The Effects of a History of Eating Disorders on Women’s Fertility and Pregnancy

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Objective

The purpose of this poster is to examine the effects of a history of eating disorders, as compared to a history of other psychiatric disorders or no psychiatric disorders, on women’s fertility and pregnancy. Specifically, this poster will demonstrate how a history of eating disorders affects women’s rates of undergoing fertility treatment, rates of twin births, and rates of complications during pregnancy.

In the last few years, eating disorders, including Anorexia nervosa (AN) and Bulimia nervosa (BN), have had increased prevalence in societal discussions. This increase in attention can be attributed to the rising percentage of Americans, especially women, suffering from eating disorders—currently, 0.5% of women suffer from AN, and 2-3% of women suffer from BN. AN is characterized by an abnormal low body weight, a disturbance in body image, and an intense fear of gaining weight; BN is characterized by two phases of binge eating and compensatory behaviors as well as a high value placed on weight and image. Both AN and BN are associated with medical complications which have a relevant impact on fertility and pregnancy.

Past studies have demonstrated that complications can arise from eating disorder behaviors during pregnancy, including preterm delivery, low birthweight and increased odds of Caesarean birth. Often overlooked—yet vital to women in these circumstances—are the effects of a history of eating disorders on the fertility and pregnancy of women. Both a lifetime history of eating disorders (AN, BN, or both) or a past history in women can affect their rates of seeking fertility treatment and rates of twin births. Additionally, this history affects women’s rates of unplanned pregnancies and their feelings regarding unplanned pregnancies. Lastly, a history of eating disorder can impact the chances of complications arising during pregnancy.

Abstract

In one study, a group of women from Generation R (a prospective general population cohort study based in Rotterdam, the Netherlands) at the Erasmus Medical Centre) was divided into those with AN history, those with BN history, those with AN+BN history, those with other psychiatric history, and those with no psychiatric history (see Figure 1). The AN, BN, and AN+BN groups were broken down further into those with lifetime history, those with past history, and those with history in the last year before pregnancy. Because of the small percentage of women that fell into the category of history within the last year, sufficient data wasn’t obtained and thus this group will not be the focus of this poster. The women were eligible for enrollment if they had a delivery date between April 2002 and January 2006; of the 8,880 recruited, 6,328 were selected based on the women’s completion of a questionnaire used to determine exposure for the study.

Data regarding patients’ psychiatric history was obtained from patients’ self-evaluation based on a provided medical vignette; data regarding fertility treatments and twin births was obtained from obstetric records, and data regarding unplanned pregnancies and women’s feelings about unplanned pregnancies was obtained from a questionnaire given to women upon enrollment.

Methods and Materials

In conclusion, a history of eating disorders has a proven impact on women’s fertility and pregnancy. A history of eating disorders is associated with increased rates of twin births. A lifetime or past history of BN is associated with increased rates of fertility treatment. A lifetime or past history of AN or AN+BN is associated with increased rates of unplanned pregnancies and continued mixed feelings regarding this pregnancy. Lastly, lifetime histories of AN and AN+BN are associated with complications during pregnancy. Fertility treatment experts should keep in mind that a history of eating disorders may underlie fertility problems and pregnancy complications.

Conclusions

Applications to Biotechnology

Advances in biotechnology allowed fertility options to be available to those women (primarily those with a history of BN) who sought fertility treatment. Of the women with a history of lifetime bulimia who sought fertility treatment, approximately 65% were treated with induced ovulation and approximately 40% were treated with IVF.

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References


Comparison of Live Birth Rates Resulting From Embryo and/or Egg Cryopreservation Via Vitrification

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Mount Carmel High School

Objective

This research will explain the comparison of two forms of fertility preservation and live birth rates resulting from embryo and egg cryopreservation via vitrification. Additionally, data will illustrate how maternal age at the time of implantation plays a crucial role in live birth rates.

Abstract

Cryopreservation, or the process in which reproductive factors such as eggs, tissue, oocytes, and embryos are frozen to be used at a later time, has become increasingly popular with women who have fertility issues, either from genetic or external factors such as cancer treatment. Within the presented research is a comparison between the two most prevalent forms of fertility preservation—egg and embryo freezing—and how effective each treatment is as indicated by successful live births. One of the major problems of cryopreserving eggs and embryos is the formation of ice crystals. A new method of freezing, vitrification, is a more effective method of cryopreservation because of its high amount of cryoprotectants. A university based hospital in East Asia conducted a study of live birth rates of embryos by vitrification versus slow freezing. The study contained 8,824 cryopreserved human cleavage stage embryos of which 7,482 were vitrified while 1,342 were frozen by slow freezing. The survival rate of the vitrified embryos was far greater compared to slow freezing, with a 15:1 ratio. A second study done, citing meta analysis data from different reproductive centers used both vitrification and slow freezing of oocytes to test survival rates. There were 1,805 infertile patients undergoing non donor oocyte cryopreservation with a total of 13,079 oocytes and 2,265 thaw cycles. A third study done by the Midland Fertility Services cites data from Human Fertilization and Embryology Authority from 2006 shows the live birth rates of patients undergoing IVF and ICSI between the ages of 38 and 45.

Methods and Materials

A University based Hospital in East Asia, conducted a study of live birth rates of embryos by vitrification versus slow freezing. The study contained 8,824 cryopreserved human cleavage stage embryos (blastocysts) of which 7,482 were vitrified while 1,342 were frozen by slow freezing. Four individual investigations studies were conducted using a protocol of ovarian stimulation either by Long agonist/rFSH or CC/RH. A second study done, citing meta analysis data from different reproductive centers used both vitrification and slow freezing of oocytes to test survival rates. There were 1,805 infertile patients undergoing non donor oocyte cryopreservation with a total of 13,079 oocytes and 2,265 thaw cycles. A third study done by the Midland Fertility Services cites data from Human Fertilization and Embryology Authority from 2006 shows the live birth rates of patients undergoing IVF and ICSI between the ages of 38 and 45.

Results

The first study contained 8,824 cryopreserved human cleavage stage embryos of which 7,482 were vitrified while 1,342 were frozen by slow freezing. The survival rate was significantly higher after vitrification as compared with slow freezing. The odds ratio was a 15.57, 95% confidence level as compared to slow freezing the odds ratio had 2.20, 95% confidence level, essentially a 15:1 ratio. The results of the second study which used both vitrification and slow freezing of oocytes demonstrated that vitrification still has higher survival rates. Out of 13,079 total oocytes that were thawed, there was an 85% survival rate of those oocytes that underwent vitrification. While reviewing both studies, it became apparent, that the factor of maternal age played a critical role in the improvement of live birth rates. The third study further demonstrates this fact by focusing mainly on the relationship between age and live birth rates. The study showed that a woman who would undergo an assisted reproductive treatment with her own fresh eggs at 42 would have a live birth rate of 6.6% per cycle. The rate, had she used cryopreserved eggs harvested at age 30, would be 40% greater per transfer when implanted at 42 years of age.

Conclusions

Vitrification, the process of freezing an embryo or egg to a glass-like state, was proven to have a higher live birth rate in both cryopreserving an embryo and egg. It has a higher level of cryoprotectant agents and ultrafast cooling and warming rates which eliminates the chance of intracellular and extracellular ice formation within and around the cell. The effects of the stage of development in which the method implemented cryopreservation as well as embryo transfer plays a critical role in the live birth rates. This fact is highlighted by data showing pregnancy rates above 50% for young patients undergoing embryo vitrification. Egg freezing, however, is a young practice in medicine, making it controversial in whether or not it is a plausible practice because it is in its initial stages. Due to lack of technology and ice crystals puncturing the membrane of the egg, an average of 30% of the cryopreserved eggs are not even viable for implantation. It was discovered that maternal age played a significant role in the rate of successful live birth regardless of whether the embryo or the egg was cryopreserved. This is important to note for both female patients and physicians that the age at which they decide to implant their embryo or egg for a pregnancy, along with the type of freezing method-vitrification or slow freezing, is vital when wanting to pursue the most effective fertility preservation method.

Relation to Biotechnology

Due to the rise of biotechnological methods such as vitrification and slow freezing, freezing eggs alone is becoming a more hopeful option for women who are currently not in a relationship, do not want a sperm donor, or who want to have children after establishing a career. Although it is a known fact that fertility rapidly declines at age 37- having less viable eggs for cryopreservation purposes—this technology could possibly change the rates of successful pregnancies, even in women who are premenopausal.

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References

The Role of Lysophosphatidic Acid as a Biomarker for Early Stage Epithelial Ovarian Cancer Compared to CA-125

Nayeli Diez de Bonilla

Objective
Ovarian cancer ranks fifth in cancer deaths among women, yet if this disease is caught in an early stage, more than 90% of patients live longer than 5 years. If there was a method of detecting ovarian cancer in an early stage, doctors could potentially lower the amount of deaths caused by this disease. The purpose of this poster is to address the urgent need for a biomarker for ovarian cancer that can be used to screen the general population of women. This poster will also compare the efficiency of using CA-125 and Lysophosphatidic acid (LPA) as potential biomarkers for early stage ovarian cancer.

