Sheath in Embryo Transfer. A Step Towards Improving Pregnancy Rate in ICSI Cycles

Original Article

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ABSTRACT

Aim: To compare classic embryo transfer versus sheath in techniques of embryo transfer.
Study Design: Retrospective case control.
Materials and Methods: Retrospective case control that was conducted in Multicenter fertility centers. Four thousands one hundred and fifteen infertile women undergoing ICSI with 3110 underwent fresh embryo transfer and 1005 underwent frozen embryo transfer. Sheath in technique conducted by confident positioning of the outer sheath before introducing embryo loaded inner sheath while classic technique both catheters introduced simultaneously. Primary outcomes Clinical pregnancy rate (defined as the presence of pulsating fetal heart after 6-8 weeks of Embryo transfer) in both groups.
Results: A total of 3110 embryo transfer were evaluated. in 1767 (56.8%) classic embryo transfer method was used compared to 1343 (42.2%) sheath in .The overall pregnancy rate is 50.8 % being 52.5 % within classic embryo transfer compared to 48.6 % within sheath in transfer that was statistically significant. Sheath in embryo transfer yield 51% pregnancy rate in non-difficult embryo transfer (comparable to classic transfer) and yield 43.3 % in difficult cases compared to failure of transfer with classic type .Pregnancy rate i8n frozen embryo transfer was significantly higher in sheath in group versus classic transfer (60.6 % versus 52.9%).
Conclusion: Sheath in Embryo transfer is a valid technique yield comparable pregnancy rate in non-complicated cases and non-comparable higher pregnancy rate in difficult cases .it is simple a traumatic techniques easy to be standardized

Key Words: Classic embryo transfer, embryo transfer, ICSI, pregnancy rate, sheath in.

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INTRODUCTION

Embryo transfer is a crucial step in the icsi success rate and all efforts have turned toward optimizing the ET procedure all through the last years with a prime goal of achieving a traumatic delivery of embryos into the endometrial cavity[1]. It was clearly demonstrated that the level of embryo transfer difficulty can have a significant effect on this result. As a supportive example for this data, a study examining the outcome of 4,807 ETs found that easy or intermediate transfers yielded a 1.7 higher pregnancy rate compared to difficult transfers[2].

Many evolving steps have been done in ET catheters over the years from firm, single-lumen catheters to soft, albeit malleable, double-lumen catheters. a significantly higher clinical pregnancy rate per ET was recorded with a soft catheter compared with a hard one[3,4] However, passing a soft catheter through the cervical canal may be difficult and sometimes not possible. Difficult ET using soft catheter has been reported to occur from 23%[5] to 37.6%[6-9].

One of the proposed technique to overcome embryo transfer difficulty is the use of sheath in procedure with maintaining the outer sheath in place however there is a little published work examine the efficacy of this technique so we conducted this study to compare sheath in versus the classic transfer technique on pregnancy rate .

AIM OF THE STUDY

To compare the classic embryo transfer technique with the sheath in technique of embryo transfer.

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MATERIAL AND METHODS

Design

Retrospective case control

Settings

Multicenter fertility centers

Participating women

Four thousands one hundred and fifteen infertile women undergoing ICSI with 3110 underwent fresh embryo transfer and 1005 underwent frozen embryo transfer .

Outcomes

Primary outcomes

Clinical pregnancy rate (presence of pulsating fetal heart after 6-8 weeks of Embryo transfer) in both groups

Secondary outcomes

1. The effect on two types of Embryo transfer catheter types on clinical pregnancy rate
2. Endometrial visualization at time of embryo transfer and difficulty of the transfer.

Inclusion Criteria

1. Age: 20-40 years.
2. Body mass index (BMI) up to 35.
3. Anti-mullerian hormone (AMH): 1 - 3.
4. No gynecological problem e.g. fibroid, endometriosis, uterine polyp, hydrosalpinx or adenomysis.
5. Both fresh and frozen embryo transfer cycles.

Exclusion Criteria

1. Patients with recurrent implantation failure.
2. Cancelled transfer cycles.

Methodology

Data of All completed ICSI (fresh and frozen cycles) were retrieved from the electronic records of two IVF center (namely Repro center in Alexandria and Elbedaya center in beniseif) from January 2018 to December 2019.

Data were rechecked through paper files also and laboratory records .any uncompleted data will be withdrawn. data include the identification serial number of patients (without obtaining patient names) demographic data , all details of ICSI cycles like doses og HMG, duration of treatment, protocol of ovarian stimulation, type of catheter used, day of embryo transfer, number of embryo transfer and the technique of embryo transfer either the sheath in technique that is conducted by confident positioning of the outer sheath before introducing the embryo loaded inner sheath while in classic technique both catheters introduced simultaneously.

Ethical approval was obtained before the start of the study from Faculty of medicine ethical approval committee IRB no: 00012098 – FWA No 00018699 under serial number 0304654 on 21 may 2020 .

