



Bệnh viện Phụ Sản Trung Ương

43 Tràng Thi, Hàng Bông, Hoàn Kiếm, Hanoi, Vietnam

Evaluation of the Efficacy of the SPERMOTREND Dietary Supplement in the Treatment of Male Infertility Related to Oligozoospermia and Asthenozoospermia



Protocol : Spermotrend in the Treatment of Male Infertility

Purpose

The purpose of this study is to determine whether the administration of the dietary supplement Spermotrend improves spermatogenesis parameters in subjects with male infertility related to oligozoospermia and asthenozoospermia. The duration of this clinical trial will be 12 weeks. The estimated number of males with infertility to be recruited for the study is 60.

<u>Condition</u>	<u>Intervention</u>	<u>Phase</u>
Male Infertility	Dietary Supplement: Spermotrend	Phase 3

Study Type: Interventional, prospective

Study Design: Intervention Model: non-placebo
Primary Purpose: Treatment

Compare the treatment result before and after 90 days using Spermotrend

Official Title Assessment of the Efficacy of Dietary Supplement Spermotrend in the Treatment of Male Infertility related to oligozoospermia and asthenozoospermia

Place National hospital of Obstetrics and Gynecology
43 Trang Thi, Hanoi, Vietnam.
Center for Assisted reproduction

Research director Nguyen Xuan Hoi,MD,PhD.
Director of Center for umbilical Cord blood and stem cell preservation
Infertility Specialist of Center for Assisted reproduction.

Primary Outcome Measures:

- ✓ Parameters of seminal analysis at weeks 12

Secondary Outcome Measures:

- ✓ Subclinical and clinical characteristics in men infertility related to oligozoospermia and asthenozoospermia
- ✓ Side effects

Estimated Enrollment: 60

Study Start Date: Oct 2014

Study Completion Date: March 2015

<u>Arm</u>	<u>Assigned Interventions</u>
Experimental: Spermotrend	Dietary Supplement: Spermotrend One Spermotrend tablet (Orally administered) twice a day, for 90 days

Eligibility

Ages Eligible for Study: 19- 50 Years

Genders Eligible for Study: Male

Accepts Healthy Volunteers: No

Criteria***Inclusion Criteria:***

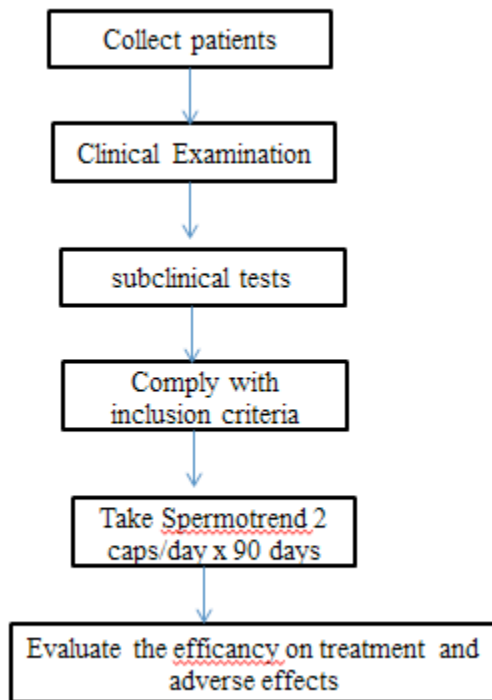
- ✓ Under 50 years
- ✓ Male infertility unrelated to major testicular conditions
- ✓ Confirmed male infertility according to WHO criteria (oligozoospermia , asthenozoospermia or either combined)
- ✓ Absence of anatomical and hormonal defect (FSH,LH,Prolactin , testosterone)
- ✓ Stop using of any infertility treatment drugs in the last 3 months

- ✓ No leucocytospermia
- ✓ Negative microbiological analysis of semen
- ✓ Negative microbiological analysis of urine
- ✓ Signed informed consent

Exclusion Criteria:

- ✓ Hydrocele, varicocele, orchitis, epididymitis, irradiation or Chemotherapy.
- ✓ System diseases such as Liver or kidney dysfunction
- ✓ Acute infectious disease, blood disorders; hypothyroidism, epileptic disease
- ✓ Azoospermia and teratozoospermia or no ejaculation
- ✓ Leukocytospermia > 1million /ml

Study Schedule



Study results

1. Baseline Clinical characteristics

Table. 1. Age's classification

Age	n	%
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< 30	6	12
30 - 39	35	70
40 -< 45	5	10
≥ 45	4	8
Total	50	100

Comment: mean age $35,16 \pm 5,33$ years (25-48 years)

