

Effectiveness of two kind of medicine on non-obstructive azoospermia

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RESEARCH

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ABSTRACT

Objective

To assess the effectiveness of medicine on non-obstructive azoospermia (NOA).

Cases

32 male patients were enrolled from March 2012 to March 2016, with age range of 23–41 years old and infertility time of 1–3 years.

Methods

According to "WHO Human Semen Detection and Processing Experiment Manual" fifth edition, semen routine was based on manual detection and serum hormones based on chemiluminescence detection, semen volume, sperm density, forward moving sperm ratio. If sperm was detected in semen for more than two consecutive times, the treatment was considered effective and was included into the statistical analysis. The detection parameters took the first test data and the last test data.

Treatment

Andriol and tamoxifen were used for idiopathic NOA while aescuven forte and aspirin used for NOA with varicocele (including two varicolectomy). The time was four months.

Results

Of the 32 patients, 13 underwent testicular biopsy, pathological results showed six patients (46 per cent) with hypospermatogenesis, five patients (39 per cent) with maturation arrest, and two patients (15 per cent) with sertoli cell syndrome. Nine patients (28 per cent) had varicocele; two patients (6 per cent) underwent surgical treatment. After treatment, sperm was detected in 20 patients (63 per cent), seven of them (22 per cent) had detectable sperm in semen after one month of treatment; five (19 per cent) had sperm after two months of treatment; eight (25 per cent) had sperm after three months of treatment. Among the 23 patients with idiopathic azoospermia, 13 patients had detectable sperm in semen after treatment (56 per cent). The level of hormone gradually increased in 15 patients, rapidly increased in four patients, but four patients had no obvious change of hormone level. Among the nine patients with varicocele, three persons (including one patient undergoing surgery) had normal sperm density after 3–4 months of treatment, continuing the treatment for another 2–3 months, wife of the patients gained pregnancies. After treatment, seven patients had gradually decreasing serum level of FSH, LH and T while two patients had increased serum level of hormones. Excluding the three pregnancy patients, it was showed that the sperm density increased ($t=-3.342$, $p=0.004$) after treatment, so did the forward moving sperm ratio ($t=-4.037$, $p=0.001$), but semen volume had no significant changes ($t=-1.698$, $p=0.109$).

Conclusion

The treatment of varicocele is important for the NOA with varicocele while andriol and tamoxifen is other method for the treatment of idiopathic NOA.

Key Words

Sperm, NOA, andriol, tamoxifen, varicocele, aescuven forte

What this study adds:

1. What is known about this subject?

Non-obstructive azoospermia could be treated by two ways. One is to change the reproductive hormone and other way is

to direct toward causes such as varicocele.

2. What new information is offered in this study?

It is maybe not androgen but estrogen which effects the expression of FSH.

3. What are the implications for research, policy, or practice?

There is urgent to known the effectiveness of reproductive hormone on spermatogenesis which is maybe different with the traditional concept.

Background

With the development of reproductive medicine, most patients can achieve the ability of birth through assisted reproductive technology (ART). But Non-obstructive azoospermia (NOA) is still a problem in the field of ART. Although the disease incidence is not high,¹ treatment is not satisfactory; most patients can only get pregnant through AID. Our group obtained ideal results by treating this type of patients with classified therapies. Now the experimental results are reported as below.

Method

Patients: from March 2012 to March 2016, 32 male patients were enrolled in the reproductive medicine centre, with age range of 23–41 years old and infertility time of 1–3 years. Inclusion criteria: Semen volume ≥ 1.2 ml, and two or more consecutive detection of no sperms in semen sediments. Biochemical tests of seminal plasma are normal. Patients with idiopathic azoospermia: FSH, LH, PRL, T were all in the normal ranges. Varicocele patients: FSH was normal or higher than the normal range. Palpation of bilateral vas deferens, epididymis revealed no abnormality. Varicocele was confirmed by scrotal ultrasonography, with two patients undergoing varicocele high ligation. All patients were excluded for abnormal factors including vas deferens obstruction, reproductive tract infections and gonadal dysfunction; chromosome testing was he normal. Related therapies should be stopped at least two months before enrolment.

