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RESEARCH ARTICLE

OUTCOMES OF FOLLICULAR FLUSHING VERSUS NONFLUSHING ASPIRATION IN POOR OVARIAN RESPONDERS WOMEN UNDERGOING INTRACYTOPLASMIC SPER INJECTION - EMBRYO TRANSFER: A RANDOMIZED CLINICAL TRIAL.

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Abstract

Aim: The main objective of this trial was to compare three - times follicular flushing aspiration (FFA) during ovum pick up (OPU) via modified single lumen needle (MSLN) to conventional direct non - flushing follicular aspiration (NFA) via single lumen needle (SLN) regards number of retrieved cumulus-oocyte complex (COCs), as well as other outcomes of assisted reproductive technology – embryo transfer cycles (ARF-ET) in women, had poor ovarian response (POR) after controlled ovarian hyperstimulation (COH).

Patients and Methods: This prospective, randomized, concealed allocation, double-blinded, controlled, superiority trial was performed at Hawa specialized IVF center, Benha, El- Qulobia, Egypt, between May 2017 and September 2018. One hundred women with POR after COH undergoing ART – ET cycles were allocated to OPU via MSLN/FFA (interventional group) or SLN/NFA (control group). Outcomes were number of retrieved COCs, Metaphase II (MII) oocytes, oocyte recovery rate (ORR), as well as outcomes of intracytoplasmic sperm injection (ICSI) procedures including fertilization rate (FR), implantation rate (IR), total cleavage embryo (ICE), number of women with positive B-HCG, clinical and ongoing pregnancy rate (CPR) (OPR) and live birth rate (LBR) per cycle as well as per ET. **Results:** The outcomes in both interventional as well as control groups was similar with no statistical significant differences regards number of retrieved oocytes (2.81 ± 1.36 vs 2.62 ± 1.82, p = 0.48), FR (68.36 ± 12.36 vs 70.38 ± 15.37, p = 0.47), IR (25.62 ± 9.36 vs 24.82 ± 10.36, p = 0.68), TCE (2.26 ± 1.28 vs 2.36 ± 1.36, p = 0.70), positive B-HCG (36% vs 38%, p = 0.83), CPR/ cycle (22% vs 20%, p = 0.80) and LBR / cycle (16% vs 14%, p = 6.78). While both groups were significantly differs in procedures time (7.81 ± 3.61 vs 14.61 ± 8.61, p < 0.0001) as well as total anaesthesia time (10.21 ± 4.61 vs 16.81 ± 8.72, p = 0.001).

Conclusion: In women with POR undergoing ART – ET cycles after COH, follicular flushing OPU is time-consuming despite similar outcomes including the number of retrieved mature oocytes to live birth rate.

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Introduction:-

Transvaginal ultra-sound guided ovum pick up (TVOP) has replaced others initially used methods of ovum pick up (OPU) earlier in the course of assisted reproductive technology (ART) evolution, secondary to its easiness, simpleness as well as effectiveness[1]. Initially, oocytes retrieval through follicular flushing aspiration (FFA) via double lumen needle (DLN) was thoughted to be more effective in oocytes retrieval than direct non-flushing follicular aspiration (DA) (NFA) via single lumen needle (SLN)[2,3,4].

On the contrary, systematic reviews and meta-analyses (SR &Ms) of randomized controlled trials (RCTs) evaluating impacts of direct aspiration (DA) versus follicular flushing aspiration (FFA) concluded that for normal responders women undergoing ART-ET, the use of DLN in OPU didn't improve the ART-ET's outcomes, despite prolonged operative time and extra costs[5,6,7]: As regards comparing FFA versus NFA in poor ovarian responders(POR) women undergoing ART-ET, two SR & M[8,9] was found, the first SR&M[8] analyzed 3 RCTs including 210 patients, investigating only women with poor ovarian respond (POR)[10,11,12], while the other SR&M[9] added to these 3 RCTs[10,11,12], a subgroup of women with POR in a trial taking in consideration comparing FFA versus DA in general[13]. These SR&Ms concluded No differences in ART-ET outcomes of comparing FFA to NFA in POR women undergoing ART-ET. However the two main contributing RCT in these SR&Ms found contradictory results regarding outcomes behind the number of retrieved cumulus-oocyte – complexes (COC) including fertilization rate (FR), total cleavage embryo (TCE), implantation rate (IR), pregnancy rate (PR), ongoing pregnancy rate (OPR) and live birth rate (LBR), thus conducting this trial to assess the impacts of modified SLN flushing follicular aspiration (MSLN) versus non-flushing direct follicular aspiration with the same SLN in outcomes of ART–ET in women with poor ovarian respond (POR) after adequate exposure to gonadotropins (Gn). The Null Hypothesis behind this work stated that there were no differences in outlined of ART-ET in women with POR whatever OPU conducted with FFA or NFA techniques[11]. However, the alternative hypothesis stated that the OPU with FFA technique might have detrimental impacts on ART-ET outcomes[10].