Methods and Materials
In a study performed at Istanbul University in Turkey, 50 healthy women, 74 patients with benign ovarian tumors, and 87 patients with epithelial ovarian carcinoma(EOC) were tested to measure the amount of LPA and CA-125 in their system. Of the 87 EOC patients, 10 patients had stage I, 63 patients had stage III, and 14 patients had stage IV. Women who were diagnosed with germ cell tumors and sex cord stromal tumors were not included. The participating women had 2 samples of 5 mL of blood drawn. One sample was then analyzed for LPA using a biochemical method that other studies had used. First, the lipids were extracted and then the LPA was separated from other lipids via thin layer chromatography. Then, after hydrolysis and derivatization, an analysis was performed using gas chromatography and mass spectrometry (GC-MS). The cutoff value for LPA was set at 1.3 µmol/L, based on previous studies. The second sample was then analyzed for CA-125 using a CA-125 II kit that utilizes the Radioimmunoassay (RIA) technique. The cutoff value for CA-125 was set at 35 U/mL, based on other studies that have been conducted. Researchers compared the levels of LPA and CA-125 within all experimental groups. If a woman's levels of LPA were not detected, their levels were assumed to be 0.1 µmol/L, for statistical analysis.

Results and Interpretations
The mean total plasma LPA level for women with EOC (n=87) was 4.29±4.52 µmol/L. Compared to women with benign ovarian tumors (n=74) who had a mean total plasma LPA level of 1.57±0.92 µmol/L and healthy women (n=50) who had a mean total plasma LPA level of 0.61±0.42 µmol/L, mean total plasma LPA levels for women with EOC were significantly different. Using the cutoff value of 1.3 µmol/L, 83 of 87 (95%) EOC patients had LPA levels greater than or equal to that value. In comparison, 46 of 50 (92%) healthy women had total plasma LPA levels lower than 1.3 µmol/L. The mean CA-125 levels of women with EOC was 764.63±1183.44. For women with benign ovarian tumors, the mean CA-125 level was 38.14±69.40 and for healthy women the mean CA-125 was 23.90±16.73. Mean CA-125 levels are significantly higher when compared to patients with benign ovarian tumors and healthy women. There is no significant difference between the mean CA-125 level in women with benign ovarian tumors and healthy women.

Conclusion
Total plasma LPA levels are significantly different between women with EOC, women with benign ovarian tumors, and healthy women. This suggests that monitoring LPA levels could help differentiate between women with EOC, benign tumors, and no cancer which could be a major contribution to the early detection of the general population. Both mean total plasma LPA levels and CA-125 levels were elevated in women with EOC compared to women with benign ovarian tumors and healthy women. Other results align with evidence from other studies that have been conducted comparing LPA levels of healthy women and women with EOC, while mean LPA levels between women with benign ovarian tumors and healthy women, we saw that mean CA-125 levels for women with benign ovarian tumors and healthy women was not significantly different. This shows us that LPA is a more sensitive option than CA-125. Further research should be conducted to compare LPA levels and CA-125 levels by stage of ovarian cancer.

Relevant Applications to Biotechnology
In a year, around 22,000 women are diagnosed with ovarian cancer and there are around 14,000 fatalities. Early diagnosis can potentially help lower the mortality rate for this disease. However, one of the many challenges to early diagnosis is that the ovaries aren’t as accessible as other organs and most of the methods used for screening today don’t achieve the necessary sensitivity or specificity required. Another challenge of this disease is that 90% of ovarian cancer cases occur in women who aren’t in an identifiable high risk group. If researchers were able to identify a biomarker for ovarian cancer, they could develop a new method of screening the general population. This new method, which could potentially involve LPA, could offer a very specific and have a high sensitivity rate if it were to be applied to the general population. LPA appears to be playing a promising role in this area, but further tests are required to confirm this.

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References
Effects of Autologous and Allogeneic Bone Marrow Transplants on Female Fertility

Introduction
The objective of this poster focuses on patients who suffer from leukemia. Several post leukemia patients have reported a loss or hindrance of fertility after treatment. In a particular study, doctors admitted 576 women into the study whose ages ranged between 10 to 60 years old. However, 26 women were removed from the study. The participants received one of three treatments: chemotherapy, analogous BMT, or allogeneic BMT. By the end of the study, only 98 patients completed the follow-up questionnaire, which provided a summary of the quality of their lives after treatment. In particular, the sexual disorder questionnaire revealed that infertility occurred in 32 (one third) of all patients, especially in the Allogeneic BMT-treated patients. Thirty-four patients who either underwent ABMT or Allogeneic BMT procedures also reported painful sexual intercourse. Doctors concluded that Allogeneic BMT resulted in more infertile patients than the other two leukemia treatments. Other doctors who have conducted similar studies also show similar results and agree that allogeneic BMT causes infertility in 83% of women to lose their fertility due to gonad damage. Gonadal damage occurs when oogenesis is affected and the production of oestrogen and progesterone is decreased. In particular, for Allogeneic BMT, such as TBI, also increases the patient’s chances of infertility from 80% to 89%. Doctors should further examine if any combination of these three treatments against one, for example, chemotherapy and autologous BMT against just autologous BMT, will increase the chance of preserving fertility. Doctors should recommend chemotherapy or autologous BMT to patients who preferentially want to save their fertility. In sum, patients will understand the effects different bone marrow treatments have on fertility and will be provided with reassurance by being aware of the potential risks before they are treated.

Methods and Materials
In a particular study, doctors used 576 women whose ages ranged between 10 to 60 years old in order to investigate the long-term effects of treatment for post-leukemia patients. They were divided into three test groups based on one of three types of treatments: chemotherapy, analogous BMT, or allogeneic BMT. Only 98 patients completed the entire follow-up study, which occurred a year after receiving treatment. Patients completed multiple QLQs (Quality of Life Questionnaire) to evaluate their QOL (Quality of Life). The demographic QLO contained questions regarding marital and employment status after fertility. The EORT (European Organization for Research and Treatment of Cancer) asked about physical, cognitive, emotional and social functioning. The leukemia BMT model QLO explored the somatic symptoms patients experienced after treatment. The sexual functioning and infertility questionnaire surveyed patients about sexual drive, pain, and infertility. The final questionnaire asked for the patients’ perception on changes in their family, profession, social and leisure life. Furthermore, doctors continued to investigate the effects of allogeneic BMT on both genders. They admitted patients who were treated between 2000-2005, and whose ages ranged from 4-28 at the time of treatment. They also participated in a long term follow-up study 3 to 12 years after treatment. Clinicians evaluated data obtained from spermiograms, testicular volume measurements, menstrual cycles, hormone analysis, and evaluated the health of any children patients had after had treatment. In addition, doctors analyzed differences in fertility rates between patients who were treated before 13 years of age and patients who were treated after 13 years of age. These patients also answered survey questions that assessed their quality of life after treatment.

Abstract
Several post leukemia patients have reported a loss or hindrance of infertility after treatment. Three major treatments (chemotherapy, Allogeneic BMT, and Autologous BMT) are possibly associated with infertility. Chemotherapy is radiation that kills off cancer cells, allogeneic BMT (bone marrow transplant) requires a donor, and autologous BMT is a bone marrow transplant from the patient’s own body. Doctors conducted multiple studies to discover any possible effects that could be observed in the fertility of post-treatment leukemia patients. In a particular study, doctors admitted 576 women into the study whose ages ranged between 10 to 60 years old. However, 26 women were removed from the study. The participants received one of three treatments: chemotherapy, analogous BMT, or allogeneic BMT. By the end of the study, only 98 patients completed the follow-up questionnaire, which provided a summary of the quality of their lives after treatment. In particular, the sexual disorder questionnaire revealed that infertility occurred in 32 (one third) of all patients, especially in the Allogeneic BMT-treated patients. Thirty-four patients who either underwent ABMT or Allogeneic BMT procedures also reported painful sexual intercourse. Doctors concluded that Allogeneic BMT resulted in more infertile patients than the other two leukemia treatments. Other doctors who have conducted similar studies also show similar results and agree that allogeneic BMT causes infertility in 83% of women to lose their fertility due to gonad damage. Gonadal damage occurs when oogenesis is affected and the production of oestrogen and progesterone is decreased. In particular, for Allogeneic BMT, such as TBI, also increases the patient’s chances of infertility from 80% to 89%. Doctors should further examine if any combination of these three treatments against one, for example, chemotherapy and autologous BMT against just autologous BMT, will increase the chance of preserving fertility. Doctors should recommend chemotherapy or autologous BMT to patients who preferentially want to save their fertility. In sum, patients will understand the effects different bone marrow treatments have on fertility and will be provided with reassurance by being aware of the potential risks before they are treated.  

Results
Of the 98 patients who completed the entire study, 32 reported infertility in the QLQs, most of whom received allogeneic BMT. Chemotherapy-treated patients had a 22% chance of becoming infertile, ABMT-treated patients had a 30% chance of becoming infertile, and Allo BMT treated patients had a 69% chance of becoming infertile. Patients who underwent ABMT or Allo BMT experienced pain during sexual intercourse. The study that focused solely on allogeneic BMT classified eighty-three percent of the women in the study as infertile. Of those classified, 80% of women who did not receive Total Body Irradiation (TBI) were classified as infertile, and 98% of women treated with TBI became infertile. Furthermore, females were more likely to loose their fertility after age 13 (91%) than before age 13 (72%). Although Doctors have not been able to pinpoint the exact time in which infertility occurs, they have learned that infertility due to treatment is progressive, not immediate.