Embryo transfer technique

Classic Embryo Transfer

Each ET procedure was carried out with the patient in the lithotomy position and without anesthesia. In most cases a transvaginal ultrasonography evaluation of the cervical canal and the position of the uterus was performed prior to ET. mock transfer was performed. The cervix was exposed with a speculum. After cleaning the cervix with sterile water, the catheter (outer and inner sheath loaded with embryos) was introduced into the cervical canal and advanced into the uterine cavity without touching the fundus. After ET the catheter was checked under the microscope and flushed to ensure that no embryos were retained. If embryos were found, they were immediately reloaded and retransferred with the same catheter.

Sheath in Embryo Transfer

The catheter was introduced through the cervical os with the outer sheath modulated and passed through the cervical canal. The stylet / or inner sheath was removed while the outer sheath remained in place. Then inner catheter containing the embryos was then gently manipulated into the outer sheath, and the embryos were transferred.

STATISTICAL ANALYSIS

Data were statistically described in terms of mean ± standard deviation (±SD), or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was done using Student t test for independent samples. For comparing categorical data, Chi-square ($\chi 2$) test was performed. Exact test was used instead when the expected frequency is less than 5. Accuracy was represented using the terms sensitivity, and specificity. Receiver operator characteristic (ROC) analysis was used to determine the optimum cut

off value for hMG dose in predicting pregnancy. Two sided *p values* less than 0.05 was considered statistically significant. All statistical calculations were done using computer program IBM SPSS (Statistical Package for the Social Science; IBM Corp, Armonk, NY, USA) release 22 for Microsoft Windows.

RESULTS

A total of 3110 embry transfer were evaluated .in 1767 (56.8%), embryo transfer was done through classic embryo transfer method while sheath in technique was used in 1343 (42.2%)

(Table 1) showing the patients and cycle characteristics and demonstrated that both groups were comparable regarding age and parameters of ICSI cycles including gonadotropins dosage s, number of retrieved oocytes and matures ones, fertilization rate as well as number of embryos to be transferred .

Table 1: Patient's characteristics

	ET method	N	Mean	Std. Deviation	Std. Error Mean	*P value*
Age	Classic	1,766	31.02	6.163	0.147	0.149
	Sheath in	1,342	30.70	6.186	0.169	
hMG dose	Classic	1,767	309.77	97.748	2.325	0.629
	Sheath in	1,343	311.49	98.313	2.683	
no.of oocytes	Classic	1,767	14.24	9.239	0.220	0.176
	Sheath in	1,343	14.69	9.116	0.249	
Mature oocytes	Classic	1,767	10.02	7.149	0.170	0.573
	Sheath in	1,343	9.87	7.164	0.195	
Fert.Rate	Classic	1,767	71.80	20.588	0.490	0.119
	Sheath in	1,343	68.83	27.690	1.301	
No.of Et	Classic	1,767	2.93	1.173	0.028	0.250
	Sheath in	1,343	2.88	1.002	0.027	

Antagonist protocol was the most commonly used protocol for ovarian stimulation being used in 1679 patient (54.3 %) followed by long agonist protocol used in 711 (22.9%) patients followed by short agonist protocol in 709 (22.8%) patients .1824 patients (58.6 %) had Embryo transfer on cleavage stage compared to 1286 (41.4 %) had blastocyst transfer .

Pregnancy rate For fresh cycle embryo transfer

The overall pregnancy rate is 50.8 % that was distributed to have 58.7% of it with classic transfer compare to 41.3 % with sheath in transfer. It was noted also that pregnancy rate was 52.5 % within classic embryo transfer compared to 48.6 % within sheath in transfer and this was statistically significant. (Table 2).

Pregnancy rate For the frozen cycles transfer

We had 1005 cases of frozen embryo transfer that yield 58.1 5 pregnancy rate .as shown in (Table 2) that pregnancy rate was significantly higher in sheath in group compared to classic transfer (60.6 versus 52.9%) (Table 2)

With more in depth analysis of sheath in embryo transfer In 1134 patients, sheath in embryo transfer was decided irrespective of level of presence or absence of difficult transfer that yield 51% pregnancy rate independent from the type of catheter used as well .on the other hand a difficult transfer was reported in 263 cases with failure of classic transfer and got 43.3 % pregnancy rate with sheath in technique.(Table 3)

Table 2: Pregnancy rate with methods of embryo transfer in fresh cycles

Clinical Pregnancy in fresh cycles			ET method		Total
			Classic	Sheath in	
	Positive	Count	928	653	1,581
		% within Pregnancy (related to number included)	58.7%	41.3%	100.0%
		% within ET method	52.5%	48.6%	50.8%
	Total	Count	1,767	1,343	3,110
		% within Pregnancy	56.8%	43.2%	100.0%
		% within ET method	100.0%	100.0%	100.0%
Clinical pregnancy in Frozen cycles			ET method		Total
			Classic	Sheath in	
Pregnancy	Negative	Count	153	268	421
		% within Pregnancy	36.3%	63.7%	100.0%
		% within ET method	47.1%	39.4%	41.9%
	Positive	Count	172	412	584
		% within Pregnancy	29.5%	70.5%	100.0%
			52.9%	60.6%	58.1%
	Total	Count	325	680	1,005
		% within Pregnancy	32.3%	67.7%	100.0%
		% within ET method	100.0%	100.0%	100.0%

