

Uncertain Impact of Anti-TNF Agents on Male Fertility: Are Men Being Counseled?

Lauren Folgosa Cooley MD, PhD¹, Isaac Lam BS¹, James Wren MD¹, Nelson Bennett MD¹, and Robert Brannigan MD¹

¹Department of Urology, Northwestern University Feinberg School of Medicine, Chicago, IL

Rationale

Over the last decade the number of couples seeking infertility consultation has increased and is now estimated at 10-15% of all couples. Male factor infertility, specifically, is found to be a contributing cause in approximately 50% of couples. While many factors can contribute to male factor infertility, there is a growing concern for the impact of medications on sperm quality, semen parameters, spermatogenesis, and future fertility. While the concern may be growing, there is little to no evidence available for many FDA-approved pharmaceuticals as to their impact on male fertility, including anti-TNF agents, which are commonly prescribed for inflammatory bowel disease, autoimmune, and dermatologic conditions.

Objectives

Adult men with autoimmune conditions are commonly prescribed anti-TNF agents. Currently only small, non-randomized studies detail the potential impact of anti-TNF agents on male fertility. These study results have been mixed, with some studies reporting adverse effects on semen parameters and sperm quality. Given the lack of clarity regarding specific reproductive effects, our objective was to see if men receiving anti-TNF agents are being: (1) counseled regarding potential for adverse reproductive effects; (2) screened for anatomic or laboratory abnormalities associated with infertility; and (3) offered sperm cryopreservation.

Methods

A single-center, retrospective analysis of 1010 male patients prescribed an anti-TNF agent between ages 18-45 from 1/1/2008 to 8/1/2017.

Our retrospective database review determined if men received: (1) counseling regarding potential risks to fertility, (2) a genitourinary exam (penis, urethra, testicles), (3) screening for varicocele, (4) diagnosis or assessment for low libido or ED, (5) hormone labs (T, LH, FSH, prolactin), (6) semen analysis, (7) sperm cryopreservation.

Chi square testing compared proportions between those who did and did not receive counseling. p<0.05 was considered significant.

Demographics

	Adalimumab	Etanercept	Infliximab	Golimumab	Certolizumab	Total
Number of patients	600	161	219	8	22	1010
Age (years)	32.8 ± 7.5	33.0 ± 6.9	30.9 ± 7.4	33.9 ± 7.5	31.8 ± 7.1	32.4 ± 7.5
Duration of treatment (days)	799 ± 700	958 ± 878	853 ± 850	794 ± 725	669 ± 466	832 ± 806
Race	n %	n %	n %	n %	n %	n %
American Indian	1 (0.17)	0 (0.00)	2 (0.91)	0 (0.00)	0 (0.00)	3 (0.30)
Asian	16 (2.67)	5 (3.11)	9 (4.10)	0 (0.00)	0 (0.00)	30 (2.97)
Black	29 (4.83)	4 (2.48)	27 (12.32)	0 (0.00)	0 (0.00)	60 (5.94)
Hispanic	1 (0.17)	1 (0.62)	2 (0.91)	0 (0.00)	0 (0.00)	4 (0.40)
Pacific Islander	1 (0.17)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	1 (0.01)
White	404 (67.33)	99 (61.5)	153 (69.86)	8 (100)	19 (86.36)	683 (67.62)
Declined	78 (13.00)	36 (22.4)	9 (4.10)	0 (0.00)	0 (0.00)	123 (12.18)
Other	70 (11.67)	16 (9.94)	17 (7.76)	0 (0.00)	3 (13.64)	106 (10.50)
Ethnicity	n %	n %	n %	n %	n %	n %
Hispanic	29 (4.83)	10 (6.21)	13 (5.93)	0 (0.00)	0 (0.00)	52 (5.15)
Not Hispanic/Latino	465 (77.50)	103 (63.98)	177 (80.82)	8 (100)	19 (86.36)	772 (76.44)
Declined	106 (17.67)	48 (29.81)	29 (13.24)	0 (0.00)	3 (13.64)	186 (18.41)
Marital Status	n %	n %	n %	n %	n %	n %
Single	342 (57.00)	77 (47.83)	153 (69.86)	6 (75.00)	13 (59.09)	591 (58.51)
Married	205 (34.17)	71 (44.10)	64 (29.22)	2 (25.00)	9 (40.91)	351 (34.75)
Divorced	4 (0.67)	3 (1.86)	0 (0.00)	0 (0.00)	0 (0.00)	7 (0.69)
Other	49 (8.17)	10 (6.21)	2 (0.91)	0 (0.00)	0 (0.00)	61 (6.04)
Diagnosis	n %	n %	n %	n %	n %	n %
Ankylosing spondylitis	61 (10.16)	42 (26.09)	7 (3.19)	0 (0.00)	1 (4.55)	111 (10.99)
Behcet's	2 (0.33)	0 (0.00)	1 (0.46)	0 (0.00)	0 (0.00)	3 (0.29)
Blau Syndrome	2 (0.33)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	2 (0.20)
Crohn's	107 (17.83)	0 (0.00)	90 (41.09)	3 (37.50)	13 (59.09)	213 (21.1)
Hidradenitis suppurativa	25 (4.17)	1 (0.62)	1 (0.46)	0 (0.00)	0 (0.00)	27 (2.67)
Psoriasis ± arthritis	256 (42.67)	83 (51.55)	11 (5.02)	2 (25.00)	2 (9.09)	354 (35.05)
Rheumatoid arthritis	24 (4.00)	20 (12.42)	18 (8.22)	0 (0.00)	1 (4.55)	63 (6.24)
Sarcoidosis	2 (0.33)	0 (0.00)	12 (5.48)	0 (0.00)	0 (0.00)	14 (1.39)
Seronegative arthritis	28 (4.67)	11 (6.83)	0 (0.00)	0 (0.00)	1 (4.55)	40 (3.96)
Sjogren's	1 (0.17)	2 (1.24)	2 (0.91)	0 (0.00)	0 (0.00)	5 (0.49)
Ulcerative Colitis	92 (15.33)	2 (1.24)	77 (35.16)	3 (37.50)	4 (18.18)	178 (17.62)

