

Curative effect of surgery in combination with compound xuanju capsule in treating subclinical varicocele induced infertility.

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Abstract

Objective: To discuss over the clinical effect of treating subclinical varicocele induced infertility with varicocelectomy in combination with compound Xuanju capsule and the effect of the therapy on levels of sex hormone and anti-sperm antibody (AsAb).

Methods: Eighty-eight patients with subclinical varicocele were selected and randomly divided into a treatment group and a control group (N=44). Patients in the control group underwent varicocelectomy, while patients in the treatment group were given compound Xuanju capsule besides surgery. Clinical effects, the level of sex hormone and the level of AsAb of two groups were observed and analyzed.

Results: The clinical effective rate of the treatment group was 84.09%, much higher than 68.18% in the control group. Sperm density, the percentage of forward movement sperm and sperm survival rate of the control group were $(29.32 \pm 3.48) \times 10^6$, (45.68 ± 3.03) and (57.17 ± 3.42) respectively after treatment, much higher than the values before treatment, and the differences had statistical significance ($P < 0.05$); the percentage of normal morphological sperms, sperm density, the percentage of forward movement sperm and sperm survival rate of the treatment group were much higher to those of the control group, and the differences had statistical significance ($P < 0.05$); except for semen volume, the other indexes of the treatment group were superior to those of the control group after treatment, and the differences had statistical significance ($P < 0.05$). The hormone level of the treatment group was higher than that of the control group, and the difference had statistical significance ($P < 0.05$); the reduction amplitude of serum AsAb positive rate of the treatment group was more obvious than that of the control group, and the difference had statistical significance ($P < 0.05$).

Conclusions: Surgery in combination with compound Xuanju capsule can effectively improve semen quality and sexual hormone level and reduce the level of serum AsAb in the treatment of subclinical varicocele.

Keywords: Surgical treatment, Compound Xuanju capsule, Infertility.

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Introduction

Varicocele can severely affect sperm activity. According to investigations, the incidence of varicocele is 15% ~ 20% among male teenagers, but is 30% ~ 40% among infertile males; hence it is considered as the major reason for male infertility [1,2]. With the development of international medical technology, patients without varicocele are also found with widening of spermatic vein and blood reflux. Such a condition is named as subclinical varicocele (SVC). Like varicocele, SVC can also induce local congestion and temperature increase of testis as well as change of local internal environment of testis, thereby weakening fertility [3,4]. Surgery is the most effective method for treating subclinical varicocele; but not sperm quality of all patients can be significantly relieved after surgery and some researches even suggest that, postoperative sperm quality decreases instead [5,6]. Therefore, it is urgent to find out a high-efficient and widely acceptable treatment method. Xuanju, the main component of compound Xuanju

capsule, has the functions of tonifying kidney, This study treated 44 patients with subclinical varicocele induced infertility using high ligation and compound Xuanju capsule, compared the changes of sperm quality as well as levels of sex hormone and AsAb before and after treatment, and discussed over the effect of subclinical varicocele on sperm quality and the possible action mechanism [7-9].

Materials and methods

Research subjects

Eighty-eight patients suffering from subclinical varicocele who received treatment in Zhengzhou People's Hospital, Henan, China from February 2010 to February 2011 were selected as research subjects. The inclusive criteria were as follows: had a history of infertility for more than 12 months, normal sexual life, be able to undergo surgery within three months, and confirmed by color Doppler ultrasonic examination. Patients

with infertility caused by female factors or with semen quality reduction caused by prostatitis, urethritis, endocrine disease, sperm duct block and systemic disease were excluded. This study has been approved by the ethical committee of Zhengzhou People's Hospital, Henan, China. All patients signed informed consent.

Methods

All patients underwent high ligation of spermatic vein in general anesthesia under laparoscope. Veins that were 3 ~ 5 cm above internal ring were expanded, ligated and cut off. Damage on artery needed to be avoided. If it was bilateral varicocele, then another side was treated in the same way. There were no severe complications after surgery. After the patients and their wives were informed and agreed, the patients were randomly divided into a control group and a treatment group. Patients in the control group underwent surgery only, while patients in the treatment group orally took compound Xuanju capsules (Zhejiang Shiqiang Pharmaceutical Co., Ltd., China, 600 Z 22640) additionally, three grains (0.42 g/grain) once, three times each day, for three months. The seminal fluid and hormone of all patients were analyzed in 6 to 9 months after surgery. The fertilization condition of their wives was followed up by outpatient service or phone.

Observation indexes

Analysis of semen: All patients underwent conventional semen examination before treatment and in the 6th month after treatment. The parameters of semen were analyzed using WLJ-9000 Color sperm quality detection system. Before examination, patients were asked to suppress sensual passion for about four days. Semen collected from patients was placed in sterilized and dried measuring glasses. Then the semen was put in a constant temperature (37°C) water bath box for liquidation. Observation content included the total number of sperms, sperm density, percentage of forward movement sperm, activity of sperm and the proportion of normal morphological sperms.

