

Scrotal Hemorrhage after Testicular Sperm Aspiration may be Associated with Phosphodiesterase-5 Inhibitor Administration

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Received date: 22 Sept 2015; Accepted date: 05 Nov 2015; Published date: 09 Nov 2015.

Citation: Zhu Y, Chu Q (2015) Scrotal Hemorrhage after Testicular Sperm Aspiration may be Associated with Phosphodiesterase-5 Inhibitor Administration. J Drug Res Dev 1(2): doi <http://dx.doi.org/10.16966/2470-1009.106>

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Abstract

Scrotal hemorrhage after testicular sperm aspiration (TESA) is uncommon in clinical operation. Unfortunately, two masturbation difficulty males experienced scrotal hemorrhage after TESA associated with phosphodiesterase-5 inhibitor (PDE5i) administration. Till now, reports about such cases are scarce. In this retrospective study, 504 men with TESA operation in Center for Reproductive Medicine, Nanfang Hospital, Southern Medical University were collected. The testis volume, coagulation function were measured. Sonographic examination with Doppler imaging was performed when scrotal hemorrhage unfortunately appeared. The incidence of hemorrhage was 0.0% in the control group and the drug group was 2.6%. The incidence of hemorrhage between two groups was different significantly ($\chi^2=11.308$, $P=0.001$). Given the potential risk of scrotal hemorrhage after the ingestion of PDE5i, it should be cautious to prescribe this medicine when the patient is likely to perform TESA.

Keywords: Scrotal hemorrhage; Testicular sperm aspiration; Phosphodiesterase-5 inhibitor

Introduction

Over the past several decades, in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI) have come into routine practice. On the day of oocyte retrieval, most male were asked to provide sufficient number sperm by masturbation. However, a small part of male, who could ordinarily retrieve sperm using ipsism, unfortunately failed to collect a semen sample by reason of psychologic stress and anxiety. Such patients were given psychological guidance and phosphodiesterase-5 inhibitor (PDE5i). While they were not able to injection with these help, testicular fine needle aspiration (TESA) was last choice. Unfortunately, several males experienced scrotal hemorrhage after TESA associated with PDE5i administration. Surprisingly, we found few azoospermia patients appeared scrotal hemorrhage after biopsy with the same TESA operation. It is assumed that scrotal hemorrhage after TESA may be associated with PDE5i administration. To our knowledge, reports about such cases are scarce. Therefore, this retrospective study was designed to summary the data and responded this question.

Materials and Methods

Study design

From 2012 to 2015, a total of 504 men with TESA operation were included in study. All patients were infertile men who referred to Center for Reproductive Medicine, Nanfang Hospital, Guangzhou, China. This study was approved by the Clinical Medical Local Ethical Review Committee of Southern Medical University.

According to different administration, these 504 men were classified to two groups. One group named drug group was experiment group, and another group was control group. Men in drug group have taken orally PDE5i before TESA. Men in control group only operated TESA, and those operated epididymal sperm aspiration (PESA) or testicular sperm extraction (TESE) was exclusive.

Testicular fine needle aspiration procedure

Testis was firstly local anesthetized using 1 ml lidocaine. A 23 G needle was passed through the scrotal skin. Suction was applied with a 5 ml syringe and the backpressure was maintained by hand. The needle was pushed in different directions into the testicular tissue. Then the needle was slowly removed from the testis tissue while the negative pressure was maintained by hand. Finally, the small tubules recovered by the needle were picking up by the assistant using two pairs of fine tweezers. Sperm in aspirated tissue was searched and retrieved for ICSI or biopsy.

Follow-up

Puncture site was kept dry and clean in three days, and strenuous exercise was avoided in one month. Sonographic examination with Doppler imaging was performed when scrotal hemorrhage unfortunately appeared. If hemorrhage did not self absorb during two weeks, evacuation operation was performed to clean hemorrhage.

Statistical analysis

Calculations were analyzed by using SPSS 19.0 software (SPSS Inc., Chicago, Illinois, USA). All numeric data were presented as the mean value \pm standard deviation. Frequencies were expressed as percentages. The statistical analysis was performed Students t-test between 2 groups, whereas χ^2 -test was used for comparison of proportions. Differences between the values were considered statistically significant when $P<0.05$.