Conclusions
Doctors have concluded that Allogeneic BMT results in the most cases of infertility. The preparation radiation for this treatment, TBI, also increases the chances of infertility by 9%. Allogeneic BMT and ABMT treated patients suffer similar side effects, however, cancer reoccurrence is more likely to occur in an ABMT-treated patient since the bone marrow is from the patient’s own body. Patients treated with chemotherapy experience the same side effects, however, they are less likely to lose their fertility. If possible, patients who want to preserve their fertility should ask clinicians if they can receive chemotherapy. However, some patients are in need of an allogeneic BMT. In this case, patients should ask their doctors if TBI is necessary since it raises a patient’s chances of infertility from 80% to 89%. The results from these studies enable doctors to thoroughly inform their patients of all the risks each treatment has, and if the patients have any doubts, they are fully aware of the consequences of treatment before hand.

Relevance to Biotechnology
In the past, leukemia patients only had chemotherapy as an option for treatment. Biotechnology has enabled doctors to treat patients who need a bone marrow transplant. New technology has empowered doctors with the ability to collect data after treatment such as analyzing menstrual cycle patterns as well as measuring and comparing levels of hormones. Biotechnology has opened several doors for doctors who wish to help leukemia patients preserve fertility.

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References
Objective

This poster investigates current oncology practices that may be adapted for use in the transgender community. Specific attention is given to ethics and quality of life for transgender youth. The word transgender is an umbrella term that is used to describe a very diverse group of individuals. This pronoun is used to respect and acknowledge the diversity of these individuals.

Relevant Applications to Biotechnology

There are a myriad of oncology treatments, both experimental and that have the potential to enhance the life of transgender youth. Transmasculine youth have one or more fertility-saving option - they can remove and freeze their eggs. At this point, the eggs can only be removed and saved for potential neomicroembryo development after puberty has begun. Kines is required to bring the eggs through follicular development. However, one of the up and coming developments in the field of transgender medicine is the ability to take an egg and bring it (almost all the way) through follicular development. Scientists predict that this will soon become an experimental fertility preservation method, such as the aforementioned egg freezing method. On the other end of the spectrum, transfeminine youth have two possible options; one standard and one experimental. Sperm banking through self stimulation is the standard method. It involves obtaining the sperm through self stimulation and then freezing it. Sperm banking through an alternate collection method is the experimental method. Sperm is obtained through testicular sperm extraction or aspiration. To date, both transfeminine methods are only possible after puberty. However, much like the research that is being done to bring eggs through follicular development, scientists are trying to develop a way to sperm to be brought to maturity before birth.

Results and Interpretation

Transgender medicine is evolving. Transgender youth are faced with many tough decisions. They must consider the consequences of their actions. Fertility is akin to a one-way street, once it is compromised or lost, it is irrevocable. Transmasculine people conclude that “standards of care for [fertility preservation] in [the transgender] clinical setting are lacking.” When asked, fertility preservation is not always a priority of the concerns of transgender youth. Transmasculine youth are becoming accepted in the medical community when applied to minors with cancer. On the other hand, personal beliefs may challenge the acceptance of the application of fertility preservation methods with individuals that identify as transgender. It is important to consider that a young person wishes to suppress puberty until they decide to use cross sex hormones or sexual reassignment surgery. They may not be considering a desire for a future family or child. By giving them the opportunity to preserve their fertility, scientists can keep the option of a family open. Viable options for post pubescent youth include egg freezing and sperm collection. A study done on transmasculine youth discussed multiple surveys, mental health screening, and risk assessment to consider fertility preservation for those patients. A study done on transfeminine youth focused on minors with cancer. They found that 40 percent of respondents stated that loss of fertility was not an important reason to delay their transition. A separate study done on transfeminine youth... Researchers found that 54 percent wished to have children, which may indicate the importance of action before transitioning. In a survey of 40 transmasculine people, 77 percent of those respondents stated that they had not considered freezing their eggs at the time of diagnosis or decision.

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Materials and Methods

A review of relevant literature was conducted to examine the composition of the transgender community, the challenges that they face, and the possibilities that oncology can provide for the community. Effort was made to understand and appreciate the evolving terminology needed to report in a sensitive manner. The review led to an understanding that existing Oncology practices must be adapted for use in transgender individuals. Currently, cross sex hormone and sperm banking is available for which have undergone puberty. Scientists are developing different methods to help to preserve the fertility of prepubertal cancer patients. These new treatments could also be applied to pre pubescent transgender youth. This conclusion led to the debate over medical treatments for transgender youth and their effects on fertility post-treatment. Although these treatments are still surrounded in controversy, this study examined cases where transgender youth have undergone oncology procedures.

References

Methods & Materials

A study sponsored by the National Cancer Institute was conducted in the United States and Spain to observe the effects of the monoclonal antibody bevacizumab on patients with metastatic cervical cancer. Bevacizumab is a monoclonal antibody that slows down angiogenesis by inhibiting vascular endothelial growth factor (VEGF). VEGF functions in blood vessel growth. A total of 452 patients were included in the study. All patients were female with metastatic cervical cancer and healthy bone marrow, hepatic, renal, and thromboembolism function. All of the patients were given a physical examination and a radiography prior to the studies initiation. The patients were divided into two overarching categories. The control group consisted of patients treated with a standard chemotherapy regiment. This regiment consisted of 50mg of cisplatin, which was administered per square meter of body surface area as well as 135-175mg of paclitaxel, administered also per square meter of body surface area. This study also measured the effect of the chemotherapy drug topotecan and the results in combination with bevacizumab. Cisplatin, paclitaxel, and topotecan are chemotherapy drugs that are known to trigger cell apoptosis. After the treatment was terminated, the effects of bevacizumab in combination with the chemotherapies were evaluated by measuring tumor size every three months for two years. Three surveys were used to measure the quality of life for patients after the treatment. The FACT-Cervix survey (0 to 4 scale) was utilized to measure overall well being and the FACT-GOG survey (0 to 4 scale) was used to measure neurotoxicity. The BPI survey (0 to 10 scale) was used to measure pain after treatment.

Results & Interpretation

The implementation of the antibody bevacizumab to cervical cancer treatment increased the survival time of patients by about 4 months. Patients treated with the chemotherapy only regimen survived for about 13.3 months as opposed to those patients who were treated with the antibody as well; they survived about 17.0 months. In addition, patients responded best to the combined regimen of the antibody and chemotherapy. Out of the 452 patients, 48% responded to the combined treatment whereas only 36% responded to the standard chemotherapy treatment. In addition, patients treated with the combined therapy answered about 1.2 points lower on the FACT-GOG-NTX survey which demonstrated quality of life on a scale of 0 to 1, 4 being the worse state of health. Patients treated with the combined regimen also had a 3% increase of gastrointestinal fistulas and thromboembolic.

Conclusions

Cervical cancer can be more effectively treated if the monoclonal antibody bevacizumab is used in combination with chemotherapy. Patients treated with the antibody survive for a longer period of time and experience a smaller amount of late effects from the treatment. Late effects such as neurotoxicity and pain are reduced with the use of the antibody. Improvement in overall quality of life is also an effect of the antibody. Patients treated with the antibody reported in a survey to have had an overall improvement in the quality of life. In addition, neither topotecan or cisplatin is a more effective chemotherapy drug. Both drugs were equally effective at treating cervical cancer.

Relevant Applications to Biotechnology

Immunology is being incorporated with technology in many different ways. Scientists have realized the immense power and influence of our own immune systems ability to cure disease. Research is focusing on detecting antibodies on cancerous cells. Such nanoparticles can be detected by advanced imaging techniques. Lasers are being used to detect these microscopic antibodies on the surface of cells. Due to such advancements in technology, the nano world is no longer an uncharted area of study and is leading to major improvements in medical therapies and treatments.

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References


Objective

The objective of this poster is to present a synthesis of the most up-to-date research on the effects of PGS/PGD on child development to help assess the risks of embryo biopsy on the embryo’s growth and development years later. The research indicates that PGS/PGD has no correlation to major differences in physical and neurological development among PGS/PGD children, IVF children, and children from natural pregnancies.

