Fertility Technology Research and the Use of Human Beings as Property

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Abstract

In January 2020, an article in the *Journal of Human Reproduction* exploring whether human embryos could be obtained via uterine lavage and to compare their quality to embryos created via *in vitro* fertilization. Any embryo that was not removed via lavage was either prevented from implanting by giving the women injections of gonadotropin releasing hormone antagonists or aborted with either methotrexate or uterine curettage. This research was done using women in Mexico, who were paid the equivalent of over two months' wages and who signed away their rights to their embryos, including agreeing to have an abortion if implantation did occur. Not only is this another instance of human beings being treated as property but is against the dignity of these women by turning them into, as one ethicist says, "human petri dishes."

Summary: Researchers continue to use people as objects to obtain their goals. In this case, it was poor women in Mexico and their embryos. The Editors of *Journal of Human Reproduction* enabled this by publishing the report.

Keywords

Abortion, Applied ethics, Beneficence, Bioethics, Dignity of the human person, Distributive justice, Ethics, Ethics of reproduction, Human dignity, Infertility therapies

In January 2020, the *Journal of Human Reproduction* published a proof of concept paper using uterine lavage to remove human embryos and assess them with embryos created via *in vitro* fertilization (IVF). In animals, it is known that embryos fertilized *in vivo* are of "more likely to be of good morphology" than embryos created *in vitro*. The researchers wanted to assess whether this also was true in humans because it could be applied to women who would otherwise want or need IVF for preimplantation genetic testing (PGT), fertility preservation, or for lesbian couples who want reciprocal implantation. The study was done in the state of Nayarit in Mexico. It was approved by ethics committees in both Mexico and the United States and was registered with ClinicalTrials.gov (Munné et al. 2020).

Women of known fertility were chosen; 8 percent had a history of infertility. They were all under thirty years of age, in good health, had two ovaries, and had no sexually transmitted infections. They all underwent a hysterosalpingogram prior to entering the study to ensure that their fallopian tubes were patent. They agreed that their oocytes and embryos would be donated for research or donation. Finally, they had to sign consent that "in the case of persistent human chorionic gonadotropin (hCG) levels

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after uterine lavage they may be treated with uterine curettage and/or the administration of methotrexate” (Munné et al. 2020); that is, any pregnancies that occurred would be terminated.

Participants were started on controlled ovarian stimulation for three days with recombinant human follicular stimulating hormone and human menopausal gonadotropins. On the fourth day, the women underwent transvaginal ultrasound and had estrogen levels drawn. If there were two or more follicles 18 mm or more, then ovulation was induced with either hCG alone or leuprolide and hCG.

Thirty-six hours later, the women were inseminated artificially with either donor or partner sperm. Uterine lavage occurred around 120 hours later. Afterward, the women were given a gonadotropin releasing hormone (GnRH) antagonist injection (Munné et al. 2020) which causes an immediate blockade of gonadotropin release in the pituitary by permanently binding to GnRH receptors in the pituitary (Khazeni and Pegah 2018). This was done to “minimize retained embryos” (Munné et al. 2020). Initially, they used two doses, but due to problems with compliance, women were given one higher dose. This reduced the rate of positive hCG levels from 41 percent to 5 percent. Thirteen days after lavage, an hCG level was obtained. If over 2 mIU/mL, levels were followed. If the levels increased, the women were treated with methotrexate and/or endometrial curettage. They were then followed for thirty days postlavage for any complications. Some women also underwent a cycle where oocytes were obtained for IVF (Munné et al. 2020).

Complications were minimal. There were no episodes of ovarian hyperstimulation. The main side effect was nausea (4 percent; Munné et al. 2020).

There were 134 cycles involved, divided into eight groups. One hundred thirty-six embryos obtained in 42 percent of those cycles overall. Results however improved as the study continued. There were eleven women who had a positive hCG. Of them, two “regressed spontaneously,” two had “endometrial curettage,” three were treated with methotrexate alone, and four with methotrexate and “endometrial curettage” (Munné et al. 2020).