Figure 1: Geography's classification

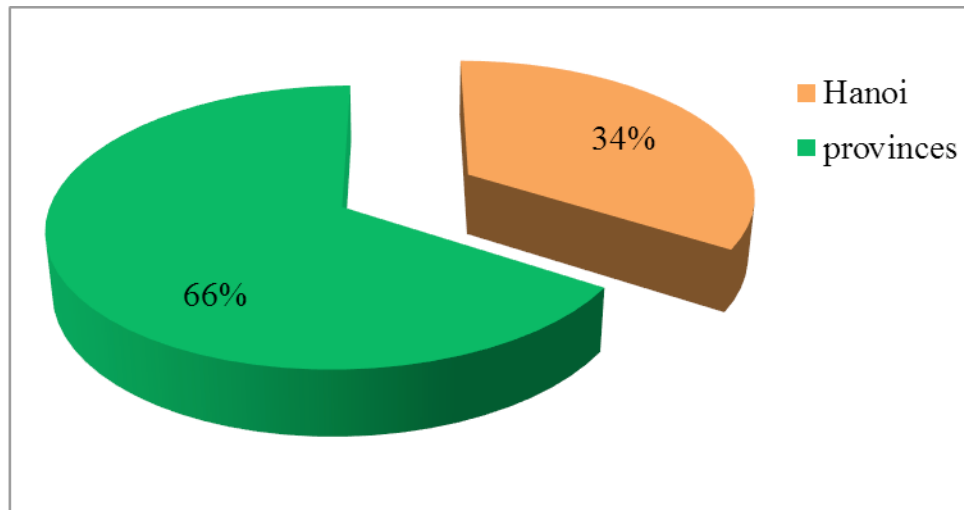


Figure 2 : Career's classification

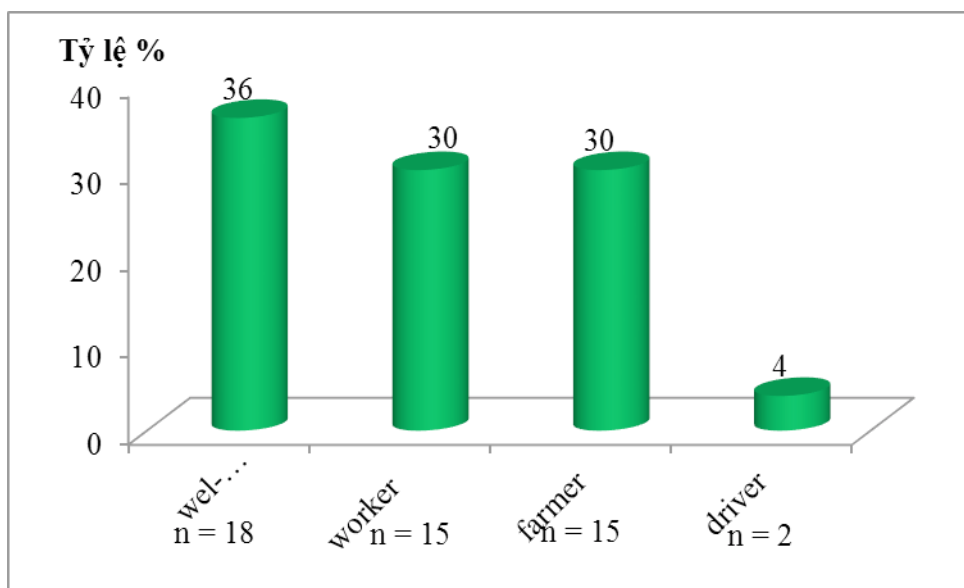


Table 2 : Lifestyle and work environment's classification

Lifestyle and working environment	n	%
Expose to toxic chemicals	1/50	2
Expose to High temperature	1/50	2
Alcohol abuse	3/50	6
Smoking	14/50	28

Table 3. BMI's classification

BMI	n	%
< 18,5	2	4
18,5 - < 25	43	86
≥ 25	5	10

Total	50	100
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Figure 3 : Infertility's classification