Abstract

Preimplantation genetic screening (PGS) and preimplantation genetic diagnosis (PGD) are new technologies that are used in vitro fertilization (IVF) treatment to generate embryos that will lead to a successful pregnancy and choose embryos with the optimal genes, respectively. PGS is commonly confused with PGD; however, they are different in that PGS only screens for genetic mutations that reduce the likelihood of implantation such as aneuploidy, while PGD screens out specific genes that the parents deem undesirable, such as the BRCA1/2 mutation. They are similar in that both utilize embryo biopsy to perform genetic tests on one or two cells from each embryo. Concerns about the possible harms of embryo biopsy used in PGS/PGD have led to several studies on their effect on child health and development. These studies are necessary to assess the risks of PGS/PGD, two invasive procedures often recommended to advanced maternal age and repetitive failure IVF patients. Research in the area of child development utilized anthropometric data at birth, two months, two years, and four years to the neurological assessment of general movements, motor skills, mental development, and behavioral development at infancy, two years, and four years to compare the development of PGS/PGD children with IVF and natural conception children. Neurological examination utilized the Hempel test to classify the mental health of children into categories: neurologically normal, simple motor neuron disease (MND), complex MND, or neurological abnormal. Other methods employed include IQ testing to assess cognitive ability and the child behavior checklist to investigate behavioral development. Physical development was measured using height, arm, waist, and head circumference; and counting morphological abnormalities, classifying them into major and minor categories. The results of these studies show that PGS/PGD children have no significant morphological or neurological health differences from other IVF children and the general population up to four years of age. Further studies are required to determine the long-term neurological and physical effects past age four before PGS/PGD are recognized as low-risk procedures for IVF/ICSI treatments.

Methods and Materials

To determine the effects of PGS/PGD on child development, research groups used a number of different metrics at different ages. Physical development was tracked using biometrics and anthropometrics. One group collected data on height, weight, and head circumference of two month old infants, comparing 995 PGS children with 1507 ICSI children at the same medical center. The study combined identification of malformations with medical history of neonatal biometrics and 2-month measurements. In another study, 70 PGS/PGD children were compared with 70 ICSI (intra-cytoplasmic sperm injection) children and 70 NC (natural conception) children for biometrics at birth and at 2 years of age, controlling for race (all Caucasian), language (Dutch, French, or English), and age (all singlets). The NC and ICSI groups matched the PGS/PGD group with mother tongue, maternal education level, gender, and birth order. The data collected included the biometrics of the first study in addition to arm and waist circumference and examination of skin and eyes. A third study comparing 50 PGS children, 72 IVF children, and 66 natural conception children examined each at 2 years of age for morphological abnormalities using photography in combination with medical records and anthropology.

Methods and Materials (continued)

At four years of age, blood pressure and anthropometrics including body fat, heart rate, pulse pressure, height, weight, waist, head circumference, and frequency of hospitalization and paediatric care were measured between 49 PGS children and 64 IVF/ICSI children.

Neurological development was measured using various one. A study measured the neurological development of infants, comparing PGS children and IVF children, at 2 weeks, 3, 4, 10, and 18 months of age. Their general movements were examined and classified as normal-optimal, normal-suboptimal, mildly abnormal, and definitely abnormal. At 18 months, five areas of functionality were assessed in the context of play in the Hempel neurologic examination: fine motor function, gross motor function, posture and muscle tone, reflexes, and visuomotor function. The neurological development at 2 years of age was assessed by another study that calculated the mental development index based on visual/auditory processing, memory, language skills, hand-eye coordination, imitation, and problem-solving ability and the psychomotor development index based on fine and gross motor skills using the Bayley Scales of Infant Development. Parents were also asked to fill out the Child Behavior Check List (CBCL) to collect data on behaviors. This study compared 54 PGS children to 77 IVF children. Four-year-olds from the anthropometric study above were tested for neurological and behavioral issues using the Hempel test outlined above converted to a neurological optimism score (NOS), CBCL, and IQ tests.

Results

Birthweight of PGS singletons (3262.8 ± 543.5 g) and multiples (2298.8 ± 581.1 g) were similar to the ICSI control group (3232.5 ± 583.2 g for singletons and 2248.1 ± 581.2 for multiples). Birth head circumference (cm) was also comparable: 34.3 ± 1.90 (ICSI) in singletons and 32.5 ± 2.38 (PGS) compared with 32.1 ± 2.36 (ICSI) for multiples. More ICSI multiples exhibited low birthweight (17.8%) compared with PGS multiples (16.2%). See Table 1 for anthropometric data of two-year-olds, Chart 1 for morphological abnormalities of two-year-olds, and Table 2 for the anthropometric measurements of four-year-olds.

The neurological study on infants indicated that 25% of PGS infants had at least one neurological problem by 18 months compared with 15% of IVF infants. 20% of the PGS group were diagnosed with MND compared with 12% of the control. The study of PGS children compared with IVF only children at two years, the mental development index was 103 for both. The neurological outcome results (PGS control) from the Hempel test showed 87% normal, 95% normal, 7% simple MND, 4% complex MND, 2% cerebral palsy. The total median CBCL results were 43.8: 46.0. The study of four-year-olds, scores of PGS control: standards were 12.2 (fluency), 49.3: 48.7 (NOS), 113.4: 114.4 (total IQ), and 45.7: 47.7 (CBCL).

Applications to Biotechnology

Given that PGS and PGD are frequently used to avoid passing on hereditary illnesses and maximize the chances of a successful implantation and pregnancy after IVF/ICSI, it is extremely important that embryo biopsy carries few risks. Tracking the neurological and physical health of PGS/PGD children is essential to determine these risks so that IVF/ICSI patients can make informed decisions and weigh the benefits of PGS/PGD with the risks.

Acknowledgements

I am grateful for this opportunity to learn about oncology in a multi-faceted and interactive way through this program. I greatly appreciate the support from my OSU sisters and Ms. Patricia Winter. I am especially thankful to Sheridan Smith’s and Dr. Ericka Sengar-Mitchell’s help and valuable discussions.

References


Chart 1. Percentages of major abnormalities per child for the PGS group (PGS+), IVF/ICSI group (PGS-), and natural conception group (reference). Purple = 0, dark green = 1, light green = 2, pink = ≥3.6

Table 1: Biometric data was collected in PGS/PGD and IVF/ICSI groups and NC at two years.

<table>
<thead>
<tr>
<th>Group</th>
<th>Weight (kg)</th>
<th>Height (cm)</th>
<th>Head Circumference (cm)</th>
<th>Left Arm Circumference (cm)</th>
<th>Waist Circumference (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PGS+</td>
<td>130.6 ± 1.3</td>
<td>134.7 ± 1.7</td>
<td>48.8 ± 1.4</td>
<td>15.7 ± 1.2</td>
<td>48.7 ± 3.0</td>
</tr>
<tr>
<td>IVF/ICSI</td>
<td>90.6 ± 2.5</td>
<td>19.1 ± 9.9</td>
<td>41.9 ± 1.4</td>
<td>15.4 ± 1.3</td>
<td>40.1 ± 3.7</td>
</tr>
<tr>
<td>NC</td>
<td>133.5 ± 1.5</td>
<td>133.4 ± 1.3</td>
<td>48.1 ± 1.6</td>
<td>16.0 ± 1.4</td>
<td>49.0 ± 3.7</td>
</tr>
</tbody>
</table>

Table 2: Blood pressure and anthropometrics of PGS and IVF/ICSI four-year-olds were measured.

<table>
<thead>
<tr>
<th>Group</th>
<th>Weight (kg)</th>
<th>Height (cm)</th>
<th>Head Circumference (cm)</th>
<th>Waist Circumference (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PGS</td>
<td>19.5</td>
<td>110.7</td>
<td>51.2</td>
<td>55.1</td>
</tr>
<tr>
<td>IVF/ICSI</td>
<td>18.7</td>
<td>109.3</td>
<td>51.1</td>
<td>51.1</td>
</tr>
<tr>
<td>NC</td>
<td>18.7</td>
<td>110.9</td>
<td>51.1</td>
<td>51.1</td>
</tr>
</tbody>
</table>
Objective

The objective of this poster is to determine if there is a relationship in the intake of fertility drugs and the risk of breast cancer in pre-menopausal women. The research focuses on fertility drugs such as Clomiphene Citrate (CC) and Follicle-Stimulating Hormone (FSH).

Abstract

Fertility drugs, such as Clomiphene Citrate (CC) and Follicle Stimulating Hormone (FSH), stimulate the release of multiple eggs when administered clinically due to the increase of estrogen in a woman’s body, which induces ovulation. This large amount of estrogen promotes the growth of hormone receptor positive breast cancer cells in pre-menopausal women. The objective of this research is to examine the relationship between fertility drugs such as CC and FSH, and the risk of breast cancer diagnoses for women under 50 years old. Within the conducted research, the National Cancer Institute recruited 1,422 breast cancer patients who underwent IVF previously, as well as their biological sisters (1,669 women) who were cancer-free. Each patient reported the use of CC, FSH, or both and whether or not they were pregnant for 10 or more weeks after fertility treatments. Women who used ovulation stimulation drugs and did not get pregnant showed a decreased possibility of breast cancer, compared to women who had never used fertility drugs. Participants who underwent assisted reproduction and successfully got pregnant—10 weeks gestation—showed an increased possibility of breast cancer in comparison with participants that were untreated. Even though fertility drugs do not increase the risk for a pre-menopausal female of getting breast cancer, the risk is not higher than expected for the general public.

