ASSESSMENT OF *SPEM1* AND INHIBIN IN PATIENTS WITH DYSFUNCTIONAL AZOOSPERMIA AND THEIR RELATION TO SUCCESSFUL SPERM RETRIEVAL

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Introduction

Infertility is becoming a major public health concern with major psychological and economic impacts. Globally, up to 15% of couples suffer from infertility, in which almost a quarter of the cases are due to the male factor. Azoospermia refers to the complete lack of spermatozoa in the ejaculate, affecting 1% of all males and up to 15% of the infertile male population**.** Azoospermia can be categorized into obstructive azoospermia (OA); that is due to blockage along the male reproductive tract and non-obstructive azoospermia (NOA): that is due to dysfunctional spermatogenesis affecting about 60% of azoospermic men. Both cases of NOA and OA can benefit from testicular sperm extraction (TESE).
In cases of NOA, micro-TESE has improved the chances of sperm retrieval by identifying foci of spermatogenesis in the testis with a success rate of 40-60%. To improve this outcome, it is necessary to have a reliable predictor of sperm retrieval. Several clinical parameters such as semen analysis, testicular size, FSH levels, inhibin B, and histopathology are among predictive factors for successful sperm retrieval in men with dysfunctional azoospermia. However, no accurate predictors have been identified..

Aim of the work

The aim of this study was to assess the gene expression of *SPEM1* in testicular tissue and the level of serum Inhibin B in patients with dysfunctionalazoospermia and to evaluate their predictive power for sperm retrieval..

Patients and Methods

Forty patients were recruited from the Andrology outpatient clinic of the Main University Hospital, Faculty of Medicine, University of Alexandria, 30 NOA patients with verified azoospermia as per the WHO 5th edition, normal semen fructose and alpha-glucosidase levels, and no evidence of obstructive causes of azoospermia in history or physical examination were included.
Patients with evidence of obstruction, anejaculation, and retrograde ejaculation were excluded from the study. Ten out of the 40 recruited patients had obstructive azoospermia (OA) and served as controls.
All patients were subjected to history taking, clinical examination, semen analysis, hormonal assessment, micro dissection testicular sperm extraction, histopathological analysis and determination of *SPEM1* gene expression by quantitative reverse transcription real time PCR.

Results

Sperm retrieval was achieved in 40% (12/30) of patients whereas micro TESE outcome was negative in 60% (18/30) of the patients with Non-obstructive azoospermia. The level of serum inhibin B was statistically significantly higher in cases with positive micro-TESE outcome (70.90 pg/mL) compared to cases with negative outcome (24.50pg/mL) (p=0.002). The relative expression of SPEM1 was statistically significantly higher in cases with positive sperm retrieval (406.3) compared to cases with negative sperm retrieval (0.25) (p<0.001). Inhibin B had a cut-off point of >50.8pg/mL with 75% sensitivity and 80% accuracy,whereas, SPEM1 had a cut-off of >1.88, sensitivity of 91.67%, and accuracy of 90%.

Table (1):Serum Inhibin B levels in relation to Micro-TESE outcome in Cases (NOA) (n = 30)

	Micro-TESE outcome		U	P
	Negative (n = 18)	Positive (n = 12)		
Serum Inhibin B (Pg/ml) relative expressions				
Min. – Max.	2.0 – 127.0	18.70 – 238.0	38.0*	0.002*
Mean ± SD.	31.77 ± 33.99	92.13 ± 66.88		
Median (IQR)	24.50(7.0–39.80)	70.90(52.65–122.05)		

Table (2):*SPEM1* relative expression in relation to Micro-TESE outcome in Cases (NOA) (n = 30)

	Micro-TESE outcome		U	p
SPEM1 relative expression	Negative (n = 18)	Positive (n = 12)		
Min. – Max.	0.04 – 33.37	0.02 – 1247.66	20.50*	<0.001*
Mean ± SD.	3.44 ± 9.05	470.50 ± 405.58		
Median (IQR)	0.25 (0.16 – 0.61)	406.3 (129.6 – 824.45)		

Table (3): Validity (AUC, sensitivity, specificity and cutoff point) of Inhibin B and *SPEM1 relative expression* to discriminate according to sperm Retrieval (n = 12 vs. 18) in cases (NOA) groups

	AUC	P	95% C.I	Cut off	Sensitivity	Specificity	PPV	NPV	Accuracy
Serum Inhibin B (pg/mL)	0.824	0.003*	0.673 – 0.975	>50.8	75.0	83.33	75.0	83.3	80.0
SPEM1 relative expression	0.905	<0.001*	0.748 – 1.000	>1.88	91.67	88.89	84.6	94.1	90.0

Conclusion

SPEM1 and serum inhibin B can both be utilized in predicting the success of sperm retrieval.*SPEM1* was a more sensitive predictor of sperm retrieval than serum inhibin B in NOA patients. *SPEM1* relative expression had a significant positive correlation with serum inhibin B, and both markers had a significant negative correlation with FSH.