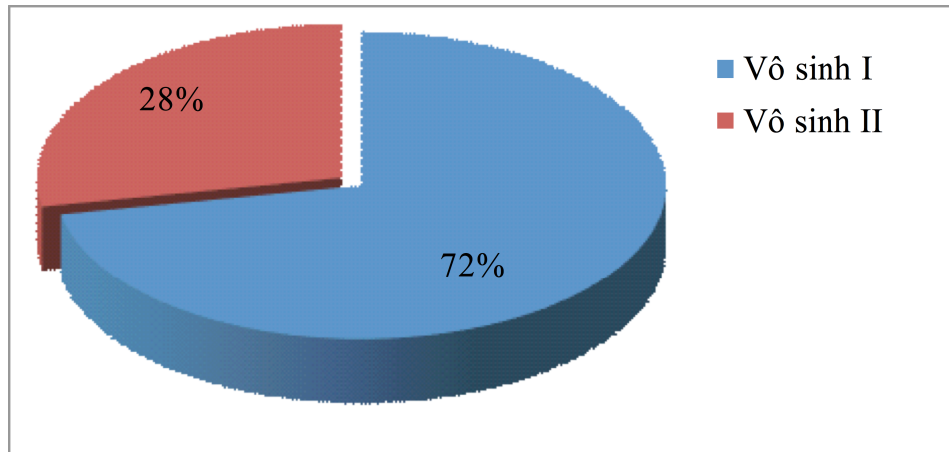


Table 4. Period of infertility

Comment: mean period of infertility $4,42 \pm 2,88$ (1-12 years)

Table 5: testicular volume

Testicular volume (ml)	n	%
≤ 15	12	24
$15 < 20$	35	70
> 20	3	6
total	50	100

Comment: mean testicular volume $17 \pm 2,11$ ml (14-23 ml)

Table 6. Hormon's profile

hormon	mean
FSH (IU/l)	$5,96 \pm 1,22$
LH (IU/l)	$6,96 \pm 1,39$
Testosterone (mIU/l)	$16,00 \pm 4,10$
Prolactin (nmol/l)	$194,68 \pm 34,15$

Comment: mean FSH level $5,96 \pm 1,22$ IU/l (4.2-9.2 IU/l)

Mean LH level $6,96 \pm 1,39$ IU/l (8.5-9.1IU/l).

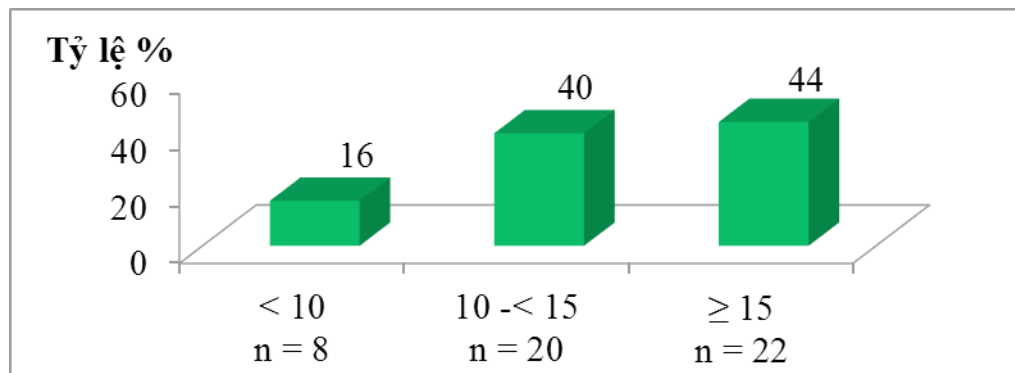
Mean testosterone level $16,00 \pm 4,10$ nmol/l (0.85 -2.5 nmol/L).

Mean prolactin level $194,68 \pm 34,15$ mIU/l (126-297 mIU/l).

Table 7. Spermogram's characteristics

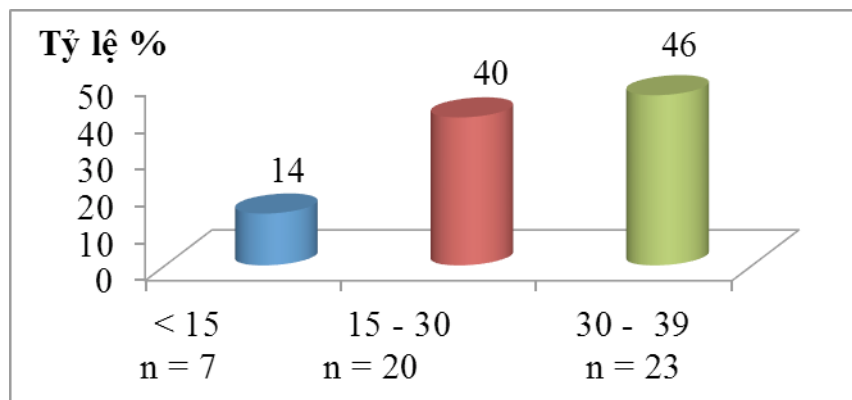
parameters	Specification	n	%
pH	Normal ($\geq 7,2$)	46	92
	abnormal	4	8
Volume	Normal ($\geq 1,5$ ml)	38	76
	abnormal	12	24
concentration	normal ($\geq 15 \times 10^6/\text{ml}$)	22	44
	abnormal	28	56
Viable sperm rate (%)	normal ($\geq 58\%$)	12	24
	abnormal	38	76
morphology	normal ($\geq 4\%$)	0	0
	abnormal	50	100