All embryos recovered via lavage were evaluated morphologically and underwent trophoctoderm biopsy. Of the embryos obtained, 30 percent were multicelled and 70 percent blastocysts. Compared to the IVF cycle, the embryos and blastocysts created *in vivo* had comparable euploidy and chromosomal abnormalities, but better morphology with 74 percent of the *in vivo* group having good morphology (3AA or better), compared to 43 percent *in vitro*. All

embryos with good morphology were vitrified and then cryopreserved in liquid nitrogen (Munné et al. 2020).

The conclusion was that uterine lavage was a nonsurgical, minimally invasive, low cost way of obtaining a greater number of embryos of good morphology for implantation for fertile women who want to preserve embryos, do PGT, or reciprocal fertilization (“shared maternity”) for lesbian couples (Munné et al. 2020). Another possibility would be for women who, for whatever reason, decide to use a surrogate.

Ethical Analysis

The Editors of the *Journal of Human Reproduction* were uneasy with the study, even publishing an editorial regarding their ethical concerns. They were concerned that “fertile women not wishing to become pregnant were exposed to ovarian hyperstimulation and were treated with intrauterine insemination with semen that did not necessarily come from their own partner. Despite uterine flushing, not all embryos were retrieved, and some women accidentally became pregnant. For termination of pregnancy, those women were then treated with methotrexate (MTX), some even with a dilation & curettage (D&C). All of the above interventions are potentially harmful to the women who did not benefit directly from participation—other than through financial compensation” (Lambalk et al. 2020). The editors were reassured that the study had been approved by two ethical committees, one in the United States and the other in Mexico. They also received and reviewed the approvals by these committees and the patient information sheets. Even so, they were still left with “a strong feeling of uneasiness” (Lambalk et al. 2020). In the end, they decided that it would be unethical to overrule two ethical boards and not publish a study that had met “appropriate ethical guidelines and principles” and where proper consent had been given (Lambalk et al. 2020). In other words, it was okay as long as someone’s “ethical guidelines and principles” were followed, even if they weren’t necessarily those of the editors.

One ethical consideration, using the principles of the Belmont Report, is the continued use of poor third-world women for whom, although they were given extensive information regarding potential risks (Lambalk et al. 2020), the fact that they were being paid more than two months’ salary could affect their autonomy (Oron 2020), more specifically their voluntariness, their freedom to choose because these

were poor women with families to support. They, not those who would benefit, bore all the burden of the research, which goes against justice. One ethicist, Laurie Zoloth, said that they were used as “human petri dishes” (Stein 2020). These women were intentionally impregnated and then these pregnancies were terminated for a possible “future technological benefit” which goes against the principle of beneficence (Oron 2020). Oron (2020) also noted high rate of need to re-biopsy the embryos (90 percent) and low recovery of embryos (41 percent). All of this is against the principle of nonmaleficence.

Researchers who work in the area of artificial reproductive technology have no problem creating human life via IVF. According to Engelhardt (1996), in modern secular society, human life before birth is the property of the woman to do with as she wills as long as her intent is not malevolent (pp. 254, 256) and barring any legal constraints. In this study, the subjects transferred their ownership rights to a third party, that is, Munné and his colleagues. These women also did this with the full knowledge of what Munné et al. would do in their study including the premeditated destruction of those embryos who managed to escape lavage. Perhaps it is this casualness toward those lives that were intentionally created and then intentionally destroyed because they managed to survive the attempt to destroy them that caused the concerns of the reviewers and Editors of the *Journal of Human Reproduction*. It is difficult to say that the intention toward those embryos was not malevolent.

This research was an assault against the dignity of women. First, these women were offered a substantial amount of money, relative to their annual income, for the use of their bodies. It is true that they did give consent, but the financial incentive could well have played a significant role in that consent. Although the physical side effects were minimal, there was still the possibility of ovarian hyperstimulation, which can be life-threatening. Women were intentionally inseminated solely for the purpose of creating human life for research. Finally, they agreed to the removal of any human life created within their own bodies and the destruction of those who were not, instead of nurturing that life.

