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Efficacy of Oral Ketoconazole in Suppressing Nocturnal Erections after Urethroplasty in Hypospadias

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KEYWORDS

Ketoconazole, Hypospadias, Urethroplasty

ABSTRACT:

Objective: To Evaluate efficacy of oral ketoconazole in suppressing Nocturnal Erections after Urethroplasty in Hypospadias

Material & Methods: From March 2025 to July 2025, a cross-sectional analytical study was conducted at Federal Institute of Health Sciences, Lahore, Pakistan. The Board of Advanced Studies and Research, Institutional Review Board, and Scientific Committee of Federal Institute of Health Sciences gave their approval to this. Parents and research participants provided their informed consent or approval. Criteria for inclusion and exclusion: All male patients between the ages of 4 and 40 were covered. The study excluded patients with co-morbid conditions such as diabetes mellitus and hypertension, those who had undergone prior surgery, and those who had psychological difficulties.

Results: Two equal groups of 80 patients each were formed. The ketoconazole group's mean age was 8.28±2.30 years, whereas the control group's was 9.42±2.91 years. During the initial follow-up, 26 patients (65%) in the ketoconazole group had erection relief, while 16 patients (40%) reported pain reduction. This is in contrast to the control group, where all patients experienced erections and six patients (15%) reported pain relief. The statistical significance of this was $p < 0.001$. Comparing the ketoconazole group to the control group at the second follow-up, 30 patients (75%) saw an improvement in erections, and 26 patients (65%) experienced a reduction in discomfort ($p=0.019$).

Conclusion: Ketoconazole successfully prevented postoperative erections, and many patients had pain alleviation with positive results

Introduction

A congenital condition known as hypospadias occurs when the external urinary meatus in the glans penis is not positioned normally. On the penis' ventral surface, the meatus may be located in a variety of places. Various surgical techniques have been documented to address this abnormality. In these individuals, painful erections during the postoperative phase are a frequent issue[1,2]. In order to establish a straight penis without chordee, meatus in its normal or nearly normal location in the glans, and a cosmetically acceptable look, surgery

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for hypopadias has evolved throughout the years[3,4]. Several surgical techniques can be used to treat proximal hypopadias; depending on where the meatus is located, these techniques may include one or two stages of restoration[5,6]. Every operation has benefits and drawbacks, but none of them have gained widespread popularity[7]. This is demonstrated by the more than 300 documented surgical techniques performed to treat hypospadias[8,9]. A variety of therapies, including dorsalnerve blocks, refrigerant sprinkles, sedatives, and amyl nitrate, are used to prevent postoperative penile erections. They are ineffective, though. Ketoconazole is an anti-androgenic medication that reduces the synthesis of testosterone. Three times a day, a high oral dosage of 400 mg of ketoconazole inhibits adrenal and testicular androgen, which lowers testosterone levels. Ketoconazole has an additional mechanism of action since it is also an androgen receptor blocker[10]. Since ketoconazole has been shown to be a safe medication with anti-steroidogenic side effects, patients use it to prevent erections during the postoperative phase[11]. Ketoconazole is used in the literature to treat painful erections, particularly in individuals with ischemic painful erections. 12–14 The purpose of this study was to record the frequency of postoperative penile erections, the severity of the discomfort they caused, and the patients' stated level of pleasure. It was also anticipated that the addition of oral ketoconazole following surgery would lower the risk of urethra-cutaneous fistula development.

Material & Methods

From March 2025 to July 2025, a cross-sectional analytical study was conducted at Federal Institute of Health Sciences, Lahore, Pakistan. The Board of Advanced Studies and Research, Institutional Review Board, and Scientific Committee of Federal Institute of Health Sciences gave their approval to this. Parents and research participants provided their informed consent or approval. Criteria for inclusion and exclusion: All male patients between the ages of 4 and 40 were covered. The study excluded patients with co-morbid conditions such as diabetes mellitus and hypertension, those who had undergone prior surgery, and those who had psychological difficulties. A sample size was determined using the OpenEpi.com online sample size calculator and the previously reported effect size of Hoeh MP12's ketoconazolein-relieving erection (87.5% vs. 12%). At 99% confidence level and 90% power, a minimum of 80 patients (40 in each group) were needed. The method employed was non-probability sequential sampling. Two groups of patients were formed: the ketoconazole intervention group and the control group. Every patient received an explanation of the ketoconazole medication and its side effects. The groups were distributed by lottery using sealed envelopes. Patients in the intervention group received ketoconazole (2 mg/kg) once daily through the seventh postoperative day and two days prior to surgery. Postoperative days 5, 8, and 10 were used to complete a questionnaire on penile erections, postoperative pain level, and overall satisfaction. The software SPSS version 21 was used for data analysis. For quantitative factors such as age, the mean and standard deviation were computed. Penile erection frequency and percentages, postoperative discomfort severity, and overall satisfaction were calculated. The chi square test was used, and a p-value of less than 0.05 was considered significant.