Figure 4: Spermogram's classification based on Sperm concentration



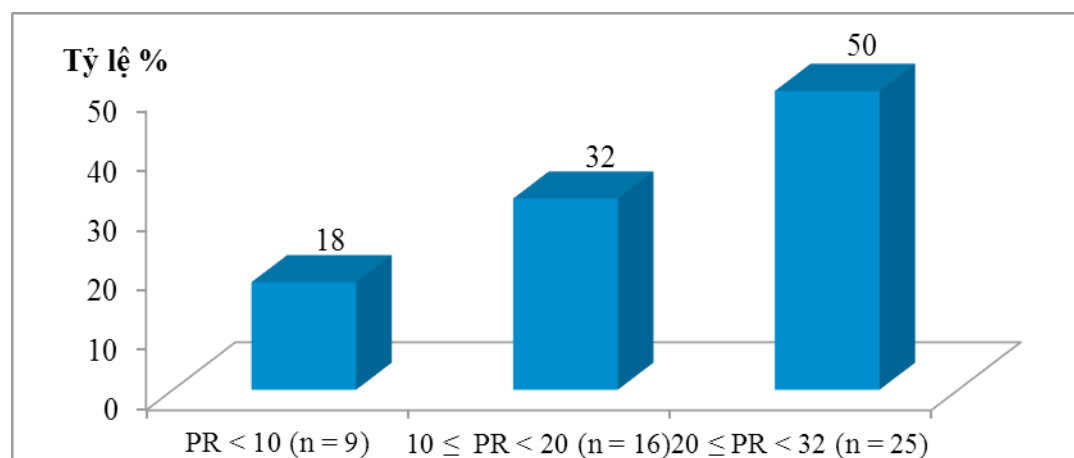
Comment: sperm concentration is from $7 \times 10^6/\text{ml}$ to $26 \times 10^6/\text{ml}$

Figure 5. Classification on total sperm count



Comment: total sperm count is from 8×10^6 to $37,5 \times 10^6$

Figure 6. Classification based on motility class A+B



Comment: Motility rate is from 8% to 31%

2. Spermotren's efficacy on the Sperm's quality and quantity

Table 8. Concentration and total sperm count : before vs after treatment

parameters	before treatment n = 50	After treatment n = 50	p
Mean concentration ($\times 10^6$ /ml)	$14,36 \pm 5,23$	$15,90 \pm 5,05$	$< 0,05$
Mean sperm count ($\times 10^6$)	$26,38 \pm 8,90$	$40,18 \pm 14,84$	$< 0,01$

Comment: after treatment, mean concentration is increased significantly from $14,36 \times 10^6$ /ml to $15,9 \times 10^6$ /ml ($p < 0,05$) ; mean total sperm count is increased significantly from $26,38 \times 10^6$ to $40,18 \times 10^6$ ($p < 0,01$).

Table 9. total sperm count on Sperm count's classification : before vs after treatment

Total sperm count ($\times 10^6$)	Before treatment n = 50	After treatment n = 50	p
< 15 (n = 7)	$11,57 \pm 2,15$	$27,07 \pm 15,64$	$< 0,05$
15 -< 30 (n = 20)	$22,43 \pm 4,49$	$36,80 \pm 13,46$	$< 0,01$
30 – 39 (n = 23)	$34,32 \pm 2,78$	$41,11 \pm 12,34$	