Patients and Methods:-

This trial was designed as a prospective, randomized, parallel groups, concealed allocation, essentially blinded except the physician performing ovum pickup (OPU), controlled, superiority trial and it was conducted in Hawa IVF specialized center, Benha, El-Qualobia, Egypt between May 2017 and September 2018. This trial was approved from Benha Faculty of Medicine ethical committee as well as all women participated in it were signed written informed consent after meticulous counseling regards the study intervention from the principal investigator (MAE).
In this trial, in total 100 poor ovarian responders(POR) women defined as women had ≤ 5 follicles of ≥ 13 mm on day of human chronic gonadotropins (hCG) administration and serum progesterone level < 1.5 ng/ml on the administration day of the hCG in groups of women diagnosed before undergoing controlled ovarian hyperstimulation (CoH) to have poor ovarian reserves (PORS) showing antral follicular count (AFC) of < 6 in both ovaries and anti-Mullerian hormone (AMH) of < 0.8 ng/ml or had prior COH cycle with poor responding were recruited sequentially and randomized to either SLN direct non-flushing follicular aspiration (SLN - NFA) group or modified SLN Flushing follicular aspiration (MSLN - FFA) group at random 1 : 1 ratio. The trial statistician used computer random number generator to produce the randomized treatment allocation schedule of a different block size of 4 and 6 to ensure that at completing each block an equal number of women with POR were included in the trial. The treatment allocation schedule transformed into opaque sealed envelops and stored at Hawa fertility center with the chief nurse. Women were randomized to either SLN-NFA (control) group or MSLN - FFA (interventional) group just before interning operative room for OPU, after randomization only the physician performing OPU was the person who was unblinded while blinding was maintained with the included women, laboratory personals as well as embryo transferring (ET) physician. Physicians performing OPU and ET at Hawa were seniors clinicians.

As the included women in this trial was anticipated to be poor responders (POR), pure recombinant follicular stimulating hormone (rFSH) (GonaPure^{R}, follitropin alpha, Minapharm, 10th of Ramadan city, Cairo, Egypt) 150 IU plus human menopausal gonadotropin (HMG) (Merional ^{R}, IBZA, Switzerland) 300 IU, starting from day 2 of menstrual follow after confirming that there were no ovarian cysts, and continue until the leading follicles reached 14 mm, gonadotropin-releasing hormone (GnRH) antagonist (orgalutian, MSD) was added to control the LH surge when ≥ 2 leading follicles reached the size of ≥ 17mm, ovulation induction was triggered by 10,000 hCG (choriomon^{R} 5000IU, IBZA, Switzerland) after 34 – 36 scheduled OPU was done . Oocyte retrieval was done in (SLN-NFA) group with 17 gauge needle (cook - Ireland, Limerick, Ireland under transvaginal ultrasound guidance