Results

Two equal groups of 80 patients each were formed. The ketoconazole group's mean age was 8.28±2.30 years, whereas the control group's was 9.42±2.91 years. During the initial follow-up, 26 patients (65%) in the ketoconazole group had erection relief, while 16 patients (40%) reported pain reduction. This is in contrast to the control group, where all patients experienced erections and six patients (15%) reported pain relief. The statistical significance of this was $p < 0.001$. Comparing the ketoconazole group to the control group at the second follow-up, 30 patients (75%) saw an improvement in erections, and 26 patients (65%) experienced a reduction in discomfort ($p=0.019$). Comparing the ketoconazole group to the control group at the third follow-up, 34 (85%) of the patients experienced an erection and 30 (75%) saw a reduction in discomfort ($p <0.001$). Details on follow-up are included in Tables I, II, and III. 18 (45%), 22 (55%) and 23 (57.5%) patients/parents expressed satisfaction on the first, second, and third follow-ups. In the ketoconazole group, 18 patients (45%) had side symptoms (table IV). The control group experienced a 2.5% urethrocutaneous fistula rate, whereas the ketoconazole group did not have any fistula.

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Table I: Erection and Pain Status at First Follow-Up(5th Postoperative Day)

Variables	Ketoconazole Group	Control Group
Erection Relieved	26(65.0%)	0(0.00%)
Pain Relieved	16(40.0%)	06(15.0)
Mild Pain	15(37.5%)	20(50.0%)
Moderate Pain	07(17.5%)	06(15.0%)
Severe Pain	02(5.0%)	08(20.0%)

Table II: Erection and Pain Status at Second Follow-Up(8th Postoperative Day)

Variables	Ketoconazole Group	Control Group
Erection Relieved	30(75.0%)	0(0.00%)
Pain Relieved	26(65.0%)	10(25.0)
Mild Pain	12(30.5%)	18(45.0%)
Moderate Pain	02(5.0%)	07(17.0%)
Severe Pain	0(0.0%)	05(12.5%)

Table III: Erection and Pain Status at Third Follow-Up(10th Postoperative Day)

Variables	Ketoconazole Group	Control Group
Erection Relieved	34(85.0%)	00(0.00%)
Pain Relieved	30(70.0%)	14(35.0)
Mild Pain	10(25.0%)	20(50.0%)
Moderate Pain	00(0.0%)	04(10.0%)
Severe Pain	00(0.0%)	02(5.0%)

Table IV: Side Effects of Ketoconazole(n=40)

Variables	Number (%)
Headache	5(12.5%)
Nausea	6(15.0%)
Feet Swelling	2(5.0%)
Pruritus	3(7.5%)
Frequent Urination	2(5.0%)
Jaundice	4(10.0%)

Discussion

When ketoconazole was added to the treatment of individuals with hypopadias, this study found a high success rate. This is a difficult abnormality, and there are several debates over the best surgical technique and when to perform it. At the moment, the procedure is best done in infancy[15]. Between 8 and 9 years old was the mean age of the patients in both groups in this study. According to a few publications, the likelihood of wound dehiscence is higher in adult patients[16,17]. one of the causes of penile erection procedure failures. Ketoconazole prevents progesterone from being

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converted to testosterone[18,19]. Ketoconazole was successful in preventing postoperative erections, according to earlier research. According to a research, 23% of individuals using ketoconazole experienced pain-free erections. 71% of inpatients who did not get ketoconazole reported having uncomfortable erections. The use of ketoconazole to prevent erections was suggested by both trials[11,13]. Comparable outcomes were seen in our trial, with 85% fewer erections and 75% less discomfort, both of which were statistically significant. Ketoconazole did not, however, effectively reduce erections, according to a randomized double-blind research, as 84% of patients receiving the medication experienced erection episodes, which was comparable to the placebo group's 83%. That RCT's sample size was insufficient[20]. Our research yielded compelling evidence supporting the use of ketoconazole with a larger sample size.

Limitations

There were a variety of age groupings among the research participants, most of whom were older kids. A better scientific investigation would include a bigger sample size of individuals with identical hypospadias in a homogenous younger age range. A multicenter study might be used for this.

Conclusion

After penile reconstruction surgery, ketoconazole successfully prevented postoperative erections, and many patients had pain alleviation with positive results.

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