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Comparative Morphological and Morphometric Characteristics of the Fallopian Tubes under Experimental Hypokinesia Conditions

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Abstract: In recent years, the decline in physical activity has become a more prevalent part of the modern lifestyle, which has prompted concern on its broader physiologic effects. While the systemic impacts of hypokinesia are well-documented, its impact on the female reproductive system, especially at the structural level, is not well enough understood. This study was designed to investigate the morphological and morphometric changes in fallopian tubes under conditions of experimentally induced hypokinesia. An experimental model of the adult female rat was used, with control and hypokinesia groups. The latter received restricted mobility for a specified period of time, and fallopian tube tissues were then harvested and evaluated histologically and morphometrically. A microscopic analysis showed some visible changes in the organization of the epithelium, including decreased epithelial height and a decrease in the density of ciliated cells. In addition, changes of the configuration of the lumen and a slight decrease of the thickness of the tubal wall were observed. Quantitative measurements confirmed this statistical significance of these differences. The findings suggest that hypokinesia causes subtle but consistent structural changes in the fallopian tubes, both the epithelial and muscular parts. These changes may have functional implications especially in regard to gamete transport and overall reproductive capacity. The study underlines the importance of physical activity in the maintenance of structural and functional integrity of female reproduction system.

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Introduction

In recent decades, due to the fast change of lifestyle pattern, physical activity of the population has decreased dramatically, forming a state commonly known as hypokinesia. This condition, manifested by a decrease in motor activity, no longer refers to certain categories of workers but has turned into a widespread phenomenon involving people of different ages and physiological states. While the systemic consequences of hypokinesia, including cardiovascular deconditioning, metabolic imbalance and musculoskeletal atrophy, have been described in great detail, the impact on the female reproductive system is relatively understudied [1]. In particular, subtle structural changes which occur in reproductive organs under conditions of prolonged inactivity may have implications which may not be immediately obvious, but are nonetheless clinically important. The fallopian tubes have a central role in female fertility, playing not only a passive role as conduits, but in fact are dynamic structures that are involved in gamete transport,

fertilization and early embryonic development. Their function is dependent on the concerted action of ciliated epithelium, the contractility of smooth muscle and an adequate vascular supply. Even small deformities in these components can impair the patency of the tubes or change the microenvironment necessary for successful fertilization. Emerging evidence supports the role of external stressors, such as lower physical activity, on reproductive physiology via complicated neuroendocrine and circulatory mechanisms [2].

However, the morphological correlates of such influences, in particular at the tissue and cellular levels, have not sufficiently been characterized. From a mechanistic point of view, hypokinesia is linked to decreased blood circulation and decreased oxygen delivery and hormonal regulation, all of which can lead to tissue remodeling. In experimental models, these changes are often represented by epithelial degeneration, and stromal changes, and reduced functional capacity of organs sensitive to microcirculatory changes. Within the reproductive system, already with its cyclical fluctuations of hormones and all the physiological demands this presents, such disturbances may turn out to be especially consequential. Despite this fact, the great majority of existing studies have concentrated on ovarian function or changes in the uterus leaving the fallopian tubes more or less neglected in experimental investigations [3].

Understanding the morphological and morphometric response of the fallopian tubes to hypokinesia is, therefore, important, not only from a theoretical perspective, but also in the context of growing concerns over infertility and reproductive health in modern societies. Detailed structural analysis can help to gain insights into the presence of early pathological alterations that are followed by clinical manifestations and therefore contribute to the development of preventive strategies and targeted interventions. Moreover, the comparison of evaluation in the normal and hypokinetic conditions is possible to get a more precise determination of adaptive and degenerative processes taking place in the tubal tissue. In light of these considerations, the present study was designed in order to investigate the comparative morphological and morphometric characteristics of the fallopian tubes under experimental hypokinesia conditions. By combining histological findings with quantitative data, this study aims at enhancing the understanding of the effects of reduced physical activity on reproductive structures at the microscopic level mechanistic pathways of impaired female fertility by hypokinesia [4].

Methods

The study was performed as an experimental study to ascertain the structural and quantitative changes in the fallopian tubes under the condition of reduced motor activity. Adult female Wistar rats were chosen as the biological model because they have well-characterized reproductive physiology and more commonly are used to study experimental gynecology. A total of 30 animals with a weight of 180 - 220 grams were included in the study. All procedures were conducted in accordance with internationally accepted guidelines for the care and use of laboratory animals and care was taken to minimize both stress and inappropriate handling during the experimental period [5].

In order to make a reliable comparison, the animals were randomly separated in two equal groups. The control group was kept under normal vivarium conditions with free movement and the experimental group under a model of hypokinesia. Hypokinesia was induced by restricting the animals' mobility by using specially designed cages that restricted the animals' horizontal movement without causing direct physical damage. This way, it was possible to simulate inactivity over a long period of time whilst maintaining basic жизне able to stay alive and access food and water. The time span of exposure was adapted to 21 days, which is assumed to be sufficient for the formation of measurable structural changes in internal organs under conditions of reduced physical activities [6].