The “World Medical Association Declaration of Helsinki” (2013) notes that while in “medical practice and in medical research, most interventions involve risks and burdens” (Declaration #16) it also states “Medical research involving human subjects may only be conducted if the importance of the objective outweighs the risks and burdens to the research subjects” (Declaration #16) and “All

medical research involving human subjects must be preceded by careful assessment of predictable risks and burdens to the individuals and groups involved in the research in comparison with foreseeable benefits to them and to other individuals or groups affected by the condition under investigation” (Declaration #17). This was a study that had no foreseeable benefit to the women involved, only risks. And although people can volunteer altruistically out of the goodness of their hearts for research that will not directly benefit themselves for the good of science, the main people (and most likely only people) who could benefit from this technology are wealthy women in first-world countries who can afford the technology and storage fees, certainly not other poor women like those in the study. This “altruism” is also tempered by the amount of the payment made to these women as well as the denial of the human dignity of the embryos, who obviously received no benefit.

There is no mention of what would happen to the women had they changed their minds after insemination but either before or after uterine lavage or after implantation, particularly no mention of an effect on their compensation, which raises the possibility of coercion.

These women could also be considered a vulnerable group requiring special protection because they were poor. Again, in the Declaration of Helsinki (2013), “Medical research with a vulnerable group is only justified if the research is responsive to the health needs or priorities of this group and the research cannot be carried out in a non-vulnerable group. In addition, this group should stand to benefit from the knowledge, practices or interventions that result from the research” (Declaration #19). Yet it is doubtful that even the women in the infertility group would be able to afford such a procedure. Finally, the “responsibility for the protection of research subjects must always rest with the physician or other health care professionals and never with the research subjects, **even though they have given consent**” (Declaration #9, emphasis added). This research done in a vulnerable population and of no potential medical benefit to them was done with the approval of two ethics committees.

This study is a further example of the secular attitude that certain human beings can be treated as property to be used or destroyed according to one’s own decision. That determination is not made by the one who will be most affected, that is, the embryo, but by those who have power over it. In this case, that power was transferred by the women subjects to the researchers conducting the study. These

researchers even have a potential financial gain through the sale of those “good” embryos that were cryopreserved for “adoption” by other women.

Abortion is part and parcel of the protocol at several levels. It was anticipated and planned without any apparent qualms on the part of the researchers. As defined in the *Ethical and Religious Directives* (2018, #45) for Catholic hospitals, abortion is “the directly intended termination of pregnancy before viability” and that includes the interval between conception and implantation. Definitely there was a postfertilization, abortifacient effect, and intent. Because a control cycle was not done where the GnRH antagonist was not given, the total effect is unknown. However, in one cycle in the study, implantation was 41 percent even with the administration of a GnRH antagonist (Munné et al. 2020). The destruction of retrieved embryos that were not of sufficient quality is assumed as well. If this were to be commercially available, this would be true even if these embryos were created within the marital act and especially those who underwent PGT.

In addition, the study seems to have disregarded the abortion laws of the state of Nayarit. At the time of the study (August 2017 to June 2018), abortion was legal only in Mexico City (Oaxaca legalized abortion in 2019). In the state of Nayarit (*Mexico News Daily* 2019), abortion is allowed for rape, “accident,” and the life and health of the mother (Grupo de Informacion de Reproduccion en Elegida [GIRE] 2014). In Nayarit, there were only fifty legal abortions performed over a twelve-year period (Statista 2020) which means that this study alone performed as many abortions (nine in eighty-three women, although it is unknown whether any had more than one) as were legally performed in a two-year period. To be in the study, the women had to agree that they would be given medicine in an attempt to prevent implantation of any embryos that might not have been removed via lavage and abort any embryos that managed to implant anyway.