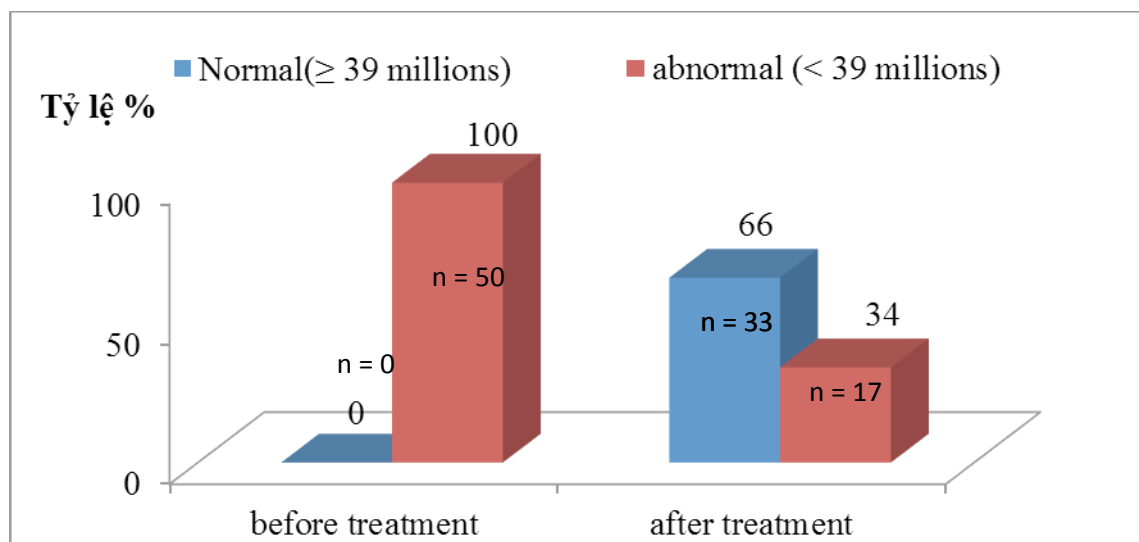


Figure 7. % pts with normal total sperm count : before vs after treatment

Comment: there is no pts with normal total sperm count before treatment while there are 33 pts (66%) with normal total sperm count after treatment.

Table 10. Motility , normal morphology and viability of sperm cells : before vs after treatment

parameters	before n = 50	after n = 50	p
Mean motility class A+ B (%)	17,92 ± 7,95	24,16 ± 9,91	< 0,01
Mean normal morphology rate (%)	1,96 ± 0,67	2,70 ± 0,89	
Mean viable sperm cells (%)	49,84 ± 7,06	50,92 ± 6,52	> 0,05

Comment: after treatment , motility is increased significantly from 17.92% to 24.16% ($p < 0.01$); morphology is increased significantly from 1.96% to 2.7% ($p < 0.01$), viable sperm cells is increased from 49.84% to 50.92% but insignificantly with $p > 0.05$.

Table 11. Motility rate based on PR classification : before vs after treatment

PR (%)	Before treatment n = 50	After treatment n = 50	p
PR < 10 (n = 9)	8,33 ± 0,5	9,11 ± 1,69	> 0,05
10 ≤ PR < 20 (n = 16)	12,25 ± 2,57	24,56 ± 9,02	< 0,01
PR ≥ 20 (n = 25)	25,00 ± 4,07	29,32 ± 5,99	

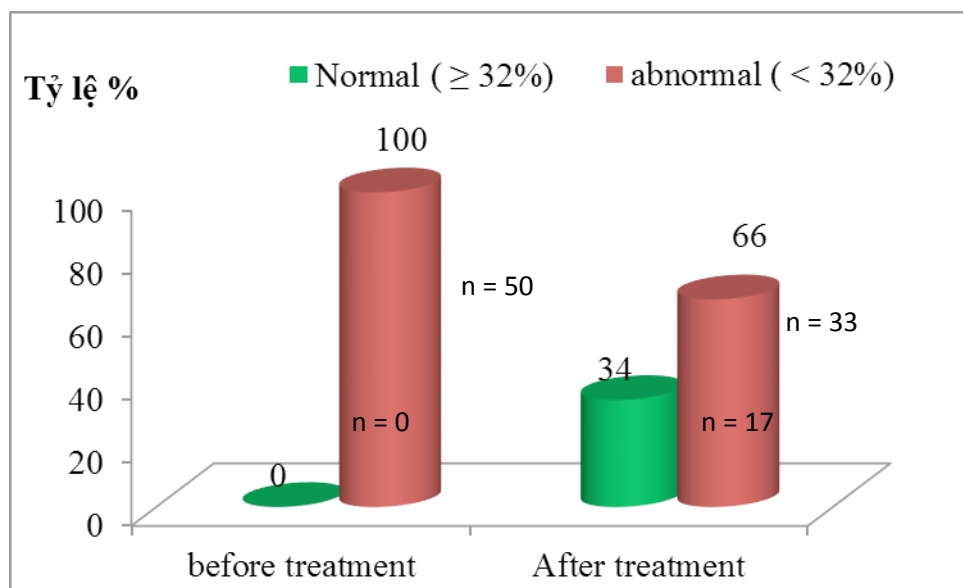


Figure 8. % pts with normal PR : before vs after treatment

Comment : after treatment there are 17 pts (34%) with normal PR in comparison with there is 0 pts before treatment.