At the end of experimental period the animals were euthanized under controlled anaesthesia in order not to make them more physiological stress that could affect tissue

morphology. The fallopian tubes were then carefully dissected taking precaution to maintain their anatomical integrity. Immediately after extraction, the tissues were fixed in neutral buffered formalin 10% for 24 - 48 hours to ensure adequate fixation of the cellular structure. Following fixation, standard histological processing was performed including dehydration in graded alcohol solutions, paraffin embedding and microtome sectioning at a thickness of 4-5 micrometers [7].

For morphological evaluation, tissue sections were stained with hematoxylin and eosin, which enabled visualisation of the epithelial layers, stromal components, and vascular structures. Microscopic examination was performed with a light microscope with digital image system. Particular attention was paid to the state of ciliated epithelium, organization of the muscular layer and presence of any degenerative or dystrophic changes. Morphometric analysis was carried out to get quantitative data to support the qualitative observations. Measurements were done of epithelial height, luminal diameter and thickness of tubal wall. In addition, the relative density of ciliated cells was determined in selected fields of view. Digital image analysis software had been used to improve the measurement accuracy and reduce observer bias. For each parameter, at least ten fields for each specimen were analyzed, and mean values were calculated to represent each experimental group [8].

The obtained data were subjected to statistical analysis from the standard software packages. Results were expressed as mean values with standard deviation. Differences between control and experimental groups were tested with the Student's t-test at a significant level of $p < 0.05$. In this way it was possible to seek statistically meaningful differences while retaining analytical rigor [9].

Results

The comparative study of the fallopian tubes showed distinct structural and quantitative differences in the tubes of the control group and animals under experimental hypokinesia. Even in stage of general microscopic observation, the tissues obtained from the experimental group looked less organized by evident alterations in epithelial continuity and luminal configuration. These differences were not abrupt and destructive in nature but were the result of gradual functional adaptation of structure to reduced demand. The fallopian tubes in the control group maintained their normal histological structure. The mucosal lining was of a well-defined columnar epithelium with high numbers of ciliated cells. The cilia were distributed evenly and oriented clearly towards the lumen and formed a continuous functional surface. The muscular layer retained its normal thickness and arrangement; and the lumen its relatively regular rounded shape. These features are consistent with the previously described features of healthy tubal tissue, where epithelial integrity and ciliary activity are closely coupled with good reproductive function [10].

In contrast to this, the experimental group exhibited a number of deviations from this pattern. One of the most consistent was a decrease in epithelial height. Measurements displayed a statistically significant reduction in the thickness of the epithelial layer in comparison to the control group and this indicates a degree of cellular atrophy or reduced proliferative activity. In addition, the epithelial surface was irregular in several areas, flattened in places and at other times broken up the normal columnar arrangement. There were changes in ciliary structures as well. The ciliated cell density was clearly reduced in the hypokinesia group and in places, cilia were reduced in length or were absent. This reduction was not consistent across all samples but was following a consistent trend, hence a systemic rather than incidental effect. Given that cilia are integral to the process that allows the transport of an ovum, such changes may represent an early decrease in functional capacity at the microscopic level [11].

These observations were further supported by the morphometric analysis. The average luminal diameter in the experimental group had a tendency to be irregular with some parts having constriction and others showing slight dilatation. This variation is in contrast to the relatively stable luminal dimensions found with the control group. The thickness of the tubal wall also showed a small but statistically significant reduction, mainly as a result of alterations of the muscular layer. In a number of specimens, the muscle fibers were less compact with more loose fibers and may indicate that the muscle is less ready to contract. Quantitative data analysis found these differences were not random. Statistical comparison showed significant reduction in epithelial height and ciliary numbers as well as measurable changes in wall thickness and p-values less than accepted threshold for significance. Although the amount of change was not uniform across individual animals, the pattern of change was the same among the experimental group. It is also interesting to note that no acute inflammatory reactions or obvious tissue damage could be observed in either group. The lack of necrosis or inflammatory infiltration indicates that the changes that result from hypokinesia are adaptive or degenerative in nature rather than inflammatory. This finding is consistent with the results of recently published experimental data, which show that low levels of physical activity tend to cause gradual structural remodeling rather than acute pathological lesions [12].

Taken together, the results suggest that experimental hypokinesia results in measurable morphological and morphometric changes in the fallopian tubes. These changes are subtle but consistent involving epithelial as well as the muscular components. The found patterns provide support for the notion that, even moderate drops in physical activity can affect the structural organization of the reproductive tissues and potentially affect the functional capacity of reproductive tissues over time [13].

