Disparities in Female Hormone Research and Therapy

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On my honor as a University Student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments

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Introduction

The landscape of women's healthcare has witnessed remarkable strides over the years, yet a persistent and intricate challenge remains in the realm of hormone research. Underlying this intricate network lies a pressing concern necessitating immediate scientific scrutiny: the pronounced disparities inherent in women's hormone research. Despite making it a legal requirement to include in clinical trials in the United States in the 1990s, women still represented less than 40% of participants in cardiovascular clinical trials (Kelly Burrowes). This overarching issue encompasses a multifaceted interplay of factors impeding the nuanced comprehension, precise diagnosis, and efficacious treatment of women's health intricacies linked to hormonal imbalances.

The historical underrepresentation of women in clinical trials casts a formidable shadow over our scientific understanding of hormonal dynamics and nowhere are the implications of this gender bias more profound than in studies related to hormonal interventions. From menopausal hormone therapy to fertility treatments, the efficacy and safety of these interventions demand precise understanding, yet women remain disproportionately underrepresented. Studies assessing hormone replacement therapy reveal that women, the primary beneficiaries of such interventions, constitute only 27% of participants (Jacobs, Emily G.). This lack of representation in research can be detrimental to women as it can lead to medical interventions that are less effective or have different outcomes in women, as the response to medications and therapies may vary based on gender.

The issue of disparities in women's hormone therapy is closely intertwined with the broader context of gender-specific research and its implications for healthcare outcomes. Gender bias in animal studies sheds light on a historical oversight that has significant repercussions for

women's health. About 80% of rodent drug studies today are conducted only on male mice before the drugs are given to male and female patients (Locke, Susannah). The underrepresentation of female mice in biomedical research is based on the assumption that females are intrinsically more variable than males, due to their estrous cycle where hormones vary every 4 days in mice (Sarah Bailey). Ironically, female mice tested through their hormonal cycle display no more variation than males do. The exclusion of females, both in animal and human clinical trials, has perpetuated a skewed understanding of how medications, including hormone therapies, affect women.

My technical topic is creating a predictive model to estimate baseline serum estradiol concentration in female laboratory mice. To complement my estradiol concentration research, my STS topic is the disparities in women's hormone therapy.

Technical Topic

Estradiol is a form of the estrogen hormone responsible for reproductive development and regulation. Previous research on this topic is outdated and predominantly focused on male mice (Depypere, H T et al.). Female mice were assumed to cause more variable results due to their hormones and, therefore, disrupt results. These assumptions have been proven false, highlighting the existence of a research bias that has hindered a comprehensive understanding of estradiol dynamics in female mice. This technical project aims to determine the baseline estradiol concentration in female mice and create a predictive model for the concentrations. By determining the baseline estradiol concentration in female mice, our study seeks to contribute valuable insights into women's health, such as muscle regeneration and hormone replacement therapy, and improve upon existing research. The development of an accurate predictive model for estradiol concentrations can significantly improve the efficiency of research efforts, with the

potential to save valuable time and resources by reducing the need for lab equipment. In addition to its immediate applications, the predictive model can have broader implications. It can be utilized to enhance the efficiency of other research projects related to estradiol where researchers can obtain rapid estimates of estradiol concentration. Additionally, it can validate older experimentation and fill the existing gaps in the understanding of the estrous cycle in female mice. The estrous cycle, consisting of four stages, plays a crucial role in reproductive processes, and our study seeks to predict the baseline estradiol concentration accurately.

The first phase of the project focuses on gathering data by determining the estrous cycle stage with vaginal cytology and blood samples of the mice. Vaginal cells will be evaluated to determine the estrous cycle stage. The stages of the estrous cycle are identified by the absence, presence, and proportion of four basic cell types (neutrophils, small nucleated epithelial cells, large nucleated epithelial cells, and anucleated keratinized epithelial cells) as well as by the cell density and arrangement of the cells on the slide, shown in Figure 1 (Depypere, H T et al.). The process entails conducting routine vaginal smears that are subsequently stained and examined under a microscope to discern various cell types and their respective ratios, and these findings serve as valuable indicators of the current phase of the estrous cycle. The quantification of estradiol concentration in mice can be achieved with the implementation of the E2 ELISA technique, and this method utilizes the collection of blood samples from the mice, followed by an analysis of the estradiol concentration. The precise amount of blood required for analysis will be ascertained, and appropriate blood collection