Treatment: Patients with idiopathic azoospermia were given testosterone undecanoate (40mg, bid, Schering-Plough CO., USA), tamoxifen (10mg, bid, Zhejiang Yangtze Pharmaceutical Co., Ltd.); Patients with varicocele (including the two patients undergoing high-approach varicolectomy) were given aescufen forte (300mg, bid, Cesra Arzneimittel GmbH & Co.KG), Aspirin (100mg, bid, Bayer, Germany). Treatments continued for 4 months.

Detection methods: In accordance with the "WHO Human Semen Detection and Processing Experiment Manual" fifth edition, semen routine was based on manual detection and serum hormones based on chemiluminescence detection.

Measurement parameters: Semen volume, sperm density, forward moving sperm ratio. The detection parameters took the first test data and the last test data.

Evaluation criteria: If sperm was detected in semen for more than two consecutive times, the treatment was considered effective and was included into the statistical analysis.

Statistics: SPSS18.0 was used for analysis; paired t test was used for comparison between two groups. $p \leq 0.01$ indicated statistical significance.

Results

Of the 32 patients, 13 underwent testicular biopsy, pathological results showed six patients with hypospermatogenesis (46 per cent), five patients with maturation arrest (39 per cent), and two patients with sertoli cell syndrome (15 per cent). Nine patients had varicocele (28 per cent); two patients underwent surgical treatment (6 per cent). After treatment, sperm was detected in 20 patients (63 per cent), seven of them (22 per cent) had detectable sperm in semen after one month of treatment; five (19 per cent) had sperm after two months of treatment; eight (25 per cent) had sperm after three months of treatment (Table 1).

Table 1: Comparison of semen before and after treatment

	N	Concentration ($\times 10^6$ /ml)
First month	20	0.00 \pm 0.00
Two month	7	0.08 \pm 0.05
Three month	5	0.13 \pm 0.23
Four month	8	2.22 \pm 2.58

Among the 23 patients with idiopathic azoospermia, 13 patients had detectable sperm in semen after treatment (56 per cent). The level of hormone gradually increased in 15 patients, rapidly increased in four patients, but four patients had no obvious change of hormone level.

Among the nine patients with varicocele, seven patients had detectable sperm in semen after treatment (77 per cent). Among them, three (including one patient undergoing surgery) had normal sperm density after 3–4 months of treatment, continuing the treatment for another 2–3

months, wife of the patients gained pregnancies. After treatment, seven patients had gradually decreasing serum level of FSH, LH and T while two patients had increased serum level of hormones; the reason needs to be discussed in the next time.

After excluding the three pregnancy patients, we found that the sperm density increased ($t=-3.342$, $p=0.004$) after treatment, so did the forward moving sperm ratio ($t=-4.037$, $p=0.001$), but semen volume had no significant changes ($t=-1.698$, $p=0.109$) (Table 2).

Table 2: Comparison of seminal parameters before and after treatment

	N	Volume (ml)	concentration ($\times 10^6/ml$)	Progressive (%)	PR+NP (%)
Before treatment	17	3.08 \pm 1.28	0 \pm 0	0 \pm 0	0
After treatment	17	3.38 \pm 1.47	1.38 \pm 1.71	17.85 \pm 18.23	19.18 \pm 27.66
T	17	-1.698	-3.342	-4.037	-2.859
P	17	0.109	0.004	0.001	0.011

Discussion

Currently, investigations on NOA are mostly composed of epidemiological studies^{2,3} or the investigations on surgical access of sperm,⁴ reports about the treatment of NOA are rare.^{1,5} In 2012, Moein et al. used tamoxifen to treat patients with normal FSH level, and gained an effective rate of about 14 per cent; the probability of finding sperm in secondary testicular biopsy was about 23 per cent.¹

This report is different from the treatment used by Moein et al.,¹ we used two different treatments on NOA patients. Among the 32 patients, seven (22 per cent) had detectable sperm in semen after one month of treatment; five (19 per cent) had sperm after two months of treatment; eight (25 per cent) showed sperm after three months of treatment. The number of sperm gradually increased, indicating the effectiveness of the treatment (Table 1). Among the 32 patients, 20 had detectable sperm (63 per cent). Both sperm density ($t=-3.342$, $p=0.004$) and the forward moving sperm ratio ($t=-4.037$, $p=0.001$) increased after treatment, but semen volume had no significant changes ($t=-1.698$, $p=0.109$) (Table 2).