Table 12. Seminal volume and pH : before vs after treatment

parameters	Before treatment n = 50	After treatment n = 50	p
Volume (ml)	2,02 ± 0,82	2,63 ± 0,79	< 0,01
pH	7,46 ± 0,161	7,54 ± 0,18	> 0,05

Table 13: Volume's classification : before vs after treatment

Volume (ml)	before n = 50	after n = 50	p
< 1,5 (n = 12)	1,02 ± 0,07	1,83 ± 0,49	< 0,01
1,5 -< 2,5 (n = 19)	1,76 ± 0,26	2,52 ± 0,66	
≥ 2,5 (n = 19)	2,9 ± 0,47	3,23 ± 0,45	< 0,05

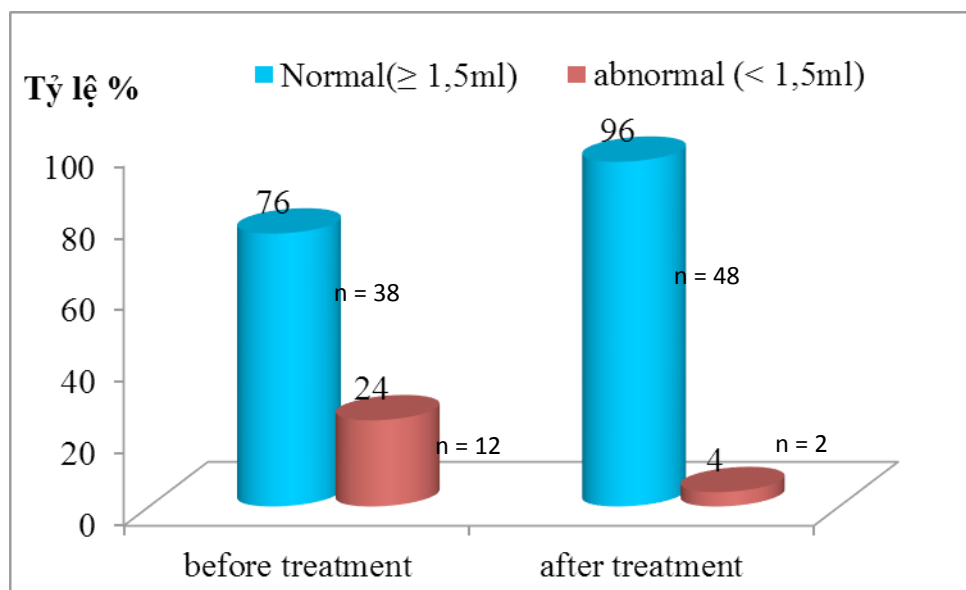


Figure 9. % pts with normal volume : before vs after treatment

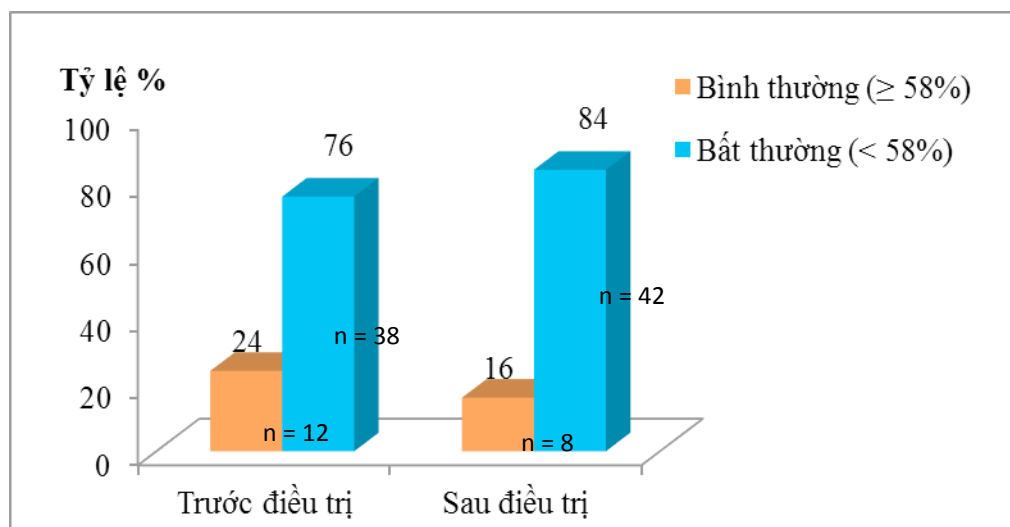


Figure 10. % pts with normal viable sperm cells : before vs after treatment

Table 14. normal morphology : before vs after treatment

Normal morphology (%)	Before treatment n = 50	After treatment n = 50	p
< 2 (n = 13)	1,00	1,92 ± 0,64	< 0,01
2 - ≤ 3 (n = 37)	2,27 ± 0,45	3,03 ± 0,76	