Methods and Materials

In order to get the most accurate results, researchers gathered data from participants who had sisters with a diagnosis of breast cancer and who were younger than 50 years old. Both sets of data were collected through a confidential telephone interview (CATI) on their health conditions, lifestyle, reproductive factors, and more. In addition, the breast cancer diagnoses were collected from the patients they had undergone, breast cancer diagnosis, and the characteristics of the tumor. Of the 3,283 participants only 3,091 qualified to participate in the study. Before the interview, sisters were shipped memory aids such as a life calendar to mark any type of surgery and births and a list of medications. Participants were also asked in the CATI if they had ever taken medication to help them get pregnant. If they did take medication they had to provide the name of the medication, when they took it, the number of menstrual cycles and if the treatment helped them get 10 or more weeks pregnant. After getting the list of medications, researchers considered two types of ovulation stimulation drugs, CC and FSH. In the first model, scientists gathered the women’s data in groups, fertility-drug use was categorized as nonuser, FSH only, CC only and both FSH and CC. Model scientists divided the groups into two simpler ones, nonusers and users.

Results

A significant decrease of young-onset breast cancer appeared on women who only took CC or CC and FSH in comparison with women who did not take these two drugs. Those who unsuccessfully used only FSH weren’t found to have any apparent risks, but the number of participants was low. When the first model of treatment of fertility drug use history with the following categories: nonusers, users of CC, users of FSH, and users of both CC and FSH was compared with the second model where fertility drugs were accumulated to create two categories such as exposed or not exposed it became clear that the effects of CC and FSH weren’t detectable in the data. Participants with a fertility drug use background appeared to have a significant decrease in the risk of young-onset breast cancer in comparison with other patients who had not used fertility drugs but did not have a successful pregnancy. As for participants who did not reach a 10 week or more pregnancy under treatment, they appeared to have decreased chances of getting breast cancer in comparison with nonusers. In conclusion, participants who did or didn’t get pregnant under the treatment, did not have a noticeable increase in young-onset breast cancer in comparison with participants that were untreated.

Conclusions

Researchers discovered that there is no significant difference in the rates of developing breast cancer between the women who have used fertility drugs in the past versus those who have not. Scientists concluded that fertility drugs do not increase the chances of breast cancer, in fact they lower the risk in females who do not sustain a 10 week or more pregnancy.

References

The Effectiveness of Targeted Therapy Using Olaparib to Resensitize Resistant Tumor Cells

Quynh Nguyen

Objective

Olaparib is a novel, orally active poly(ADP-ribose) polymerase (PARP) inhibitor that induces synthetic lethality in homologous BRCA-deficient cells. With that background information, this poster will demonstrate the effectiveness of these groups combined: Combined administration of 400mg Olaparib and platinum-based chemotherapy, monotherapy Olaparib and monotherapy Bevacizumab to see which group makes treatment resistant tumor cells more sensitive.

Abstract

Ovarian cancer is the fifth leading cause of cancer death in women, approximately 10% of all ovarian cancers are hereditary and of these, more than 90% are associated with BRCA1 or BRCA2 germline mutation. Scientists discoverers that targeted therapies are a new type of cancer treatment that uses drugs or other substances to find and attack cancer cells while doing little damage to normal cells. There are 2 types and each works different: Bevacizumab and Olaparib. Bevacizumab works as angiogenesis inhibitor, which helps, block the formation of new blood vessels and as a combination use with standard chemotherapy for cancers. Meanwhile, Olaparib is one new type therapy of PARP inhibitor, which is a repair of DNA single-stranded breaks (SSB) through via homologous-recombination repair pathway. This is why the focus of this study is to see what is the most effective therapy that can revert tumor cell from resistance state to sensitivity state in ovarian cancer. In this study, we will compare three different groups of therapy: Combined administration of 400mg Olaparib and platinum based chemotherapy, monotherapy Bevacizumab; monotherapy Olaparib. The result of this study is the objective response rate (ORR) in group-combined Olaparib and platinum-based therapy is 22% for administration of monotherapy Bevacizumab 15mg is 21%. However, the objective response rate for group monotherapy Olaparib 400mg is 33%. In addition, the Progression-free survival (PFS) of Bevacizumab group itself is 4.7 months, combined administration of 400mg Olaparib and platinum-based therapy is 8.4 months and for Olaparib group itself is 9 months. Combined study of this is to prove that monotherapy Olaparib 400 mg twice daily has antitumor activity heavily on ovarian cancer. Monotherapy Olaparib shows that it has a most effective in revert treatment resistant tumor cells to sensitive stage in recurrent ovarian cancer patients.

Materials and Methods

Patients were eligible if they were 18 years of age or older and had recurrent ovarian cancer. All studies start in Phase 2 of clinical trial. However, the materials and methods for each study will be different. In Ledermann’s study (combined Olaparib and platinum-based therapy) includes 68 patients were randomly administered at a dose of 400mg twice daily. These patients receive two or more platinum-based regimens and had a partial or complete response to their most recent platinum-based chemotherapy. The second study was conducted by Gynecologic Oncology Group, Burger’s study (monotherapy Bevacizumab) included 34 patients were administered with Bevacizumab 15mg repeated every three weeks. Audeh’s study (monotherapy Olaparib) includes 34 patients were administered with Olaparib 400mg twice daily. All patients were followed until progression of disease. PFS was assessed with the use of computed tomographic scans obtained every 12 weeks and was calculated on the basis of measurement of tumor size.

Results

The result of Ledermann’s study is the median PFS is 8.4 months for the group combined Olaparib and platinum-based chemotherapy. Based on the RECIST guidelines, the response rate is 12% in the study group. At that time, the data had to cut-off due to few deaths had occurred for a survival analysis to be performed. The toxicity of group combined Olaparib 400mg and platinum-based therapy was majority of adverse events grade 1 or 2 and did not require interruptions of the treatment. In Burger’s study, the activity of Bevacizumab was analyzed in 62 patients, the response rate is 21% and the median PFS is 4.7 months. In addition, 40% patients were progression-free for at least 6 months. So far in the study, there are only two patients discontinuated the study because of adverse effect and these adverse effects are manageable and mild in majority of cases so the toxicity in Bevacizumab was graded 3. Finally, Audeh’s study showed that greater Olaparib activity is seen at high dose of 400mg, the response rate of this monotherapy Olaparib is 33% which higher than other therapy groups. The median PFS is 9 months. However, throughout the process of treatment with monotherapy Olaparib 400mg, there were the most frequently reported adverse events and most events were mild in intensity, toxicity was graded 3 or 4.

Conclusion

In conclusion, monotherapy Olaparib 400mg can make treatment resistant tumor cells most effective. Throughout all 3 studies, monotherapy Olaparib showed that the therapy itself has an antitumor effect that slows growth of ovarian cancer tumors. However, giving patients a high dose of Olaparib 400mg itself can lead to adverse events which may cause relapse in patients because of an overdose in Olaparib. Furthermore, the ORR didn’t differ between the group with combined Olaparib and platinum-based therapy and monotherapy Bevacizumab because each study had a different amount of patients that participated in the study, which could have affected results. In the end, results showed that monotherapy Olaparib 400mg is a promising therapy and can be used to revert resistant tumor cells to a sensitive, responsive state.

References


Acknowledgment

I would like to thank Oncofertility Saturday Academy for giving me this opportunity to learn about Oncofertility, IVF, Cancer and Bioethics in medical. I would like to specifically thank Dr. Ericka Senegar-Mitchell, Ms. Partrica Winter, Dr. R. Jeffrey Chang, Dr. Sender and big sister Sheridan for sharing their knowledge with me. Thank you to my OSA sisters and special sister Hailey for being my guidance and support me throughout the academy.

Figure 1. Protein structure of Bevacizumab

Figure 2. Chemical structure of Olaparib
The Effects of Mitochondrial DNA on Embryonic Implantation

Kathleen Pulvers
Academy of Our Lady of Peace

Objective
What are the effects of Mitochondrial DNA levels on embryonic implantation? The embryos from women ranging of twenty-six to forty-two years old were transferred and observed for any signs of implantation. The amount of mtDNA in the embryos were measured using real-time PCR and then compared to the implanting and non-implanting embryos to observe if there is any relationship. This poster will demonstrate the effects that high and low levels of mitochondrial DNA have on the success rate of embryonic implantations.

Abstract
As maternal age increases, the chance of embryonic chromosomal abnormalities as well as complications with implantation increases. Abnormal mitochondrial activity can damage oocytes by causing augmentation of reactive oxygen super-oxides in the cell, affecting implantation rates. The mitochondrial genome proofreading system is not as strong as the nuclear genome’s, so chromosomally normal (euploid) blastocysts have lower levels of mtDNA than chromosomally abnormal (aneuploid) blastocysts. In one study done, 92.9% of euploid embryos developed into blastocysts while 42.1% of aneuploid embryos developed into blastocysts: a possible connection could be the 75% chance of aneuploidy in the oocytes of women over 40 years old. Through real-time Polymerase Chain Reaction (PCR), microarray comparative genomic hybridization (aCGH), and next generation sequencing (NGS), the mtDNA levels in the embryonic genome can be measured. The data will reflect the amount of mtDNA in the embryos and will then be observed for implantation potential. The patients were in IVF clinics in the US and UK; gender and age ranges were kept constant for the duration of the study. The ranges for reproducibly younger women were age 26-37 and reproducitively older women were age 38-42. Successful implantations were shown where maternal age was low and where mtDNA levels were 0.003 or lower. Where mtDNA levels were higher than 0.003, and came from maternally older women, the embryos had a lower tendency to implant. The data suggests that high levels of mtDNA increase embryonic implantation failures which points to a connection among maternal age, mtDNA, and embryonic implantations for both euploid and aneuploid blastocysts. Knowing the health of blastocysts, pre-implantation, is important so that pregnancies can occur.