Nayarit law states that human life is to be protected from conception (GIRE 2014). The resultant pregnancies were called an “accident” by the Editors of the *Journal of Human Reproduction* (Lambalk et al. 2020), but they were not. They were the natural consequence of fertilization. It was an anticipated possibility. If the abortions were performed because the researchers would argue that the pregnancy threatened the life or health of the mother, the women should not have been allowed to undergo in the first place a procedure that carried a real risk of pregnancy, particularly because the chance of such pregnancy was unknown at the start of the

study. Munné et al. are careful not to use the words “abortion” or even “termination” in their article. Were the women fully aware of why they were being given MTX or having endometrial curettage that they were undergoing abortions? How was this addressed by the ethics committees, especially the one in Nayarit?

Conclusion

Scientifically, the goal of increasing knowledge of the biology of reproduction was met. The conclusion validated the hypothesis of the investigators. The data demonstrate that there is something lacking in the artificial IVF environment compared to *in vivo* fertilization. As in animal models, *in vivo* fertilization produces a better-quality embryo than *in vitro* with the added benefit of being able to obtain them in a nonsurgical, minimally invasive manner and done at a lower cost than IVF. This would allow women (and couples) to delay pregnancy to a time of their choosing by being artificially inseminated and then freezing the embryos to be implanted at a later date. Women (or couples) who have a single-gene genetic defect could undergo this procedure while still allowing for PGT. At the same time, it could increase their chances of a successful pregnancy while avoiding the invasive surgery needed for IVF. Finally, lesbian couples could use it when they wish to have shared maternity, that is, where one partner donates the egg and the other gestates it.

However, we still do not know whether the rate of aneuploidy is different in ovulations created by hyperstimulation versus normal, which is important to know if deciding whether IVF embryos should be routinely evaluated for it (Oron 2020). There was one cycle that was not hyperstimulated (cohort 3) in the study (Munné et al. 2020), but the results were not reported.

It is troubling that, although the Editorial Committee of the *Journal of Human Reproduction* had serious concerns, they published the paper anyway. Approval by two ethics committees who, according to them followed “appropriate ethical guidelines and principles,” does not absolve them of their duty to refuse to publish manuscripts that they deem a failure of ethics, even if the results are deemed scientifically significant (Lambalk et al. 2020). Otherwise, they become complicit in the promotion of unethical research and embolden others to do so.

It would also be useful to see the reasoning used by the two ethics committees that approved it to justify the study. What were the “appropriate ethical guidelines and principles” (Lambalk et al. 2020) that

were used? Considering the cited concerns, they should be open to public scrutiny as well.

It is telling that this study involved using poor women in Mexico, a third-world country, to test a procedure that had no benefit to them, which is against the directives of the Declaration of Helsinki.

This cannot be considered an altruistic urge on the women's part. This is not like cancer research where a treatment is researched that may be more helpful to other patients with cancer down the line, even poor women like these. The emphasis was on a technique that would be beyond the reach of the poor women who were involved in it. These women were treated as property for the use by wealthier women, most of whom live in first-world countries, who will receive the "benefits" of this procedure without any risk to themselves.

Acknowledging that these women will benefit ignores the harm to the person in the form of the human embryo by also reducing it to mere property to be used or discarded at the whim of those who have power over it. These embryos were created as objects for research. Abnormal embryos that were retrieved were destroyed. There was intentional, even casually planned, destruction of those who did not meet the requirements of the study, those embryos that were created, but then not removed via lavage. All of this further devalues preborn human life.

Both women and embryos were used as means to an end and with the planned destruction of those human embryonic lives that did not meet those ends.

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Biographical Note

Cynthia Jones-Nosacek, MD, is a family physician, retired after being in practice for over thirty-five years. Her practice covered the full range from obstetrics and newborn care to hospice, inpatient, and outpatient care. She graduated from Loyola-Stritch School of Medicine. Her residency was at Resurrection Hospital in Chicago. She practiced at Ascension Columbia St. Mary's Hospital in Milwaukee, Wisconsin. She has written a wide range of articles in medical bioethics from beginning to end of life. Presently, she divides her time between mission work in Uganda, studying for a master's degree through Ohio State University, and caring for her grandchildren.