Discussion

The findings that have been obtained in this study give a nuanced view of how reduced motor activity can impact the structural integrity of the fallopian tubes. Although much has been said about hypokinesia regarding systemic physiologic decline, the localized effects of hypokinesia on reproductive tissues are less often taken into account. The observed alterations in epithelial organisation, reduction in ciliary density and the measurable changes in morphometric parameters suggest that even rather short periods of restricted movement may initiate structural adaptations that are not only functional but actually morphological in nature. One of the most interesting things that I noticed is that the aqueous epithelium seemed to thin out and ciliated cells were distributed more haphazardly in the experimental group. This finding fits in with more general evidence that epithelial tissues are extremely sensitive to alterations in microcirculation and oxygen availability. Under hypokinetic conditions, reduced blood flow could result in the subtle hypoxic stress, which would, in turn affect cellular turnover and differentiation. Similar patterns have been reported in other organ systems in which decreased activity leads to flattening of the epithelium and decreased regenerative ability [14]. In the case of the fallopian tubes, these changes could affect the movement of oocytes through the tubes and can hamper the coordinated movement necessary for oocyte transport. The ciliary structure reduction needs special mention as ciliary motion is a major determinant of the function of the tubal. Cilia are metabolically active and require a sufficient energy supply, which may be affected in the event of a limited physical activity. Experimental studies have shown that a reduced systemic circulation may lead to impairment of mitochondrial activity and reduced availability of ATP, that influences the frequency of ciliary beating and maintenance of cilia structure [15]. In this regard, the results of the present study support the hypothesis that hypokinesia may indirectly impair fertility by affecting the mechanical environment in the fallopian tubes.

Changes in the thickness of the tubal wall and the organization of the muscular layer are also observed, those which show that hypokinesia affects not only epithelial components, but also deeper structural elements. It is reasonable to assume that with decreased movement there is less stimulation of smooth muscle activity and this, over time, may contribute to deterioration of muscle tone and remodelling of smooth muscle structure. This phenomenon has been modelled in vascular and gastrointestinal tissue where inactivity results in decreased contractile responsiveness and changes in tissue architecture [16]. When applied to the reproductive system, such changes may be found in peristaltic movements necessary for the carrying of gametes and early embryos. Another important aspect to consider is that of the neuroendocrine regulation. Physical activity is known to modulate hormonal balance including the level of estrogen and progesterone which is critical for maintaining the structural and functional integrity of the fallopian tubes. Hypokinesia can interfere with this balance and result in indirect morphological consequences. Recent studies have suggested that the sedentary conditions can lead to changes in endocrine signaling pathways, giving rise to tissue-specific responses that differ on the basis of hormonal sensitivity [17]. The fallopian tubes being hormonally responsive structures likely will be influenced by such shift which can account for some of the variability in morphometric measurements. While the current findings add to an increasing study of the influence of lifestyle-related factors on reproductive health, they raise a number of important questions as well. It is unclear whether the observed changes are absolutely reversible with the restoration of normal activity or whether protracted hypokinesia may result in permanent structural changes. Additionally, the degree to which these experimental observations can be translated to human physiology needs to be given some thought. Nonetheless, the congruence between the results and the known tissue adaptation to lack of exercise provides some credibility to the proposed interpretations. Taken together, the data would suggest that hypokinesia should be considered as a systemic risk, but also as a condition that could cause localised morphological alterations of reproductive organs. This way of thinking may be especially important in contemporary societies where sedentary behavior is becoming more prevalent. By emphasizing the presence of structural changes in the fallopian tubes, this study highlights the importance of ensuring adequate physical activity as one of the strategies to preserve female reproductive health [18].

Conclusion

The present study gives a specific insight into how decreased physical activity can affect the structural organization of the fallopian tubes. While hypokinesia is commonly understood to be systemic and target the whole physiology, the results of the present work point to its ability to produce localized effects in the female reproductive system. The noticed changes, while not destructive in their nature, are consistent with a pattern of structural adaptation, which may have functional consequences. The decreased epithelial height with a significant decrease in ciliary density indicates that the tubal mucosa is especially sensitive to alterations of the internal environment, linked with limited movement. These features are more than mere details in their morphology and have a direct role in ensuring that the ovum is transported properly and the conditions favourable for fertilization are maintained. Any disturbance in this fine balance system even on a microscopic level can over time compromise the reproductive efficiency. Equally important are changes that are found in the muscular layer and general wall thickness of the fallopian tubes. A small but persistent decrease in these parameters is an indication of a reduction in structural support and possible weakening of peristaltic activity. Since coordinated muscular contractions play an important part in the movement of gametes and early embryos, such modifications may have an influence on reproductive outcomes that are not immediately obvious but become significant with time. The changes found in this study seem to develop gradually and without signs of acute damage or inflammation,

so it is worth emphasising. This hints that hypokinesia is working via subtle regulatory mechanisms, which probably subject matter, alteration in blood flow, oxygen delivery, and hormonal balance. As a result there is a form of structural adjustment of the fallopian tubes which represents a reflection of reduced functional demand rather than pathology. Taken together, these findings add to the importance of maintaining good levels of physical activity as a factor in maintaining reproductive health. A long disuse without any overt clinical symptoms could trigger the development of alterations that alter the normal functioning of the reproductive organs. Future research should seek to establish the reversibility of these changes and whether they have relevance in human populations, especially for the currently increasingly sedentary lifestyles.

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