(TVS) at 80 mmHg suction pressure in 50 women with the poor ovarian response. In women allocated to MSLN - FFA group, under TVS guidance and superadded triple way valve and an extension intravenous line, as well as 10 ml of overnight, warmed incubated culture media, any punctured follicle after suctioning its content flushed with 2-4ml until its prior diameter reached and aspirated again, each follicle subjected to 3 cycles of flushing aspiration after initial aspiration at pressure of 80 ml utilizing an SLN identical to that used in SLN-NFA group (cook Ireland). In both groups, OPU was performed under Intravenous general anesthesia with propofol 1% (Fresenius Kabi, Homburg, Germany). According to two HawaIVF center protocol, all retrieved COC was denuded, and intracytoplasmic sperm injection (ICSI) performed within two hours from retrieval as well as fresh transfer in POR women usually done in day 3. All embryo transferred women started luteal phase support of 400 – 800 progesterone daily and continued until testing for pregnancy 14 days later when women with adequate B-hCG level ≥ 5IU / ml were considered positive chemical pregnancy, and Clinical pregnancy was diagnosed with TVS demonstrating positive fetal heart Pulsation. Ongoing pregnancy (OP) was considered if pregnancy was ≥20 weeks while live birth (LB) was considered when women delivered viable baby, implantation rate (IR) was calculated as the number of gestational sacs divided by the number of ET, while pregnancy rate (PR) either chemical (CPR) or clinical (CPR) was calculated as number of women with either positive BHCG or positive fetal heart pulsation in TVS divided by number of women shot transferred respectively. OPR calculated as the number of women with pregnancy ≥ 20 weeks divided by the number of transferred procedures. LBR was calculated as the number of women with LB divided by the number of women who had transferred procedures. The primary study outcomes measures were the number of retrieved COCs, fertilization rate (FR) defined as number fertilized oocytes divided by all oocytes undergoing ICSI precedence. Implantation (IR) defined as the number of intrauterine sacs by TVS per number of embryos who transferred, chemical PR, clinical PR, OPR, LBR as well as miscarriage rate (MR) which defined as the number of any failed pregnancy before 20 weeks gestation divided by the number of women with positive BHCG.

According to hypothesis behind this work and data on average total cleavage embryo (TCE) which was 2.8 (1.2) with NFA versus 1.9 (0.7) with FFA on Mok-Lin et al. trial[10] as well as utilizing the android app for sample calculation[14]. A total sample size of 100 women with POR were needed to detect average difference of one from two to three in TCE at SD of 1.2 at double-sided 5% significance (type / error (α) = 0.05) and a power of 80% (type II error (B) = 0.2) as well as to compensate for 20% losses to follow up.

Statistical analysis included all women who randomized in this trial [intention to treat (ITT) analysis policy] and was conducted by SPSS 21 for the window (IBM, Chicago, IL, USA). Continuous variables were introduced as mean ± standard deviations (ranges) and were tested for significance difference with two sample independent student's t-test while categorical data was introduced as numbers (percents) and compared between then with the chi-square test. Point estimate difference with 95% confidence interface (95% CI) as well as p-value was used to predicate statistical significance and a p-value of < 0.05 was used to show statistical significance.

Results:-

In this trial, 100 poor ovarian responders women undergoing ICSI – ET were choices to be tested for impacts of flushing follicular oocyte aspiration with modified single lumen against no-flushing direct follicular oocyte aspiration, from assessed 140 women showing the criteria of POR after COH. These 100 POR women were randomized to either of MSLN/FFA(interventional) group (50) and SLN/NFA(control) group (50) and all of them undergoing OPU as well as included in final intention to treat (ITT) analysis as presented in figure (1).

Table (1) introduces the study participants baseline demographic, clinical, COH and hormonal criteria and shows that both groups didn't differ significantly regards these items, as the 95% confidence interval included the null value of zero for continuous variables as well as the null value of 1 in assessing the risk ratio for categorical variables. So the studied women were more or less similar in preinclusion baseline characteristics, and any later differences in outcomes could be attributed to methods of OPU.

Table (2) presents the outcomes of OPU techniques as well as outcomes of whole ART-ET cycles and shows that there were no statistically significant difference between both OPU techniques regards the entirely retrieved COCs (2.81 ± 1.62 in MSLN/FFA versus 2.62 ± 1.82 in SLN/NFA $p = 0.48$) but the time need for OPU as well as the total anesthesia time were statistically significant shortened by 6.8, 6.6 minutes, respectively. Also there were no statistically significant differences regarding others ICSI - Et outcomes including fertilization rate (FR), total

cleavage embryos (ICE), transferred embryo (TE), embryo cryopreserved (EC), implantation rate (IR), women with positive BHCG, clinical pregnancy rate either per-cycle or per-ET, line birth rate (LBR) either per-cycle or per-ET as well as cancellation rate and its related causes between women undergoing MSLN/FFA or SLN/NFA in the poor ovarian responders follicular aspiration (PORFA) trial.