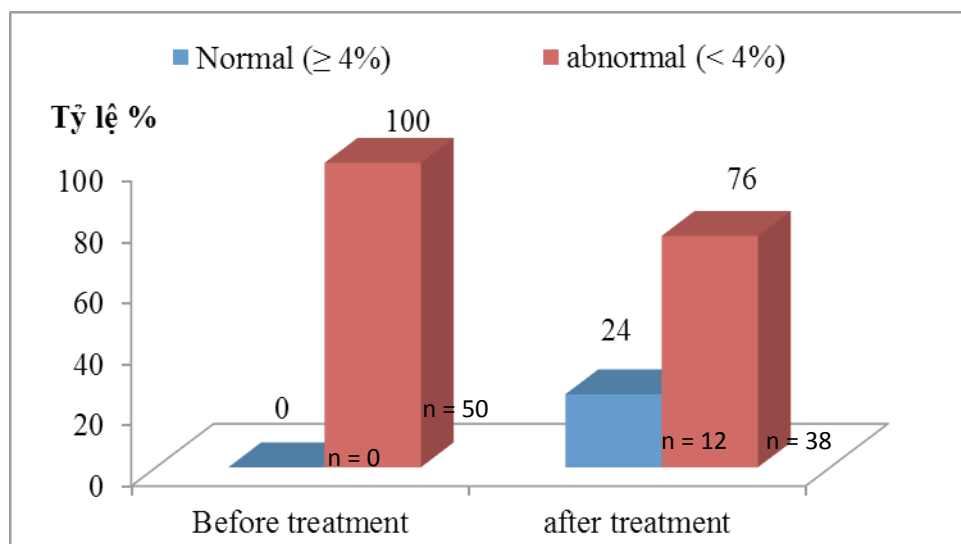


Figure 11. % pts with normal morphology : before vs after treatment

Analysis the relationship between Age and treatment result

Table 15. total sperm count($\times 10^6$)

Aged group (year)	Before treatment n = 50	After treatment n = 50	p
< 30 (n = 6)	25,5 ± 9,95	36,5 ± 12,18	< 0,05
30 - 39 (n = 35)	27,26 ± 8,24	41,12 ± 15,58	< 0,01
40 - < 45 (n = 5)	23,4 ± 10,05	44,00 ± 10,84	> 0,05
≥ 45 (n = 4)	23,5 ± 14,46	28,00 ± 11,66	

Comment : after treatment there is a significantly increase on total sperm count for the aged group < 39 years .

Table 16. Mobility class A+ B(%)

Aged group (year)	Before treatment n = 50	After treatment n = 50	p
< 30 (n = 6)	11,33 ± 2,94	21,67 ± 12,03	< 0,05
30 - 39 (n = 35)	18,69 ± 8,02	24,34 ± 10,02	< 0,01
40 - < 45 (n = 5)	18,40 ± 7,64	30,00 ± 7,48	< 0,05
≥ 45 (n = 4)	20,00 ± 8,58	19,00 ± 6,68	> 0,05

Comment: After treatment , the rate of mobility class A+B is significantly increased from 11,33% to 21,67% ($p < 0.05$) ; from 18.69% to 24.34% ($p < 0.01$) and from 18,4% to 30% ($p < 0.05$) for the age of < 30 , 30-39 and 40-45. At the age ≥ 45 the rate of mobility class A+B is decreased from 20% to 19% but insignificantly ($p > 0.05$)

Table 17. Seminal volume (ml) : before vs after treatment

Aged group (year)	Before treatment n = 50	After treatment n = 50	p
< 30 (n = 6)	2,00 ± 0,55	2,92 ± 0,80	< 0,01
30 - 39 (n = 35)	2,11± 0,89	2,67 ± 0,81	
40 -< 45 (n = 5)	1,60 ± 0,42	2,50 ± 0,50	
≥ 45 (n = 4)	1,75 ± 0,96	2,00 ± 0,82	> 0,05

Comment: after treatment , seminal volume is significantly increased (p<0.01) for the age < 45 . It is insignificantly increased (p>0.05) for the age ≥ 45 .