Among the 23 patients with idiopathic azoospermia, 13

patients had detectable sperm in semen after treatment (56 per cent), this ratio is much higher than that reported by Moein et al., and this difference may be related with the higher proportion of sertoli cell syndrome patients in Moein's report as compared to our report. Our treatment was different from that by Moein et al., we used tamoxifen - testosterone undecanoate. From the treatment efficacy of NOA patients, the treatment efficacy for patients with NOA is lower than the treatment of oligospermia,^{6,7} suggesting that the etiology of idiopathic azoospermia is complicated. And the analysis of hormones demonstrated this point. Among the 23 patients, 15 had gradually increased level of hormone, four had rapidly increased level of hormone and four patients had no obvious changes of hormone level. From our observation, if the level of hormone increased rapidly or did not change after treatment, the possibility of finding sperm in semen was low.

Among the nine NOA with varicocele, seven patients had detectable sperm in semen after treatment (77 per cent). Among them, three (including one patient undergoing surgery) had normal sperm density after 3–4 months of treatment, pregnancies occurred after another 2–3 months of treatment. After treatment, seven patients had gradually decreasing serum level of FSH, LH and T, and two patients had increased serum level of hormones. Aescufen forte is produced by Cesra Arzneimittel GmbH & Co.KG, it can improve the venous return and venous function,⁸ and is currently widely used in venous disease.^{8,9} In this study, decreased levels of sex hormones may be the result of a recovery of testicular function after the improvement of venous return. But why some patients had increased level of FSH and LH after treatment remains to be investigated.

Although treatment of varicocele is controversial,¹⁰ we observed that good surgical treatment or drug treatment could achieve good therapeutic effect for varicocele patients with NOA.¹¹

Conclusion

For NOA patients, varicocele is still an important factor that needs more attention, using surgery or drug treatment may make patients gradually restore spermatogenic function. For idiopathic NOA patients, tamoxifen - testosterone undecanoate is a good treatment.

References

1. Moein MR, Tabibnejad N, Ghasemzadeh J. Beneficial effect of tamoxifen on sperm recovery in infertile men with nonobstructive azoospermia. *Andrologia*. 2012;44:194-8.

2. Hess CB, Thompson HM, Benedict SH, et al. Exposure Risks Among Children Undergoing Radiation Therapy: Considerations in the Era of Image Guided Radiation Therapy. *Int J Radiat Oncol Biol Phys.* 2016;94(5):978-92.
3. Shoshany O, Shtabholtz Y, Schreter E, et al. Predictors of spermatogenesis in radical orchiectomy specimen and potential implications for patients with testicular cancer. *Fertil Steril.* 2016;2(16):45-8.
4. Ran R, Kohn TP, Ramasamy R. Innovations in surgical management of nonobstructive azoospermia. *Indian J Urol.* 2016;32(1):15-20.
5. Wenker EP, Dupree JM, Langille GM, et al. The Use of HCG-Based Combination Therapy for Recovery of Spermatogenesis after Testosterone Use. *J Sex Med.* 2015;12(6):1334-7.
6. Adamopoulos DA, Pappa A, Billa E, et al. Effectiveness of combined tamoxifen citrate and testosterone undecanoate treatment in men with idiopathic oligozoospermia. *Fertil Steril.* 2003;80(4):914-20.
7. Bo S, Zhiming C. Efficacy of combined testosterone undecanoate with tamoxifen citrate treatment for spermatogenic arrest. *J Mod Urol.* 2011;16(5):426-8.
8. Zhishang Y, Junping X. Effects of aescurenforte on varicocele. *J Mod Urol.* 2004;9(4):226-7.
9. Xie Songhong, Ou Shu'an. Effect of ascufenforte on 36 patients with varicella. *China Trop Med.* 2007;7(7):1162-6.
10. Weedin JW, Khera M, Lipshultz L. Varicocele repair in patients with nonobstructive azoospermia: a meta-analysis. *J Urol.* 2010;183(6):2309-15.
11. Youssef T, Abd-Elaal E, Gaballah G, et al. Varicolectomy in men with nonobstructive azoospermia: is it beneficial? *Int J Surg.* 2009;7(4):356-60.

PEER REVIEW

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

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ETHICS COMMITTEE APPROVAL

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