INVO/ICSI:
A PIONEER IDEA AND A REAL ALTERNATIVE FOR ART

CECOLFES
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Definition

INVO: Enables us to return to **a natural and semi-natural environment** where gamete culture and development occurs in the best natural incubator, the vagina, where gas concentrations, temperature, and humidity are physiologically appropriate. Since **mild ovarian stimulation** is used, it's a safe treatment associated with healthy babies at home, (at lower cost), and a favorable cost-benefit ratio derived from in-vivo conceptus development.

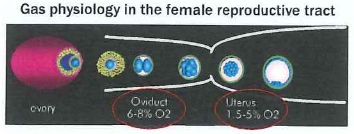
Objective

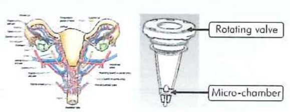
Intravaginal Culture of Oocytes (INVO) is an Assisted Reproductive Technique (ART) that allows oocyte fertilization and early embryo development inside an air free, gas-permeable (CO_2 and O_2) plastic device called INVOcell. This study reports an application of INVO/ICSI procedure for patients displaying male factor. After Intracitoplasmatic Sperm Injection (ICSI), Microinjected Oocytes (OMI) are placed into an INVO device to be incubated within the vaginal cavity. A total of 172 cycles of couples with male factor as cause of infertility were included in the INVO/ICSI protocol, from January-December 2012 in CECOLFES showing **similar results to classical ICSI procedures**, as a new optional treatment in ART.

Principles

O_2 concentration

Gas physiology in the female reproductive tract



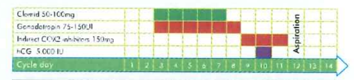


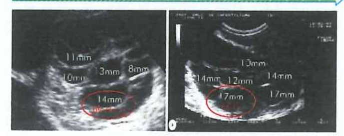
- The vaginal cavity provides **correct pCO_2, pO_2** and body temperature.
- INVO is **gas-permeable**, the device permits pCO_2 and pO_2 balance between the vagina and the culture medium.
- It **avoids risk factors** related with culture under high O2 concentrations and temperature variations.
- It allows embryo culture in low O_2 conditions (5% O_2, 5-6% CO_2 y N_2).
- It allows the patient to participate **"anew" in conception.**

Methodology

A total of **172 couples** underwent INVO/ICSI protocol. **Natural cycle or mild ovarian stimulation** with **Clomid** (OMIFIN®) and **hMG** (Merional®) were used. An average of 4.7 OMIs per patient were placed in the **INVOcell™** preloaded with **G2 PLUS®** (VitroLife). Semen samples were capacitated using **PureSperm®** density gradients and the **Proinsert® device** (Nidacon). ICSI was performed, OMIs were loaded into the INVO device, which was then placed in the vagina. After 72 hours, the device was removed and embryos were recovered for uterine embryo transfer.

Mild Stimulation





Sperm preparation

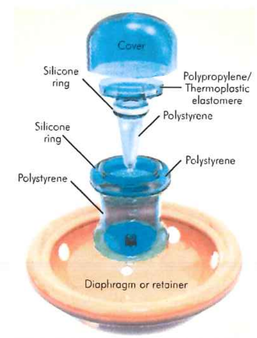
Density Gradient 40/80

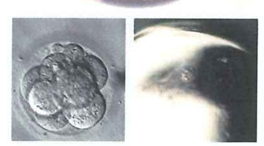
A density gradient will effectively remove lymphocytes, epithelial cells, abnormal or immature sperm, cell debris, seminal fluid, bacteria and to some extent viruses.

ProInsert®

- 80/40 Density Gradient, easy to load without mixing the layers.
- Easy to retrieve the pellet via the central channel of the ProInsert without recontamination.
- Easy to discard the post-capacitation residues.

Intravaginal Culture





Results

A total of **172 cycles** were performed. An average 6.5 oocytes per cycle were retrieved, a mean of 4.7 OMIs were placed into **INVOcell** device, and a mean number of transferred embryos per cycle was 2.0. The cleavage rate obtained after INVO culture was 53.1%. A total number of 65 clinical pregnancies (59 single and 6 multiple pregnancies) were achieved, corresponding to 37.9% of pregnancy rate per cycle and to **40.3% of pregnancy** per transfer.

INVO/ICSI RESULTS

Groups[a]	Cycles (n)	Transfers[b](n)	Recovery[c]	INVOcell[d]	Cleavage[e]	Et[f]	Pregnancy[g]
<29	33	32 (96,9)	6,93	4,63	3,1 (66,9)	2.1	10 (54,5)
30-34	53	50 (94,3)	7,82	4,52	3,2 (70,7)	2.2	22 (41,5)
35-39	71	66 (92,9)	6.42	5,01	2,6 (51,8)	1.8	23 (32,3)
≥40	17	13 (86,6)	5.12	4,93	1,7 (34,4)	1.5	2,0 (13,3)
Total	172	161 (93.6)	6,5	4,7	2,5 (53,1)	2,0	65 (37,9)

Note: INVO= Intravaginal culture of oocytes; ET= Embryo Transfer. Values in parentheses are percentages. [a]Ranges of ages. [b]Cycles that ended up in transfer. [c]Mean number of retrieved oocytes per punction. [d]Mean number of oocytes placed for fertilization per INVOcell device (cycle). [e]Mean number of retrieved viable proper developed embryos per INVOcell device (cycle). [f]Mean number of transferred embryos per cycle. [g]Number of clinical pregnancies per cycle

Number of cycles	172
Number of single pregnancies	59
Number of multiple pregnancies	6
Total number of pregnancies	65
Miscarriage	18
Healthy babies home	47
Clinical pregnancy rate/cycle	37,9%
Clinical pregnancy rate/transfer	40,3%

Conclusions

- **INVO**/ICSI can be an effective, alternative, and viable option in ART to achieve pregnancy in male factors cases.
- **INVO**/ICSI showed comparable results to those reported using classical ICSI.
- **INVO** produces high-quality embryos that result in a good rate of clinical pregnancy per cycle and a lower rate of multiple gestations.
- **INVO** has good acceptance because of patient involvement during the initial stage of embryo development, with very positive and significant psychological impact.
- The lower costs of treatment, places **INVO** within the reach of a larger population of infertile couples.

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