No apparent complications were recorded in either group of PORFA trial could be attributable to techniques of follicular aspiration as well as there were no recording of congenital in the delivered babies.

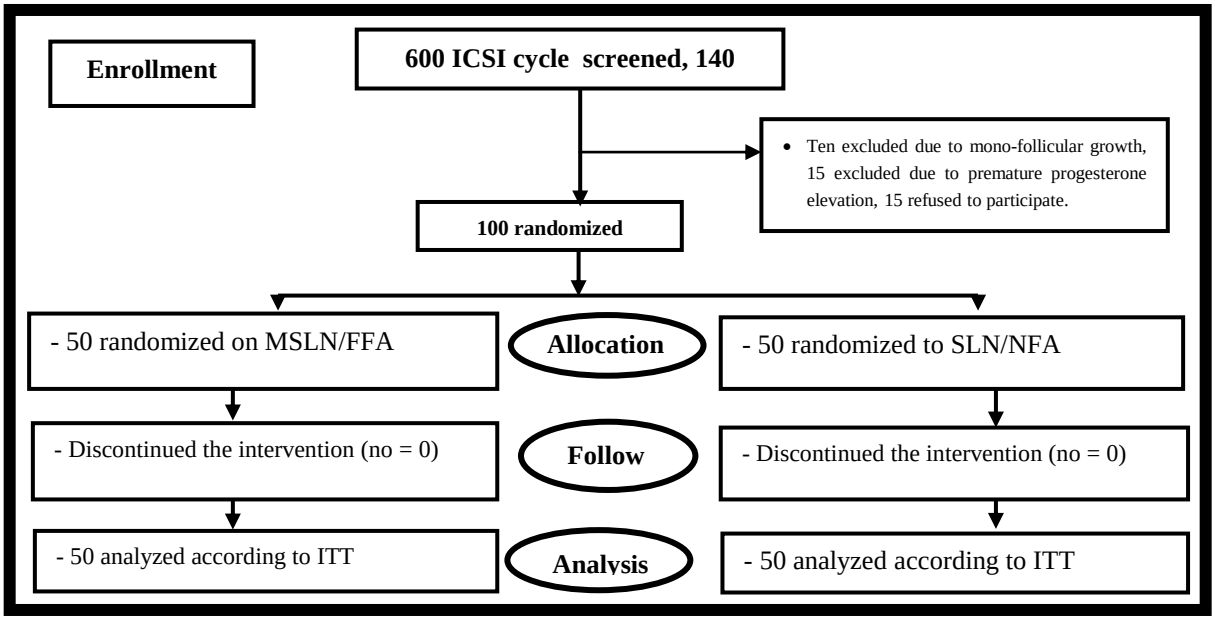

Figure1:-Consort Participants Flow Chart In MSLN/FFA(Interventional) Group Versus SLN/NFA(Control) Group Included In PORFA Trial.

Abbreviation:-
CONSORT:- Consolidated Standards of reporting trials, **MSLN/FFA:** Modified single lumen/flushing follicular aspiration, **SLN/ NFA:** Single women needle / no direct flushing aspiration, **PORFA:** Poor ovarian responders follicular aspiration.

Table 1:-Baseline characteristics of women in MSLN/FFA(interventional) group and SLN/NFA(control) group during ICSI-ET cycle in PORFA trial.