Table 1. Demographics of study participants. All participants were male, age 18-45 at time of initiation of anti-TNF inhibitor, and had only been prescribed one anti-TNF agent. Red outline denotes most common response in each category.

Results

	(+) Counseling		(-) Counseling		p
	n	%	n	%	
Total	104	10.30	906	(89.70)	<0.0001
GU Exam	83	(79.81)	267	(29.47)	<0.0001
Varicocele	26	(25.00)	17	(1.88)	<0.0001
Libido/Sexual Function	46	(44.23)	108	(11.92)	<0.0001
Hormone Labs	29	(27.88)	28	(3.09)	<0.0001
Semen Analysis	18	(17.31)	26	(2.87)	<0.0001
Sperm Cryopreservation	6	(5.77)	10	(1.10)	0.002

Table 2. The association between counseling and reproductive assessment/sperm cryopreservation. GU exam – any reference of examination of penis, urethra, testes, epididymis. Varicocele – examination and grading of varicocele. Libido/Sexual function – asking patient about libido or sexual function. Hormone Labs – obtaining testosterone, LH, FSH, and/or prolactin. p value <0.05 considered significant and calculated by chi square of proportions.

	(+) Counseling (n = 104)	
	n	%
Ankylosing spondylitis	12	(11.54)
Behcet's	0	(0.00)
Blau Syndrome	0	(0.00)
Crohn's	20	(19.23)
Hidradenitis suppurativa	2	(1.92)
Psoriasis ± arthritis	34	(32.69)
Rheumatoid arthritis	8	(7.69)
Sarcoidosis	0	(0.00)
Seronegative arthritis	4	(3.85)
Sjogren's	3	(2.88)
Ulcerative Colitis	21	(20.19)

Table 3. Percentage who received counseling by diagnosis. In descending order by % who received counseling: Psoriasis > Ulcerative colitis > Crohn's > Ankylosing Spondylitis > Rheumatoid arthritis > Seronegative arthritis

Conclusions

- The impact of anti-TNF agents on male fertility is unknown.
- Our study is the first to demonstrate that only 10.3% of men prescribed anti-TNF agents are receiving counseling regarding potential risk to fertility.
- Those patients who are counseled are also significantly more likely to be screened for anatomic, hormonal, and semen analysis parameters prior to anti-TNF agent therapy.
- Those who receive counseling are more likely to elect for sperm cryopreservation.
- Overall rates of sperm cryopreservation are low (counseling 5.7%, no counseling 1.10 %).
- Patients with psoriasis were most likely to be counseled followed by those with inflammatory bowel disease.
- More research is needed to better understand the potential impact of anti-TNF agents on male reproductive potential. This will help guide the discussion and recommendation for baseline, pre-treatment reproductive assessment and sperm cryopreservation.