Results

As shown in table 1, there were a total of 504 infertile men with TESA operation from 2012 to 2014. Mean age was 28.63 ± 4.22 years. Mean testis volume was 11.8 ± 2.6 ml. Coagulation function showed there was no difference in two groups. The incidence of hemorrhage was 0.4% in overall men. The control group was present in 0.0%, and the drug group was 2.6%. The incidence of hemorrhage between two groups was different significantly ($\chi^2=11.308$, $P=0.001$).

	Control group	Drug group	Overall	P value
No	428	76	504	
Age (y)	28.40 ± 3.86	29.07 ± 4.11	28.63 ± 4.22	P>0.05
Testis volumn (ml)	12.0 ± 4.3	11.5 ± 2.9	11.8 ± 3.6	P>0.05
Coagulation function				
Thrombin time(s)	15.24 ± 2.11	14.98 ± 2.03	15.11 ± 2.14	P>0.05
Activated partial thromboplastin time(s)	25.71 ± 3.23	26.01 ± 3.17	25.89 ± 3.26	P>0.05
International normalized ratio	0.89 ± 0.23	0.91 ± 0.22	0.90 ± 0.22	P>0.05
Prothrombin time (s)	11.65 ± 1.09	12.02 ± 1.16	11.87 ± 1.18	P>0.05
Fibrinogen (g/L)	2.55 ± 1.03	2.64 ± 1.06	2.62 ± 1.07	P>0.05
Incidence of hemorrhage (%)	0(0.0)	2(2.6)	2(0.4)	χ ² =11.308; P=0.001

Table 1: Characteristics of patients

Comment

TESA, which developed initially from 1992, was a defined method in retrieving sperm for assisted reproduction [1]. Moreover, it was also used to perform testis biopsy. Compared to testicular sperm extraction (TESE), TESA was simplified and with minimal physiological consequences [2].

It was reported that 29% of diagnostic testicular biopsies resulted in intratesticular haematoma formation [3]. However, scrotal hemorrhage was a relatively rare clinical event after TESA in our clinical operation. Since 2013 to 2015, the incidence of hemorrhage was only 0.4% in 504 men in this study. Such tremendous differences may be due to popularization of sonographic examination. While patients did not feel uncomfortable after TESA, they were not regularly asked to perform sonographic examination, which lead to parts of the small hemorrhage was overlook.

Since 2013 to 2015, 76 patients had been ejaculation by masturbation successfully more than two times, but they were not able to ejaculation on the day of oocyte retrieval. These men passed through a procedure of relaxation, mood adjusting and PDE5i drug taking, selected TESA operation finally to retrieve sperm. Although the proportion who unfortunately appeared scrotal hemorrhage was only 2.6%, it is not found any scrotal hemorrhage events after same operation in other 428 patients who did not take PDE5i. These two patients' adverse reaction may be attributed to tadalafil as the temporal relationship between usage of the drug and the hemorrhage.

PDE5i, such as sildenafil (Viagra), vardenafil (Levitra) and tadalafil (Cialis), is used for therapy of erectile dysfunction. PDE5i increases nitrous oxide (NO) and cyclic guanosine monophosphate (cGMP) in the smooth muscles of the corpus cavernosum. For PDE5i to be effective, sufficient sexual stimulation is essential [4]. The masturbation difficulty males were so anxiously in such environment, could not relax to get enough sexual arousal, were not able to complete ejaculation even took PDE5i. PDE5i are generally safe and well tolerated [5], have not been reported in association with scrotal hemorrhage events. Although there was no clear evidence to association with scrotal hemorrhage and tadalafil, the presumed mechanisms contained following: firstly, redistribution of arterial blood flow associated with rupture of vessels. Second, NO and cGMP pathway might be responsible for inhibition of platelet aggregation and activation. Finally, PDE5i was considered as an antithrombotic agent [6].

Although there were no sufficient evidences which could support that scrotal hemorrhage after TESA was caused by the administration

of tadalafil. Given the potential risk of scrotal hemorrhage after the ingestion of tadalafil, it should be cautious to prescribe this medicine when the patient is likely to perform TESA, and ice scrotum may be beneficial after TESA.

Author Contributions

YTZ conceived of this study, collected data, performed data analysis, and prepared the manuscript. QJC conceived of this study, performed data analysis, and prepared the manuscript. All authors read and approved the final manuscript.

Competing Interests

The authors declare that they have no competing interests.

Acknowledgments

This research was supported by Scientific Initiative Research Foundation of Southern Medical University (No.PY2014N031).

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