Table 3: Level of Difficulty with Embryo transfer in Sheath in Transfer

			Difficulty		Total
			D	E	
Pregnancy	Negative	Count	149	530	679
		% within Preg	21.9%	78.1%	100.0%
		% within Difficulty	56.7%	49.1%	50.5%
	Positive	Count	114	550	664
		% within Preg	17.7%	82.3 %	100.0%
			43.3%	50.9%	49.5%
	Total	Count	263	1080	1,343
		% within Preg	18.8%	81.2%	100.0%
		% within Difficulty	100.0%	100.0%	100.0%

Pregnancy rate with Type of catheter

Two types of catheters were used for embryo transfer Wallace catheter that was used in 58 % of cases versus 42 % using gynetic catheters. Wallace catheter was the predominant type used in classic transfer use in 69.4 % of cases while gynetic was the predominant in sheath in transfer being used in 58.6 of those cases transferred by sheath in technique.

The overall pregnancy rate is 52.5 % in the classic group being 53.1 % with wallace usage compared to 50.6 % in gynetic usage and this was not statistically significant. on the other hand The overall pregnancy rate is 48.5 % in sheath in group being 47.6 % with wallace usage compared to 49.4 % in gynetic usage and this was not statistically significan (Table 4)

Table 4: Pregnancy rate with each type of catheter in classic and sheath in transfer

Classic Embryo transfer			Catheter type		Total
			Gynetic	Wallace	
Pregnancy	Negative	Count	267	572	839
		% within Pregnancy	31.8%	68.2%	100.0%
		% within Catheter type	49.4%	46.7%	47.5%
	Positive	Count	274	654	928
		% within Pregnancy	29.5%	70.5%	100.0%
			50.6%	53.3%	52.5%
Total		Count	541	1,226	1,767
		% within Pregnancy	30.6%	69.4%	100.0%
		% within Catheter type	100.0%	100.0%	100.0%
Sheath in transfer			Catheter type		Total
			Gynetic	Wallace	
Pregnancy	Negative	Count	388	302	690
		% within Pregnancy	56.2%	43.8%	100.0%
		% within Catheter type	50.6%	52.4%	51.4%
	Positive	Count	379	274	653
		% within Pregnancy	58.0%	42.0%	100.0%
		% within Catheter type	49.4%	47.6%	48.6%
Total		Count	767	576	1,343
		% within Pregnancy	57.1%	42.9%	100.0%
		% within Catheter type	100.0%	100.0%	100.0%

DISCUSSION

A total of 3110 Embryo transfer were evaluated .in the present work , in 1767 (56.8%), embryo transfer was done through classic embryo transfer method while sheath in technique was used in 1343 (42.2%) with a difficult transfer in 263 cases of sheath in group yielding 19.5 % difficulty rate that is consistent with other series of transfers with soft coaxial transfer catheters. 21.7% to 26.4 %[10] All patients were well matched in both groups regarding demographic data as well as history of infertility.

There was a significant difference in clinical pregnancy rate with using classic technique compared to sheath in techniques with a difference 4 % that was significant statistically however , With more in depth analysis of sheath in embryo transfer it can be noted that in 1134 patients, sheath in embryo transfer was decided irrespective of level of presence or absence of difficult transfer that yield 51% pregnancy rate independent from the type of catheter used as well .on the other hand a difficult transfer was reported in 263 cases with failure of classic transfer and got 43.3 % pregnancy rate with sheath in technique and this add a good value for sheath in techniques as we can consider it zero percent with classic transfer. So after adjusting these difficult cases, we found comparable pregnancy rate in non-difficult embryo transfer. In spite of similar findings have been reported before[9-11] The technique in these studies, unlike our technique, use an obturator or tenaculum to assist outer sheath insertion.

Another supporting finding for our data that clinical pregnancy rate was significantly higher in sheath in technique with frozen embryo transfer that is possibly resulting from the previous information of embryo transfer status and its difficulty so be prepared with sheath in technique .

We proposed that the introduction of the transfer catheter for one time maintaining the outer sheath in place just behind the internal os then passing the inner sheath smoothly and not the touching the fundus making the transfer a traumatic and hence increase the pregnancy rate even with difficult cases.

Soft Embry transfer catheters were demonstrated to be more superior in achieving higher pregnancy rate compared to firm catheters .in the present study , we compared the pregnancy outcome between two types of soft catheter namely Wallace and gynetic catheter and results showed non-significant difference between them in both fresh cycle and frozen cycle transfer .

Since embryo transfers were done with more thann one clinician in the two centers participating in this work, the danger of bias by inter-operator variability is present in this study[12] To avoid this bias, all clinicians were trained to transfer the embryos in an identical way according to ASRM guideline of Embryo transfer[13] and by this way the inter-individual differences between the clinicians almost completely disappear[14].

CONCLUSION

Sheath in technique of Embryo transfer is a valid technique that yield comparable pregnancy rate in non-complicated cases and non-comparable higher pregnancy rate in difficult cases .it is simple a traumatic techniques easy to be standardized .

CONFLICT OF INTERESTS

There are no conflicts of interest.

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