Analysis of hormone: All patients underwent hormone determination before and after treatment. Fully automatic luminescence labeling immunoassay analyzer and corresponding reagents (Abbott Laboratories, USA) were used. The operation strictly followed the instructions on the kit. Normal value of hormone was as follows: Follicle-Stimulating Hormone (FSH): 1 ~ 8 IU/L, luteinizing hormone: 2 ~ 12 IU/L, testosterone (T): 9.4 ~ 37 ng/L.

Analysis of AsAb: The positive rate of AsAb was detected using Enzyme Linked Immunosorbent Assay (ELISA). The kit used was provided by Beijing Aikang Biotech Co., Ltd. And Lihua Bioengineering Co., Ltd., China. The operations were performed as per the instructions on the kit.

Evaluation criteria of curative effect: Curative effect was evaluated referring to the evaluation criteria of curative effect mentioned in Clinical Study on Traditional Chinese Medicine (1993, 1st edition) released by the Ministry of Health of the

People's Republic of China. If the density of sperm was over $15 \times 10^6/\text{ml}$, the proportion of forward movement sperms was over 32%, sperm activity was higher than 40%, and (or) their mates were pregnant during treatment, then patients were determined as cured. If sperm density improved for more than 50% after three months of treatment, the activity of sperm improved for more than 50% or the proportion of forward movement sperm improved for 25% ~ 50%, the treatment was determined as significantly effective. If the density of sperm improved for 25% ~ 50%, the activity of sperm improved for 25% ~ 50%, or the proportion of forward movement sperm improved for 25% ~ 50%, then the treatment could be determined as effective. But if the density of sperm improved for less than 25%, the activity of sperm improved for less than 25%, and the proportion of forward movement sperm improved for less than 25% as well, or those indexes even decreased compared to before treatment, then the treatment was determined as ineffective. Overall effective rate could be calculated using the formula of overall effective rate=(the number of cure cases + the number of significantly effective cases + the number of effective cases)/total number of patients.

Statistical method

Data were analyzed by SPSS ver. 20.0. Measurement data were expressed as mean \pm SD. Comparison between groups was performed using t test. Enumeration data were processed by chi-square test. $P < 0.05$ indicated the difference had statistical significance.

Results

Comparison of general data

In the treatment group, there were 44 patients, aged 24 ~ 38 years old (average 26.5 ± 4.6 years old); there were 32 cases of left-side varicocele, 4 cases of right-side varicocele, and 8 cases of bilateral varicocele; there were 7 cases of level 0 varicocele, 23 cases of level I varicocele, and 14 cases of level II varicocele. In the control group, there were 44 patients as well, aged 26 ~ 39 years old (average 26.8 ± 5.9); there were 30 cases of left-side varicocele, 5 cases of right-side varicocele and 9 cases of bilateral varicocele; there were 6 cases of level 0 varicocele, 25 cases of level I varicocele, and 13 cases of level II varicocele. There was no statistically significant difference in general data such as age and disease condition between the two groups; hence the results were comparable.

Analysis results of semen of patients in two groups before and after treatment

The control group showed insignificant changes in the semen volume and proportion of sperm with normal form, and the differences had no statistical significance ($P > 0.05$); but sperm density, the proportion of forward movement sperms, and sperm survival rate of the control group after treatment were significantly higher than those before treatment, and the differences had statistical significance ($P < 0.05$). Sperm volume of patients in the treatment group showed insignificant change

after treatment ($P>0.05$); the percentage of sperm with normal form, sperm density, the proportion of forward movement sperms and sperm survival rate of the treatment group after treatment were much higher than those before treatment

($P<0.05$). Except for semen volume, the other indexes of the two groups demonstrated statistically significant differences ($P<0.05$; Table 1).

Table 1. Comparison of semen parameters between two groups (mean \pm SD).

Group		Semen volume(ml)	Sperm with normal form(%)	Sperm density($\times 10^6$)	Forward movement sperm proportion (%)	Sperm survival rate (%)
Treatment group (N=44)	Before	3.51 \pm 0.31	27.41 \pm 2.42	15.82 \pm 3.73	27.56 \pm 17.75	42.53 \pm 3.29
	After	3.62 \pm 0.34	53.69 \pm 59.21*#	35.24 \pm 6.73*#	53.21 \pm 12.96*#	65.95 \pm 3.83*#
Control group (N=44)	Before	3.62 \pm 0.28	26.95 \pm 1.53	15.73 \pm 2.67	27.68 \pm 17.18	41.83 \pm 4.01
	After	3.66 \pm 0.37	27.19 \pm 3.67	29.32 \pm 3.48*	36.68 \pm 16.24*	57.17 \pm 3.42*

Note: * means $P<0.05$ compared to before treatment; # means $P<0.05$ compared to control group

Analysis results of sexual hormone levels between two groups

The T level of patients in the control group showed a remarkable increase after treatment, and the difference was statistically significant ($P<0.05$). The FSH and LH levels of the control group both declined and the difference had no statistical significance ($P>0.05$). T level of patients in the treatment group had a significant improvement, but the FSH and LH levels showed significant decline, and the differences had statistical significance ($P<0.05$). The improvement of sexual hormone levels of the treatment group was better than that of the control group, and the difference had statistical significance (Table 2).