Results
From the 302/340 blastocysts that were analyzed through aCGH, 99 were aneuploid and 203 were euploid. Table 1 depicts the relationship between mtDNA quantity, maternal age, and chromosomal status. Out of the 38/340 blastocysts that were analyzed via NGS, 24 were aneuploid and 14 euploid. Through real-time PCR was used on the 38/340 blastocysts to compare the amount of mtDNA in the aneuploids and euploids. Figure 2 illustrates the low levels of mtDNA in euploid blastocysts and high levels of mtDNA in aneuploid blastocysts. From the 89 blastocysts transferred through SETs and DETs, 42 resulted in ongoing pregnancies while 47 failed to implant. Real-time PCR analysis indicated that the implanting blastocysts had noticeably lower amount of mtDNA than the non-implanting (3%). 100 of the 42 blastocysts that implanted had mtDNA quantities lower than 0.003, while 30 of the 47 that failed to implant had mtDNA quantities higher than 0.003. What was found was that the baseline of mtDNA for embryos that implant is 0.003, or lower. The embryos that had an mtDNA quantity of 0.003 or lower, tended to be from the reproducitively younger women. These results suggest that maternal age is connected to embryonic mtDNA quantity and that an older maternal age increases the chances of failure to implant.

Conclusion
Maternal age is an influencing factor on chromosomal status. With increasing maternal age, particularly over 37 years old, the cases of embryonic aneuploidy in this study were more prevalent. Moreover as maternal age increased, the amount of mtDNA in blastocysts increased as well, and the instances of embryonic implantations decreased. In women 36 years and younger, cases of aneuploidy were lower and success rate of embryonic implantation were higher. This is important to note for women experiencing fertility issues, as their age could play a major role.

Methods and Materials
In IVF clinics in the US and UK, 340 blastocysts from 161 couples (average maternal age 38 years) were cytogenetically tested for aneuploidy. One of the cytogenetic techniques used was microarray comparative genomic hybridization (aCGH) in which 302 blastocysts were analyzed. Out of the 302 blastocysts from aCGH, 148 blastocysts were from reproductive younger women with a range 26-37 years and an average age of 34.8 years. The remaining 154 blastocysts came from reproductive older women with ages ranging from 38-42 years and an average age of 39.6 years. These 302 blastocysts were studied through real-time Polymerase Chain Reaction (real-time PCR) to determine their chromosomal status and amount of mtDNA; additionally, 38 blastocysts were studied through NGS to search for the same (see figure 1 for reference).

After the relationships between mtDNA, aneuploidy, and maternal age were analyzed, 89 blastocysts from 85 patients (average maternal age 38.3 years) were transferred into uteruses. 81 blastocysts went through single embryo transfers (SETs), and 8 through double embryo transfers (DETs). The mtDNA copy number quantification was found via real-time PCR assessment of the implanting and non-implanting 89 blastocysts. In this study, the factors were maternal age (younger vs. older), embryonic chromosomal status (euploid vs. aneuploid), and embryonic implantation (pregnancy vs. failure to implant).

Relevant Applications to Biotechnology
Through cytogenetic testing methods such as real-time PCR, aCGH, and NGS, aneuploidy can be found in blastocysts before transferred into the uterus. Using real-time PCR is important to measure the amounts of mtDNA in blastocysts so that it can be known if implantation of the blastocysts, and ultimately a successful pregnancy, is possible. For the future of biotechnology, perhaps medicine can be developed to lower/decrease the mtDNA levels in older women trying to have children. Analysis and future medicine can include the chances of having an ongoing pregnancy because more healthy blastocysts would be able to be transferred in utero and will implant.

Acknowledgements
I would like to thank Dr. Ericka Senegar-Mitchell for teaching, motivating, and inspiring us in how to be better scientists. I would also like to thank Ms. Winter for helping to run the OSA program. Additional thanks to Dr. Chang for instructing us on the dynamics of Oncotelligence and answering all of our questions. My OSA sisters, including Sheriden Smith, have given me guidance and support throughout this program and it is much appreciated. Lastly, to my friends and family that have unknowingly helped me by supporting me in all that I do, especially my sister who watches over me in all that I do.

References
CRISPR-Cas9 Mediated Treatment of HPV16-Related Cervical Malignancy
Mikaila Reyes  Torrey Pines High School

Objectives
With the advancement of technology, it is still often questioned why there is not yet a "cure" to cancer. The objective of this experiment, in which CRISPR-Cas9 systems are used in order to disrupt the E6 oncogene introduced by HPV16, is to serve as a stepping-stone toward solving this age-old question.

Figure 1. HPV16 Virus
Each year, about 12,000 women are diagnosed with cervical cancer. Human Papillomavirus (HPV) is the leading cause, and anyone who is sexually active is at risk. Although transmissible with an HPV vaccine and easily preventable, it causes cervical cancers to arise in millions of women worldwide each year.

Abstract
High-risk Human Papillomavirus (HPV), notably HPV16, is responsible for virtually all cases of cervical cancer. When a host cell is infected, the E6 oncoprotein proliferates and disrupts the p53 tumor-suppressor protein, leading to unregulated cell growth. With the intent to eliminate cervical cancer in women without causing harm to healthy cells, CRISPR-Cas systems can be used to manipulate the E6 oncogene introduced by HPV16, essentially curing cervical malignancy. CRISPR (Clustered Regularly Interspaced Short Palindromic Repeat) is a new gene-editing tool in which a targeted segment of DNA can be excised with great specificity. Four different cell lines were transfected and studied in vitro, two of which were HPV16-positive cervical cancer cell lines (CaSki and SiHa) and two were HPV16-negative (C33A and HEK293). Each cell line was transfected with a plasmid encoding the Cas9 enzyme and a gRNA sequence. Three different segments of guidance RNA (gRNA) were used in order for the CaSki (Cas9) associated enzyme to cut the E6 gene in the HPV genome at a specific site. When the double stranded breaks (DSB) in the DNA are repaired by the error-prone nonhomologous end joining (NHEJ) repair system, a frameshift mutation occurs, deactivating the gene. An annexin V-FITC (fluorescein isothiocyanate) apoptosis detection kit demonstrated that apoptosis increased from an average of 5% to 40% in the HPV-positive CaSki and SiHa cells while the HPV-negative C33A and HEK293 cells were unaffected. Western blot analysis indicated a reduction in E6 activity by nearly 50% while p53 activity nearly tripled as compared to the control. The CRISPR-Cas9 system has great potential as it allows for a less toxic and efficacious way to cut DNA.

Methods and Materials
Four types of cells were used in order to test the efficacy and specificity of the CRISPR-Cas9 system: HPV16-positive SiHa and CaSki cells, and HPV16-negative C33A and human embryonic kidney (HEK)-293 cells. The cells were maintained in media containing fetal bovine serum in a 37°C, 5% humidity in Modified Eagle’s Medium at 37°C. For the SiHa, C33A, and HEK293 cells, the DNA transfection reagent X-tremeGENE HP was used while JetPEI was used for the CaSki cells. Transfected into the cells was a plasmid containing the Cas9 gene and a short gRNA sequence intended to guide the Cas9 enzyme to the target area on the E6 gene. Three gRNA sequences were created (referred to as gRNA-1, gRNA-2, and gRNA-3); each plasmid contained only one of the three sequences.

Results and Interpretations
The results were as follows:
1. After transfected the CaSki and SiHa cells with the three different gRNA/Cas9 plasmids, the T7E1 assay demonstrated that the gRNA-2 and gRNA-3 groups cleaved the E6 gene into products with approximately 200 - 300 bp. In the CaSki cells, cleavage occurred with a frequency of up to 19% (gRNA-3). In the SiHa cells, cleavage occurred with a frequency of up to 22% (gRNA-2).

Conclusions
Thus far the minimal cytotoxicity, great specificity, and proven effectiveness of CRISPR promise a bright future for this powerful technology. Cervical cancer is only the beginning, as all cancers are thought to be caused by HPV16. The cells used to mutate or replace genes in vivo or in vitro, meaning that a person’s genes can be edited at any time and permanently. As it is cheap, easy to use, and successful, CRISPR is the future of targeted medicine. CRISPR has yet to be tested on human cells in vivo. Therefore, there are concerns regarding the off-target effects. Off-target effects, like the ones mentioned in our experiment design, must be either reduced to nearly zero or controlled entirely before it can be even considered for FDA approval. Further studies should consider using CRISPR in cell models in order to determine the side effects of genome editing. Although more trials must be conducted annually, CRISPR offers a hopeful solution for an array of genetic diseases and abnormalities.

Applications to Biotechnology
CRISPR is a great breakthrough for the medical community. As the CRISPR-Cas9 systems were only discovered in 2012, there are still many tests to be done in order to perfect the technology. As of now, CRISPR can be used for genome-editing, cancer therapy, and prevention. CRISPR is currently being used to model cancer in mice both in vivo and in vitro, which has many implications for the future study of cancer and the testing of chemotherapeutics. CRISPR is also in the preliminary stages of being used for systemic genetic modifications in mammalian cells, with the potential to crop modification, making them pest-resistant or more heat-resistant.