Variable	MSLN/FFA(group) (no = 50)	SLN/NFA(group) (no = 50)	Δ (95% C.I)	P value
-Age (Y)*	33.36±6.51(28.6-43.8)	34.63 ± 7.61(27.5-42.8)	1.27 (-1.54,4.08)	0.37
- BMI (kg/m^2)*	28.22±5.81(23.5-33.6)	29.62 ± 4.62(22.6-35.6)	1.30 (-0.78, 3.38)	0.21
- Infertility duration (y)*	9.61±3.72(4.5-13.5)	10.52 ± 4.82(3.5-15.6)	0.91 (-0.79, 2.61)	0.29
- Gravidity *	1.91±1.21(0-4)	2.12 ± 1.61(0-5)	0.21 (-0.35, 0.77)	0.46
- Parity *	0.03±0.08 (0-2)	0.06 ± 0.09 (0-2)	0.03 (-0.00, 0.06)	0.08
- Cause of infertility :**				
Diminished ovarian reserve	38 (76%)	36 (72%)	4%(-13.04, 20.75)	0.65
Endometriosis	4 (8%)	8 (16%)	9%(-5.27, 21.41)	0.22
Mole factor	8 (16%)	6 (12%)	4% (-10.07, 18.04)	0.56
- AMH (ng/ml)*	0.68±0.12 (0.12-0.79)	0.69 ± 0.21 (0.15-0.72)	0.11(-0.05, 0.07)	0.77

- AFC (n)*	3.81 ± 2.82 (2 - 6)	4.21 ± 2.62 (2 - 6)	0.40 (-0.68, 1.48)	0.46
- Previous poor response **	28 (56%)	32 (64%)	8% (-10.89, 26.11)	0.41
- Starting Gn(Iu)*	425±130 (375-525)	415±140 (375-600)	10 (-63.61, 43.61)	0.71
- Total Gn(Iu)*	4560±2300(3900-5550)	4660±2400(3850-6000)	100(-832,1032)	0.83
- Stimulation Days *	10.91±3.26 (9 - 13)	11.11±4.36 (9 - 12)	0.2(-1.32, 1.72)	0.79
- Peak E2 (pg/ml)*/* **	736 ± 300 (450 -1200)	695±280(500 - 1300)	40 (-155.16, 75.16)	0.49
- Peak P4 (ng/ml)*/* **	1.03 ± 0.62(0.81-1.62)	1.09±0.72(0.75 -1.56)	0.06(-0.20, 0.32)	0.66
- Follicules≥ 13 mm at hCG*	3.71 ± 0.82 (2 - 6)	3.82 ± 0.92 (2 - 6)	0.11(-0.23, 0.45)	0.52
- Follicules≥ 10 mm at hCG*	5.61 ± 1.23 (3 -10)	6.21 ± 1.86 (4 -11)	0.39(-0.23, 1.01)	0.21
-Endometrial thickness (mm)*	8.26 ± 3.26 (5 -11)	9.21 ± 4.61 (4 - 12)	0.95(-0.63, 2.53)	0.23

Abbreviations:-

MSLN/FFA:-

Modified single lumen / flushing follicular aspiration, **SLN/NFA :**Single lumen needle / non-flushing direct aspiration,

PORFA:

Poor ovarian responders follicular aspiration. **AMH:** Anti-Mullerian hormone, **AFC:**Antral follicular count, **Gn:** Gonadotropins,

E2:

estradiol, **P4:**Progestrone,

BMI :

Body mass index, **Δ (95% CI):** Point estimate difference with 95% confidence interval.

- Values were given as mean ± Standard deviation (range)* or number (percentage)**
- P <0.05 : Statistically significant.
-*** Peak E2 & P4 at day of HCG.

Table2:-Outcomes of ART-ET cycles among women undergoing MSLN/FFA(interventional) group and SLN/NFA(control) in PORFA trial.