Table 2. Comparison of sexual hormone levels between two groups (mean \pm SD).

Group		T(μ g/l)	FSH(IU/L)	LH(IU/L)
Treatment group (N=44)	Before	6.34 \pm 1.38	4.63 \pm 0.24	12.64 \pm 4.42
	After	18.56 \pm 5.85*#	1.78 \pm 0.62*#	6.75 \pm 1.34*#
Control group (N=44)	Before	6.37 \pm 1.43	4.58 \pm 0.19	12.28 \pm 4.72
	After	14.29 \pm 3.43*	3.53 \pm 0.47	11.34 \pm 3.85

Note: * means $P<0.05$ compared to before treatment; # means $P<0.05$ compared to control group.

Changes of AsAb of two groups

The positive rate of serum AsAb of the treatment group was 90.91% before treatment and 27.27% after treatment. As to the control group, the percentage was 88.64% and 52.27% respectively. The change of the positive rate of serum AsAb of the two groups had statistical significance ($P<0.05$).

Discussion

Male infertility refers to infertility of wife caused by male factor after a couple live together for more than one year and adopts no contraception measures. About 10% of married couples have infertility, of which, 30% is caused by male [10].

Subclinical varicocele is considered as an important factor for male infertility. With the advancement of examination means in recent years, subclinical varicocele has captured more and more attentions from clinical doctors in andrology [11,12]. Like clinical varicocele, subclinical varicocele is induced by blood back flow caused by the lack of or insufficiency of spermatic venous valve [13-15]. The main characteristic of patients with subclinical varicocele is widened internal spermatic vein and blood back flow observed by color doppler flow imaging when there are no obvious pathological changes and examination results are negative; hence it is easily to be ignored clinically [16]. Thus the early diagnosis and treatment of subclinical varicocele are quite necessary.

This study treated subclinical varicocele induced infertility patients with different treatment schemes. Results demonstrated that, sperm density, forward movement sperm proportion and sperm survival rate of patients in the control group were higher after treatment compared to before treatment ($P<0.05$). The percentage of sperm with normal form, sperm density, forward movement sperm proportion and sperm survival rate of patients in the treatment group were much higher after treatment compared to those before treatment ($P<0.05$). Various indexes of patients in the treatment group were much higher than those of the control group ($P<0.05$). Besides, the natural fertilization rate of the treatment group was much higher than that of the control group. It indicated that, surgery in combination with compound Xuanju capsules could effectively improve treatment effect of varicocele.

Testis has endocrine function. FSH is mainly responsible for promoting the development of seminiferous epithelium and spermatogenesis, while LH regulates the synthesis of mesenchymal cell and the release of T cells by acting on interstitial cells and thus accelerates the generation and maturity of sperms. Currently, the research results concerning the relationship between varicocele and internal secretion are inconsistent. Some scholars [17] thought that, varicocele induced hypothalamic-pituitary-gonadal axis disorder was correlated to the injury of leydig cells. Varicocele can damage functions of leydig cells and sertoli cells in testis, leading to the

reduction of hormone level (testosterone inhibin). Such kind of abnormal secretion of hormone can further affect levels of hypophysis LH and FSH, change endocrine environment, and weaken fertility through feedback mechanism. Song Wei et al. [18] found that, serum FSH level of patients significantly decreased and T level had no obvious change after undergoing surgery for varicocele. Ishikawa et al. [19] considered that, serum free T level increased after treatment of varicocele and moreover sperm activity and density were improved. In this study, it was found that, serum FSH and LH levels had significant reduction and serum T level showed obvious increase in the treatment group after surgery, which were statistically different with hormone levels of the control group. It suggested that, surgery in combination with compound Xuanju capsules could reduce levels of serum FSH and LH and improve serum T level, and improve endocrine environment for spermatogenesis in the treatment of clinical-type varicocele induced infertility.

Conclusion

All in all, high ligation in combination with compound Xuanju capsule can relieve disordered sex hormone and AsAb levels and promote the improvement of sperm quality. Therefore, we consider that, high ligation in combination with compound Xuanju capsule is an ideal scheme for treating varicocele and it is worth promotion and application in clinic.

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