Table 18. Viability of sperm cells : before vs after treatment

Aged group	Before treatment n = 50	After treatment n = 50	p
< 30 (n = 6)	48,83 ± 6,82	51,00 ± 6,03	> 0,05
30 - 39 (n = 35)	49,37 ± 7,02	50,83 ± 6,47	
40 -< 45 (n = 5)	53,80 ± 4,03	52,40 ± 2,51	
≥ 45 (n = 4)	50,50 ± 11,24	49,75 ± 12,04	

Comment: after treatment , viable sperm cells is increased in all aged groups but insignificantly (p > 0.05)

Table 21: Normal morphology : before vs after treatment

Aged group	Before treatment n = 50	After treatment n = 50	p
< 30 (n = 6)	1,83 ± 0,75	3,00 ± 0,89	< 0,05
30 - 39 (n = 35)	1,86 ± 0,70	2,60 ± 0,91	< 0,01
40 -< 45 (n = 5)	2,20 ± 0,47	3,20 ± 0,47	< 0,05
≥ 45 (n = 4)	2,50 ± 0,57	3,00 ± 0,82	> 0,05

Comment: after treatment , there is a significant increase on the rate of normal sperm morphology at the age < 45 . It is increased from 2.5% to 3.0% at the age ≥ 45 , but insignificantly with p > 0.05.

Analysis on the relationship between some risky factors and treatment result

Table 22: Concentration and total sperm count based on risky factors: before vs after treatment

Risky factor		Before treatment n = 50	After treatment n = 50	p
Group I (n = 15)	concentration (x10 ⁶ /ml)	14,28 ± 5,06	18,00 ± 5,52	< 0,01
	Total sperm count (x10 ⁶)	27,23 ± 8,36	48,17 ± 8,88	
Group II (n = 2)	concentration (x10 ⁶ /ml)	17,00 ± 7,07	18,00 ± 9,90	> 0,05
	Total sperm count (x10 ⁶)	34,50 ± 2,12	29,00 ± 5,66	
Group III (n = 33)	concentration (x10 ⁶ /ml)	14,30 ± 5,36	14,81 ± 4,38	> 0,05
	Total sperm count (x10 ⁶)	25,50 ± 9,24	37,23 ± 15,97	< 0,05

Group I: alcohol abuse or/and smoking

Group II: expose with toxic environment (heavy chemical or high temperature)

Group III: non-risk factors

Table 23. mortality class A+B (%) based on risky factors: before vs after treatment

Risky factors	Before treatment n = 50	After treatment n = 50	p
Group I (n = 15)	19,13 ± 8,10	30,80 ± 6,49	< 0,01
Group II (n = 2)	14,50 ± 7,78	16,50 ± 10,61	> 0,05
Group III (n = 33)	17,58 ± 8,03	21,61 ± 9,86	< 0,01

Table 24. Normal morphology (%) based on risky factors: before vs after treatment

Risky factors	Before treatment n = 50	After treatment n = 50	p
Group I (n = 15)	1,93 ± 0,59	2,93 ± 0,80	< 0,01

Group II (n = 2)	1,50 ± 0,71	2,00 ± 1,41	> 0,05
Group III (n = 33)	1,97 ± 0,73	2,70 ± 0,89	< 0,05

Summary

1. Subclinical and clinical characteristics in men infertility related to oligozoospermia and asthenozoospermia

- Mean age: 35,18 ± 5,33 years
- Infertility I is 72%, Infertility II is 28%.
- Mean period of infertility : 4,42 ± 2,88 years
- Abnormal concentration(< 15x10⁶) : 56%
- Abnormal seminal volume (< 1,5ml) : 24%,
- Abnormal morphology (< 4%) : 100%

2. The efficacy of Spermatotend on Sperm's quality and quantity in men infertility related to oligozoospermia and asthenozoospermia

- Seminal volume is significantly increased from 2.02 ± 0.82 (ml) to 2.62 ± 0.79 (ml) (p < 0,01)
- Concentration is significantly increased from 14.36 ± 5.23 (x10⁶/ml) to 15.9 ± 5.05 (x10⁶/ml) (p < 0,05)
- Total sperm count is significantly increased from 26.38 ± 8.90 (x10⁶) to 40.18 ± 14.84 (x10⁶) (p < 0,01)
- Mortality class A+ B is significantly increased from 17.92 ± 7.95 (%) to 24.16 ± 9.91 (%) (p < 0,01)
- The rate of Viable sperm cells and pH is insignificantly changed (p > 0,05)
- Sperm's quality and quantity is improved the best at the age of 30 - 39 after treatment
- No adverse effect is found

Recomendations

1. Spermotrend demonstrated positive influence on treatment for men infertility related to **oligozoospermia and asthenozoospermia** . **It should be recommended to use on clinical practice , especially for the age of 30-39 years.**
2. It should be evaluated furthermore with longer period of treatment