Variable	MSLN/FFA group (no = 50)	SLN(NFA group) (no = 50)	Δ (95% C.I)	P value
Total aspirated follicules (n)*	156	162		0.48
Total retrieved oocytes (n) *	106	112		0.48
Retrieved oocytes (n) *	2.81±1.62 (0-5)	2.62±1.82(0-5)	0.19(-0.72,0.34)	0.48
Retrieved MII oocytes (n) *	2.18±1.36 (0-4)	1.92±1.21(0 - 3)	0.26(-0.77, 6.26)	0.31
Retrieved GV oocytes (n) *	0.63 ± 0.26(0-3)	0.70 ± 0.61(0-3)	0.07 (-0.11, 0.25)	0.45
Time of OPU (min)*	7.81 ± 3.61 (5-8)	14.61 ± 8.61(10 - 18)	5.80 (4.17, 9.42)	<0.0001
Total OPU anesthesia time*	10.21 ± 4.61 (8 -15)	16.81 ± 8.72(12-24)	6.60 (3.44, 9.75)	0.0001
Oocytes maturity rate*	82.61±10.61 (55-100)	79.81±10.25(60-100)	2.80 (-6.94, 1.34)	0.18
Retrieved COCs/punctured follicule*	0.71±0.31(0-100)	0.79 ± 0.34 (0-100)	0.08 (-0.04, 0.20)	0.22
Zero COCs follicular aspirate(n%)**	8 (16%)	9 (18%)	2% (-12.97, 16.91)	0.79
Mature oocyte recovery rate*[(1)].	70.26±10.36(0-100)	69.36 ± 11.32(0-100%)	-0.90 (-5.20, 3.40)	0.67
ICSI**	42 (84%)	411 (82%)	2% (-12.97, 16.91)	0.79
Ferilization rate*	68.36±12.36(0-100)	70.38±15.37(0 - 100%)	2.02 (-3.51, 7.55)	0.47
Total cleavage embryos*	2.26±1.28(0 - 4)	2.36 ± 1.36 (0 - 4)	0.10 (-0.43, 0.62)	0.70
Transferred embryos*	1.84 ± 1.11 (1-3)	1.63 ± 0.99(1-3)	0.21 (-0.62, 0.20)	0.32

Embryo grade*[(2)]	2.26 ± 1.21 (1- 5)	2.36±1.36 (0-4)	0.10 (-0.41, 0.61)	0.69
Embryo cryopreserved*	0.12 ± 0.81 (0 - 3)	0.18 ± 0.92(0-3)	0.06 (-0.28, 0.40)	0.73
Implantation rate*	25.62±9.36 (0 - 100)	24.82±10.36(0-100)	-0.80 (-4..71, 3.11)	0.68
Positive B-HCG**	18 (36%)	19 (385)	2% (-16.42, 20.23)	0.83
Clinical pregnancy rate/cycle**	11 (22%)	10 (20%)	2% (-13.98, 17.87)	0.80
Clinical pregnancy rate/ET**	13 (26%)	12 (24%)	2% (-14.80, 18.66)	0.81
Live birth rate/cycle**	8 (16%)	7 (14%)	2% (-12.39, 16.35)	0.78
Live birth rate /ET**	9 (18%)	8 (16%)	2% (12.97, 16.91)	0.79
Cancellation rate**	15 (30%)	18 (36%)	6% (-12.15, 23.29)	0.52
Causes of cancellation :**				
No oocyte in OPU	8 (16%)	9 (18%)	2% (-12.39, 16.35)	0.78
Total fertilization failure	4(8%)	5 (10%)	2% (-10.22, 14.35)	0.72
Cleavage arrest	3(6%)	4 (8%)	2% (-9.30, 13.53)	0.69

Abbreviations:-

ART-ET:- Assisted reproduction technology and embryo transfer, **MSLN/FFA:** Modified single lumen / flushing follicular aspiration, **SLN/NFA :** Single lumen needle / non-flushing direct aspiration, **PORFA:** Poor ovarian responders follicular aspiration trial, **MII:** Metaphase II, **ICSI:**Intracytoplasmic sperm injection, **GV:** Germinal vesical oocyte, **OPU:** Ovum pick up, **COCs:** Cumulus oocytes complexs, **ET:** Embryo-transfer, **B-HCG:** Beta subunit of human chronic gondotropins, **Δ (95% CI):** Point estimate difference with 95% confidence interval.

Values were given as mean ± Standard deviation (range)* or number (percentage)
P <0.05 : Statistically significant. **(1)** = Matur oocyte recovery rate calculated as (MII) follicles ≥ 13 mm at HCG x 100%. **(2)** =Grade of cleavage embryo from 1 to 5 where 1 means best while 5 mean worst quality.

