
6-12	18	42.9%
13-18	12	26.6%
19-24	10	23.8%
25-36	2	4.8%
Total	42	100%

Table 9: Distribution of patients with bilateral undescended testis according to testes locations.

Location	Number of cases	Percentage
Retractile	4	9.5%
Both suprascrotal	20	47.6%
Both inside inguinal duct	4	9.5%
Both in a high location	0	0%
One suprascrotal and the other in the inguinal duct	8	19%
One suprascrotal and the other in a high location	0	0%
One in a high location and the other in the inguinal duct	6	14.3%
Total	42	100%

Table 10: Response to treatment in patients with bilateral undescended testis after 1, 3 and 6 months of therapy.

		Full response	Partial response	Failure of therapy
After 1 month	No.	2	8	32
	%	4.8%	19%	76.2%
After 3 month	No.	4	10	28
	%	9.5%	23.8%	66.7%
After 6 month	No.	8	12	22
	%	19%	28.6%	52.6%

Table 11: A comparison of hormonal therapy results between the two age groups.

		Any kind of response	Failure of therapy	P Value
6-18 Months	No.	18	12	0.011
	%	60%	40%	
19-36 Months	No.	2	10	
	%	16.7%	83.3%	

Table 12: A comparison of hormonal therapy results according to the primary positions of the two testes.

		Any kind of response	Failure of therapy	P Value
Retractile	No.	13	1	0.001
	%	92.9%	7.1%	
Both suprascrotal	No.	5	5	
	%	50%	50%	
Both suprascrotal	No.	0	4	
	%	0%	100%	
One suprascrotal and the other in the inguinal duct	No.	1	7	
	%	12.5%	87.5%	
One suprascrotal and the other in the inguinal duct	No.	1	5	
	%	16.7%	83.3%	

Table 13: Response to hormonal therapy of undescended testis that moved down to the scrotum during follow-up, compared to unilateral and bilateral undescended testis groups.

	No. of testis that descended to scrotum	No. of testis that failed to descend	Total	P Value
Bilateral undescended testis	28(33.3%)	56(66.7%)	84(100%)	0.001
unilateral undescended testis	11(12.6%)	76(87.4%)	87(100%)	

Table 14: Response to hormonal therapy of impalpable undescended testis that went down to the scrotum during follow-up, compared to unilateral and bilateral undescended testis groups.

	No. of impalpable testis	Full response	Any kind of response
Bilateral undescended testis	32	0(0%)	2(6.25%)
unilateral undescended testis	20	0(0%)	1(5%)

Table 15: Side effects of hormonal therapy.

Side effect	Number of cases			Percentage		
	1 month	3 months	6 months	1 month	3 months	6 months
Penile enlargement	24	7	0	18.6%	5.42%	0%
Increase of number of hair and scrotal wrinkles	49	12	0	38%	9.3%	0%
Both	32	3	0	24.8%	2.32%	0%
No side effect	24	107	129	18.6%	82.94%	100%