Acknowledgments
I would like to thank my parents for their unconditional love and support. They have taught me so much and I would not be where I am without them. I would also like to thank Dr. Ericka, Mrs. Winter, Steven and everyone else involved in the Oncofertility Saturday Academy for giving me this amazing opportunity and experience. Lastly, I would like to thank my OSA sisters for creating lifelong memories.

References
The Role of Fertility Sparing Surgery in Early Stage Epithelial Ovarian Cancer

Hailey Sokoloff • Poway High School

Abstract

Ovarian cancer is a disease that impacts not only the many women that it threatens, but also their fertility. To combat the disease, new methods of treatment, such as fertility sparing surgery (FSS) have emerged. FSS aims to preserve patient fertility. To accomplish this, FSS requires only a unilateral oophorectomy, where one ovary is removed while the other ovary and the uterus remain, as opposed to a more traditional bilateral oophorectomy and hysterectomy where both ovaries and the uterus are removed. Although this is relatively new method of treatment, significant effects have already been observed. This poster will examine the impact of standard treatments on patient fertility in relation to treatment effectiveness in managing early stage epithelial ovarian cancer.

Introduction

As a top concern for young cancer patients, fertility preservation must be addressed. Ovarian cancer is among those cancers whose treatment threatens fertility. 21,290 women are diagnosed with ovarian cancer annually. However, through fertility sparing surgery (FSS), patients have greater ability to maintain fertility while treating cancer. The purpose of this study is to demonstrate the potential of FSS to help preserve patient fertility while effectively treating early stage epithelial ovarian cancer. To evaluate the success of various cancer treatments in preserving fertility, while curing disease, researchers compared women, less than 50 years of age, who had early stage, low-grade, non-clear cell epithelial ovarian cancer and received treatment. Patients were assigned to one of two study groups: women who underwent bilateral oophorectomy or women who received FSS. Researchers found rates of recurrence between 33% in a 109 patient study and 100% in a 3 patient study. Researchers also found 98% to 100% of patients resumed menstrual cycles and pregnancy success rates between 38% and 71%. Beyond this, ultimately, researchers found that the survival rates of patients who underwent fertility sparing surgery were not significantly impacted. One study reported that the five year survival rate for patients who had undergone fertility sparing treatment was 84%, and the five year survival rate for patients treated with standard, more radical surgery was 82%. As a result, it is clear that fertility sparing surgery provides a place of other procedures with the potential to severely limit fertility, should be considered for patients with early stage epithelial ovarian cancer. By offering FSS to patients, they will have potential to better preserve fertility and have a higher quality of life. Future studies with increased numbers and necessary for future evaluation.

Methods and Materials

All patients underwent staging surgery and were classified using the FIGO system. Histology, stage, and grade were evaluated. Patients included in the study had epithelial, stage 1A or 1C, grade 1 or 2, non-clear cell ovarian cancer, and were less than 50 years of age. Patients were assigned to one of two groups: those receiving bilateral oophorectomy or those receiving FSS. Patients considered to be at high risk of recurrence, with a grade higher than 1 or stage higher than 1A received platinum-based chemotherapy. Five year survival and recurrence rates were calculated, as well as rates of amenorrhea and pregnancy.

Results and Interpretations

In studying FSS, reproductive function, recurrence, effects of additional chemotherapy, and five-year survival rate were monitored. Overall, FSS allowed continued reproductive function, without increasing rates of recurrence or decreasing five year survival rates, in cases with or without additional chemotherapy.

Effects of Chemotherapy:

Chemotherapy was found not to change the reproductive outcomes in FSS patients. One study found chemotherapy didn’t cause permanent amenorrhea and didn’t impact conception or age of menopause. In another with 15 patients who received menopausal treatment, seven of the fifteen had received adjuvant chemotherapy.

Reproductive Function:

After FSS, most patients resumed menstruation. One study found that 15 of 17 patients who had received FSS subsequently experienced regular menstruation. Another study reported 94% of patients continued to have menstrual function. In one study, all FSS patients resumed regular menses. Another study reported that 72% of the women treated with FSS attempted to become pregnant, but only 38% of them actually succeeded with full-term delivery. However, two other studies reported much higher success rates of 68% and 71%, respectively.

Recurrence:

Overall, there was a significant difference in five-year survival rates for women with FSS and women who didn’t have FSS. One study found a five-year survival rate of 84% in the fertility-sparing group and an 82% five-year survival rate in the standard surgery group. Figure 1 also demonstrates this; the overall five-year survival rate of women who underwent a bilateral oophorectomy was 91%, while women who had ovarian preservation had a similar survival rate of 94%. However, it is possible that there is an initial, more rapid drop in survival in women who underwent FSS while women who had more radical surgery showed a less extreme, more gradual drop in survival. This is depicted in Figure 2. As stated though, by the five year mark, survival rates are the same.

Conclusion

This poster reports on treatment of early stage, low grade epithelial ovarian cancer. Laparoscopic surgery is an increasingly investigational bilateral surgery and results in significantly decreased postoperative morbidity.

References

Ovarian Stimulation for Premenopausal Breast Cancer Patients: Aromatase Inhibitors vs. Selective Estrogen Receptor Modulators

Daisy Valdivieso

Saturday Academy

Canyon Crest Academy

Abstract

About 15% of breast cancer patients are ages 45-54, and knowing that after treatment they may no longer be fertile, many breast cancer patients have chosen to undergo embryo cryopreservation. However, the rise in estrogen levels that accompanies the use of common ovarian stimulants is dangerous for breast cancer patients, as estrogen plays a significant role in tumorigenesis of breast tissue. This study will evaluate two solutions to this problem: aromatase inhibitors and selective estrogen receptor modulators. They each work differently, and a comparison will be conducted to determine their relative efficacy and their positive and negative aspects. Representing each of these groups, a study with 60 patients compared letrozole (AI) and tamoxifen (SERM). Patients did not exceed stage three breast cancer, and were between the ages of 24 and 43. Experimental groups took 60mg/d tamoxifen, 60mg/d tamoxifen with FSH, or 5mg/d letrozole with FSH. After egg retrieval and IVF, the embryos were cryopreserved. In total, the tamoxifen group resulted with 13 cycles in 12 patients, the tamoxifen-FSH group had 9 cycles in 7 patients, and the letrozole-FSH group had 11 cycles in 11 patients. Tamoxifen-FSH and Letrozole-FSH produced the highest embryo yield, but Tamoxifen-FSH resulted in very high E 2 levels. Therefore, Letrozole-FSH was found to be the best combination for successful egg retrieval while not threatening estrogen levels. Furthermore, cancer recurrence rates were about the same in the IF group as the controls, with three in twenty-nine and three in thirty-one, respectively. From this study, letrozole-FSH, the aromatase inhibitor, was concluded to be the most effective. However, both aromatase inhibitors and selective estrogen receptor modulators are successful in keeping estrogen levels low, and minimizing or eliminating other factors that contribute to successful ovarian stimulation for breast cancer patients, both should be considered in making a personalized decision for every patient.

Methods and Materials

For this topic, a study from the Center for Reproductive Medicine and Infertility at Weill Medical College of Cornell University conducted a controlled comparison between tamoxifen and letrozole for ovarian stimulation in breast cancer patients, representing the SERM and aromatase inhibitors, respectively. Human, female subjects were all between the ages of 24-43 and none exceeded stage III breast cancer. This study included three experimental groups: a group of 12 women who received tamoxifen, a group of 7 who received tamoxifen with FSH, and a group of 11 who received letrozole with FSH. The control group consisted of 31 eligible women who elected natural cycle IVF (NCIVF) and went without ovarian stimulation. Reasons for this decision include cost and a lack of time to conduct this process before cancer treatment was needed. For those in the tamoxifen group, baseline FSH, LH, and E 2 levels were recorded, and on the second to third day of menstruation, 60 mg/d of tamoxifen was taken until FSH levels were below the baseline. For those in the tamoxifen-FSH group, along with the 60 mg/d of tamoxifen was a 150 UI injection of recombinant FSH. This was continued daily until hCG was administered. For those in the letrozole-FSH group, an oral 5 mg of letrozole was initiated on the second to third day of menstruation, and after two days 150U/d of FSH was added. Like the tamoxifen-FSH group, this was continued daily until hCG was administered. If FSH levels after ovocyte retrieval, E 2 levels were above 250 pg/ml, letrozole was continued until levels were below 50 pg/ml. For all of the patients, FSH, LH, and E 2 levels were recorded every one or two days until the oocytes were removed. If E 2 levels exceeded 250 pg/ml, a GnRH antagonist was released to avoid a premature LH surge. When the follicle reached an average diameter of 17-18 mm, hCG was administered, oocytes were retrieved 36 hours later, IVF was performed by ISCL, and embryos were frozen at the 2-4 pronuclear stage.