Discussion:-

The trial demonstrated that, in women, with poor ovarian response to COH in ART-ET treatment cycles follicular flushing ovum pick up three – times by modified single lumen needle with triple value and an intravenous extension line resulted in lengthy procedures as well as prolonged anesthesia time without any significant differences in the number of COCs. Also, this trial did not show any significant differences between both techniques of OPU regards fertilization rate, implantation rate, +ve B-HCG number, ongoing pregnancy rate as well as live birth rate.

This trial was the 4th trial comparing FFA and NFA of OPU in women with POR in ART-ET cycles. The present study was in agreement with either RCT[s(10,11,12)], and SR&Ms[(8,9)] regards that FFA versus NFA prolong the procedure as well as the anesthesia time without any gaining values in the number of retrieved COCs as well as MII oocytes. Also the outcomes of the present trial were in agreement with results of the two RCTs[(11,12)] and the two SR &Ms[(8,9)] regards that the FFA didn't induce a detrimental impacts on retrieved oocytes with consequently lower fertilization rate (66.7 FFA vs 81.7 NFA) and a statistically significant lower total embryo cleavage (1.9 ± 0.7 in FFA vs 2.8 ± 1.2 in NFA, p = 0.01), lower embryo grade (2 ± 0.4 vs 2.2 ± 0.6, p = 0.03), lower implantation rate (5.3% vs 34.2%, p = 0.006), lower clinical pregnancy rate per cycle (4% vs 36%, p = 0.01) and lower live birth rate per cycle (4% vs 20%, p = 0.19) as reported in Mok-Lin et al. trial[(10)]. The presented trial was on the contrary to Mok-Lin et al.[(10)] trial regards the proposed detrimental mechanisms associated with flushing follicular aspiration of OPU including introduction of culture media, impacts of high flushing pressure as well as proposed increased retrieval of immature oocytes and alteration of COCs granulosa cell numbers and function with its consequences on the outcomes of ICSI as well as outcomes of ART-ET cycles[(10)].

Strengths in the present study include its prospective nature, randomization, blinding of included embryologist, embryo transferring physician as well as Participating patients and follow up physician. Taking a step further in

RCTs assessing impacts of FFA versus NFA techniques on OPU outcomes through adequate power choosing total cleavage embryo as determining item in assessing the prior sample size compared to previously published RCTs[10,11,12,13] whom determining their sample sizes on the differences in the number of retrieved COCs. Storage of treatment allocation schedule by the chief nurse at the Hawa IVF center by utilizing closed sealed enveloped techniques insured concealment of the allocation procedures.

The main limitations of this trial include an inability to complete blinding of the physician performing OPU. However, this physician did not include any more in any other part of the trial, and this could not be avoided owing to the nature of procedures. Inadequate power of this trial likes others prior RCTs[10,11,12] taking in consideration impacts of OPU techniques in women with POR in ART-ET cycles regards evaluation of more important outcomes of the ART-ET cycles namely ongoing pregnancy rate as well as live birth rate, however such items required 200 - 400 POR patients per group which was behind the capacity of most IVF center and required a long period of time as well as considering participating of multiple IVF centers, however accumulation of patients with POR from different RCTs[10,11,12,13] could resolve such problem. Another limitation of the presented study is the exclusion of natural cycles and women with mono-follicular growth. So, it is recommended to conduct a larger sample size trial or multicenter one taking into consideration live birth rate as a prior determining factor of sample size.

This RCT likes others 2 RCTs[11,12] and 2 SR &Ms[8,9] found neither beneficial nor detrimental impacts of three times follicular flushing ovum pick up via modified single lumen needle over conventional single lumen needle direct non-flushing follicular ovum pick up regards any outcomes from the number of retrieved oocytes to live birth rate.

Conclusion:-

The current trial did not recommend any more follicular flushing in women with poor ovarian response to controlled ovarian hyperstimulation in ART-ET cycles over simple non-flushing direct follicular fluid aspiration ovum pick up

Conflict of interest:-

The author has nothing related to this article to be disclosed

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