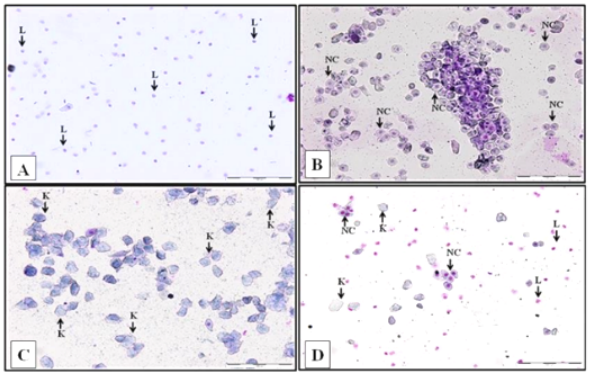

Figure 1: Cell Types Per Estorus Cycle Stage

techniques will be employed. There will be monitoring of behavioral and environmental factors that may impact the estrous cycle and overall data. This will include observing sickness and reactions to blood collection, adjusting collection methods if necessary, and monitoring environmental factors such as light exposure, food given to mice, and temperature.

The next phase will entail creating a predictive model to output accurate concentration. Data obtained from the animal experimentation will be utilized to construct a predictive model that can incorporate the established baseline concentration of estradiol and estrous phase, in an attempt to improve our understanding of the physiological processes involved. The data output will include the predicted hormone concentration [E2] and the stages, solely based on the estrous stage. The predictive model will have both the original data and the model's output. Both will be compared using statistical tests to identify how similar the model is. The data output will contain statistics such as accuracy, sensitivity, and specificity to interpret the model and to confirm if the model is working.

STS Topic

For decades, women's hormones have been shrouded in a veil of scientific neglect and bias. This neglect and underrepresentation have manifested as disparities in research funding, study design, and representation, ultimately impacting the diagnosis, treatment, and understanding of women's health issues deeply intertwined with hormone fluctuations. Understanding the extent and consequences of these disparities is essential for advancing gender-inclusive healthcare and the question of how these disparities in women's hormone research contribute to gaps in understanding addresses a critical gap in our knowledge, impacting the precision and efficacy of medical interventions for women.

In terms of funding, women's health research receives only 4% of the total National Institutes of Health (NIH) budget, despite representing over 50% of the population (Finley, C et al.). Within this meager allocation, research on specific hormonal conditions like endometriosis or polycystic ovary syndrome (PCOS) receives even less, further compounding the problem. This issue is further compounded by racial bias, leading to an even smaller share of resources allocated to studying hormonal health issues in women of color (Pershad, Anita et al). The underrepresentation of minority women, including Black, Hispanic, and Asian women, remains a pervasive issue and according to data from the U.S. Food and Drug Administration (FDA), Black women constitute only about 6% of participants in clinical trials, while Hispanic women make up approximately 1.8% ("Race Matters When Prescribing Hormone Therapy for Menopausal Women."). This inadequacy can lead to inaccurate conclusions and ineffective treatments that fail to address the specific needs of diverse populations.

Historically, research has often relied on male-dominated study populations, ignoring the unique hormonal experiences of women. This can lead to inaccurate conclusions and treatments that fail to address the specific needs of female patients. For example, most cardiovascular disease research excludes women despite their rising risk in later life, potentially missing crucial hormonal factors. This is worsened by the fact that women are underrepresented in leadership positions within research institutions and funding agencies, further perpetuating the cycle of bias. This lack of diversity in decision-making hinders the prioritization of research relevant to women's health concerns.

This lack of representation can have catastrophic, long-term impacts. The lack of research on specific hormonal conditions can lead to delayed diagnosis and ineffective treatment, causing unnecessary suffering and potentially worsening health outcomes. For example, women with

endometriosis often face years of diagnostic struggles due to inadequate research on the condition. In addition, treatments developed based on predominantly male study populations may be ineffective or even harmful to women, leading to medication side effects and missed opportunities for effective interventions tailored to female hormonal needs.

The question that I aim to answer in my STS project is how disparities in women's hormone research contribute to gaps in understanding hormonal imbalances. My research will include a comprehensive review of existing literature on gender disparities in clinical trials and hormone studies that will provide insights into historical trends and gaps. I will then conduct an analysis of data from clinical trials that will involve assessing the gender distribution of participants, the representation of women in hormonal studies, and the outcomes reported for different genders. I will then utilize medical databases, such as those containing information on hormonal therapies and women's health outcomes, which will offer a real-world perspective on the impact of gender disparities in research. This methodology will allow for an understanding of how these disparities specifically impact women’s health.

Conclusion

In order to address the lack of an existing model for determining baseline estradiol concentrations for mice, I will perform vaginal cytology and collect blood serum samples to create a predictive model for the concentrations. This model will have the potential to significantly improve the efficiency of research efforts and allow for rapid estimates of estradiol concentration. A comprehensive review of existing literature on gender disparities in clinical trials and hormone studies as well as an analysis of data from clinical trials will be conducted in order to understand how disparities in women's hormone research contribute to gaps in women's health outcomes.

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