Results and Interpretations

In the results of the study, a variety of comparative data was recorded. The tamoxifen group resulted with 13 cycles in 12 patients, the tamoxifen-FSH group had 9 cycles in 7 patients, and the letrozole-FSH group had 11 cycles in 11 patients. There was an exception for the tamoxifen group, 1 of which had two cycle cancellations due to spontaneous ovulation right before the oocytes were retrieved. The age of IVF and control patients was similar, with the average being 37.7±6.8 years of age for controls and 36.5±0.7 years of age for IF patients. Letrozole-FSH and tamoxifen-FSH groups both had higher numbers of mature oocytes and oocytes retrieved than the tamoxifen group, thus they resulted in higher embryo counts as well. Average total embryos per patient for tamoxifen, tamoxifen-FSH, and letrozole-FSH were 1.3±0.2, 3±0.8, and 5±3.5 respectively. However, tamoxifen-FSH resulted in much higher peak estradiol than other groups, at an average of 1,182×77 pg/ml. Letrozole-FSH was able to maintain peak estradiol levels very well, averaging at 380±37 pg/ml, and tamoxifen alone peaked at 4198±99 pg/ml. Letrozole-FSH group proved to have the shortest follow-up time as well, averaging at 272±31 days versus 609±89, 418±109, and 666±71 days for tamoxifen, tamoxifen-FSH, and controls, respectively. Fortunately, there was no difference in recurrence rates between controls and IF patients.

Discussion

The purpose of this project was to determine the efficacy of AIs in comparison to SERMs. From the data above, it can be concluded that letrozole-FSH, the AI, was more effective in keeping estradiol levels low while stimulating the ovaries than tamoxifen-FSH or tamoxifen, the SERM groups. However, this does not rule out tamoxifen for ovarian stimulation. Both aromatase inhibitors and selective estrogen receptor modulators have proved to minimize estrogen levels with their different mechanisms. Furthermore, the small numbers used for this study indicate that further research should be conducted to confirm these findings. Another SERM that was not brought up in the study is clomiphene citrate; this is the standard drug for IVF in fertile patients. According to a clinical pharmacology review, letrozole has become more and more common and could potentially replace clomiphene. Therefore, not only is letrozole, and thus AI, good for fertility preservation in breast cancer patients, but also fertility preservation for general infertile patients. In addition, tamoxifen, as a partial agonist, is associated with an increased incidence of uterine cancer while letrozole is not. Perhaps the least to be feared are the aromatase inhibitors... However, while tamoxifen is antiestrogenic to breast cells, it is an estrogen agonist in bone tissue, and extended use of it can prevent postmenopausal osteoporosis. As conveyed, there are a number of benefits and risks that accompany the use of these drugs. It is important to involve both options when discussing fertility preservation with breast cancer patients so that a decision can be made that best fits their personalized care.

References


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The Effect of Testicular Sperm Extraction (TESE) During Adolescence on the Reproductive Success of Males with Klinefelter Syndrome

Vivien Vaucher

Objective
This poster aims to identify how having Klinefelter Syndrome (KS) can affect a male’s fertility; one of the more viable options, testicular sperm extraction, has been tested for fertility preservation; and how utilizing sperm from adolescent KS males obtained through testicular sperm extraction affects their reproductive success in the future.

Abstract
Klinefelter Syndrome (KS) is a disorder that occurs when a male has any number of additional X chromosomes to the X chromosome in the XY that determines his sex. This syndrome is one of the most common sex chromosome disorders, affecting an estimated one in 500-1,000 males at birth; however, many cases go undiagnosed because the symptoms often present mildly. Most KS males face infertility and a deficit in testosterone, and if diagnosed, patients can be put on testosterone treatments to regulate hormone levels in the body for the development of secondary sex characteristics. Males with KS often seek assisted reproductive technology, a common method being testicular sperm extraction (TESE), where a biopsy is performed to retrieve testicular tissue, and it is then cryopreserved for future sperm extraction. Due to the knowledge that the success of TESE decreases as testosterone increases, it is ideal for this procedure to be performed before the onset of puberty when testosterone does not have any effect. This particular study was conducted on eight adolescent males with Klinefelter Syndrome who served as an experimental group to examine the success of TESE on KS males. Following an analysis of a semen sample to detect azospermia, these males were given the option to have testicular tissue cryopreserved. After examination of the testicular tissue extracted, one patient was found to have viable spermatozoon in one testis, and another was found to have a low, but present amount of germ cells in one testis. Seven of the males were shown to have azospermia. TESE was used as the preservation method due to it having proven to allow for successful spermatogenesis of the sperm retrieved, and additionally, egg fertilization through ICSI in vitro fertilization procedure. Thus far, TESE has proven effective in the fertilization of eggs via in vitro fertilization, but it has not yet been tested enough to determine statistics regarding the prevalence of full reproductive success. However, the results of testicular tissue biopsies performed on adolescent KS males show potential for the future reproductive success of the patients.

Methods and Materials
In a French study conducted from 2008 to 2011, eight adolescent males diagnosed with Klinefelter Syndrome were evaluated for their fertility and served as an experimental group for the possible fertility preservation method of testicular sperm extraction, or TESE. A group of four males with tissue cryobanked via TESE prior to gonadotoxic treatment served as the control group. Each KS male was asked to provide a semen sample in order for the researchers to detect azoospermia. Following the analysis, these males were then given the option to have testicular tissue cryopreserved. TESE was used as the method of preservation due to it having proven to allow for successful spermatogenesis of the sperm that are retrieved, and additionally, fertilization of eggs through the ICSI in vitro fertilization procedure.

Results
When tested, all of the patients had hyposperma, which causes lower sperm count in semen. In addition, seven of the males had azospermia, and therefore a complete absence of motile sperm in their semen. This made the extraction during adolescence essential, since testosterone levels are highest during puberty and therefore will have the greatest effect on the sperm of young adult males. After analysis of the testicular tissue extracted, one patient was found to have viable spermatozoon in the right testis, and another was found to have a low, but present amount of spermatozids in the right tests. All of the patients’ seminiferous tubules were empty or degenerative, and therefore were not producing any gametes that would allow for the production of viable spermatozoon. Overall, spermatozoon count was significantly lower in the experimental group of KS males observed in the study compared to any other control group involved in similar studies.


Figure 2. Often males with Klinefelter Syndrome will have fertility problems that come from hyposperma, or low sperm count as is pictured on the right. Low sperm count. (2015). Retrieved August 11, 2015

Conclusions
So far, results have not been entirely conclusive on how preserving fertility through TESE has affected the reproductive success of males with Klinefelter Syndrome since the males in the study have not yet sought out assisted reproduction to conceive. However, past attempts at conception through the ICSI in vitro fertilization procedure using sperm extracted via TESE have shown to be successful in the fertilization of eggs and creation of embryos. Further studies would be required to get adequate information regarding the effect of utilizing TESE to preserve the fertility of KS males on their future reproductive success.

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References
The Enhancement of Cancer Immunotherapy with Gold Nanoparticles

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Objective

Cancer immunotherapy is a cancer treatment that utilizes adjuvants and antigens to stimulate the immune system to detect and eradicate cancer cells. By utilizing immunotherapy, immune system is stimulated to recognize tumor-specific antigens, leading to the suppression of tumor growth. This can be accomplished by various methods, such as using antigen-presenting cells (APCs) or engineered T cells that specifically recognize and kill cancer cells.

Abstract

Cancer immunotherapy is a treatment that utilizes adjuvants and antigens to stimulate the immune system (the patient’s natural defense against disease). By using these agents, the immune system can target and destroy cancer cells. This can be achieved through various methods, such as using programmed cell death (PCD), engineered T cells that specifically recognize and kill cancer cells, or using cancer vaccines.

Methods and Materials

Many studies have been conducted to analyze the effect of utilizing gold nanoparticles (AuNPs) in cancer vaccines with the intention of suppressing tumor growth. In one study, researchers investigated the efficacy of AuNPs in cancer vaccines. The mice were injected with AuNPs conjugated with antigens and tumor suppressor genes. The results showed that the AuNPs significantly suppressed tumor growth compared to the control group.

Results and Interpretations

All three studies concluded that AuNPs helped enhance cancer vaccines by inhibiting tumor growth. In the first study, tumor growth in mice treated with AuNP/OVA257–269 was suppressed (40%) compared with the saline/control (100%). After 27 days, the tumor in mice treated with AuNP/OVA257–269 was suppressed to ~480 mm compared to the free antigen (OVA) vaccine which was suppressed to ~900 mm. These results indicate that the AuNP-based vaccine was effectively delivered to the local lymph nodes and created an antigen-specific immune response.

Conclusions

It was concluded from these three studies that AuNPs helped enhance the therapeutic effect of cancer vaccines. The AuNP-induced cancer vaccines efficiently inhibited tumor growth compared to the free antigen/adjuvant shots due to the fact that gold nanoparticles have several properties that enable efficient drug delivery. Through this breakthrough, the creation of new and efficient cancer vaccines can be possible. Even though cancer immunotherapy can be improved through the use of gold nanoparticles, more research needs to be conducted on the complete eradication of malignant cancer cells through vaccines. Through further research, cancer immunotherapy can be utilized to eradicate cancer while reducing toxicity, increasing eradication rate, and potentially increasing long-term survival rates. As a result, the lives of many cancer patients can be positively impacted through cancer vaccines.

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