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Review Article

Estrous Cycle Ratio as a Reproductive Index in the Rats

MJ Adeniyi[1]* and FO Agoreyo[2]

[1]Department of Physiology, Edo University Iyamho, Nigeria

[2]Department of Physiology, University of Benin, Nigeria

***Corresponding author:** MJ Adeniyi, Department of Physiology, Edo University Iyamho, Edo state, Nigeria.

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Abstract

Estrous cycle is an endogenous rhythm. Previously, studies have evaluated and analyzed the cycle based on its regularity and length and diestrus proportion. The aim of the review is to introduce estrous cycle ratio as a reproductive index and highlight its relevance. Twenty murine studies were retrieved from electronic databases published between 1999 and 2019. Estrous cycle ratio was calculated according to the method of [1]. The result shows that the average estrous cycle ratio is 0.81 with a nadir of 0.5 and a zenith of 1.5. Increase in estrous cycle ratio may signify prolongation of follicular phase length and delay in ovulation. Decrease in estrous cycle ratio may indicate delay in luteal regression with attendant delay in the initiation of new folliculogenesis. Therefore, estrous cycle ratio is an estrous cycle evaluation index.

Keywords: Estrous Cycle Ratio; Follicular Phase; Folliculogenesis; Estrous Cycle; Ovulation

Introduction

Experimental rats are spontaneous ovulators with characteristic short reproductive cycle length lasting 4-5days [2]. Like the menstrual cycle, cyclic changes occur in murine reproductive structures, including the parenchyma of the ovaries-the primary reproductive organ. Examples of such changes are fluctuations in gonadotropin and gonadal hormones, changes in density of uterine glands and cervical mucus and perturbations in pH, sexual receptivity and body temperature [3].

Rats' estrous is divided into four phases based on cell type and density. Proestrus is characterized by squamous epithelial cells. Estrus, metestrus and diestrus are identified and differentiated based on the presence and proportions of cornified cells, leucocytes and squamous epithelial cells. Like menstrual cycle, proestrus is related to pre-ovulatory phase. Metestrus and diestrus are related to post-ovulatory phase [2].

Several studies have evaluated estrous cycle using estrous cycle indices such as estrous cycle length, estrous frequency, estrous phase interval, estrous regularity and diestrus index [1]. The present study looked at the possibility and relevance of using estrous cycle ratio as a reproductive index in murine studies.

Methodology

Studies were retrieved through electronic databases of English language literature only. Search was achieved through the use of phrases and key words such as estrous cycle, estrous phases, estrus and estrous length. Murine studies published between 1999 and 2019 were selected. Only studies that displayed estrous phases in form of tables were used. Using these criteria, a total of 20 murine studies were selected. For each reviewed article, information was extracted on authorship and year of study.

Only the placebo groups of these studies were analyzed. Calculation of estrous cycle ratio (ECR) was done using the method prescribed by [1].

ECR = (Proestrus+Estrus) / (Metestrus+Diestrus)

Result

See in the following (Table 1 & Table 2)

Table 1: Estrous cycle phases.

S/N	Estrous Cycle Phases				References
	Proestrus	Estrus	Metestrus	Diestrus	
1	25.0±0.3	17.0±1.8	29.0±0.3	29.0±0.3	Agoreyo & Adeniyi [1]

2	2.5±0.34	4.2±0.2	0.5±0.2	7.8±0.3	Sortur & Kaliwal [23]
3	6.2±0.4	5.8±0.4	4.6±0.4	3.4±0.34	Hassan, [9]
4	25.0±0.0	25.0±0.0	25.0±0.0	25.0±0.0	Oyesola et al. [4]
5	26.0±1.8	24.0±4.7	18.8±3.2	33.3±1.8	Mustapha et al. [13]
6	1.0±0.0	2.1±0.0	1.2±0.0	4.6±1.1	Ahirwar et al. [8]
7	3.8±0.4	6.2±1.4	6.0±1.3	14.2±2.4	Sharanabasappa et al. [19]
8	4.0±0.6	4.8±0.7	3.5±0.8	3.7±0.7	Santos et al. [21]
9	0.86±0.1	0.9±0.1	0.8±0.1	1.8±0.5	Abu & Uchendu [7]
10	32.0±0.0	59.0±0.0	50.0±0.0	31.0±0.0	Ranjan et al. [22]
11	5.0±0.2	7.7±0.3	4.9±0.3	12.3±0.4	Oluyemi et al. [16]
12	6.4±0.2	7.2±0.2	10.6±0.2	6.4±0.2	Sarita [18]
13	20.9±0.0	20.0±0.0	44.8±0.0	14.3±0.0	Iranloye & Owokunle [10]
14	21.7±0.0	22.3±0.0	20.4±0.0	37.6±0.0	Raji & Hawt [17]
15	4.8±0.2	6.8±0.3	5.5±0.3	10.2±0.3	Sayed et al. [20]
16	15.0±0.0	20.0±0.0	40.0±0.0	25.0±0.0	Ngadjui et al. [15]
17	5.0±0.0	7.5±0.0	2.5±0.0	12.0±0.0	Nayanaturu et al. [14]
18	2.08±0.5	3.3±0.3	4.0±0.3	5.6±0.4	Koneri et al. [12]
19	1.8±0.0	2.9±0.0	1.3±0.0	3.5±0.0	Monima et al. [5]
20	4.0±0.0	6.0±0.0	5.0±0.0	15.0±0.0	Kage et al. [11]

Table 2: Estrous cycle ratio.

S/N	Estrous Cycle Ratio	References
1	0.7	Agoreyo & Adeniyi [1]
2	0.8	Sortur & Kaliwal [23]
3	1.5	Hassan [9]
4	1	Oyesola et al. [4]
5	1	Mustapha et al. [13]
6	0.5	Ahirwar et al. [8]
7	0.5	Sharanabasappa et al. [19]
8	1.2	Santos et al. [21]
9	0.7	Abu & Uchendu [7]
10	1.1	Ranjan et al. [22]
11	0.7	Oluyemi et al. [16]
12	0.8	Sarita [18]
13	0.7	Iranloye & Owokunle [10]
14	0.8	Raji & Hawt [17]
15	0.7	Sayed et al. [20]
16	0.5	Ngadjui et al. [15]
17	0.9	Nayanaturu et al. [14]
18	0.6	Koneri et al. [12]
19	1	Monima et al. [5]
20	0.5	Kage et al. [11]

Discussion and Conclusion

During active female reproductive life, cyclical morphological and physiological changes occur in the ovarian parenchyma [3]. Each cycle begins with development of ovarian follicle to graafian follicle which then ruptures under the influence of luteinizing hormone, paving way for corpus luteum formation. The whole process involved in corpus luteum formation is termed luteogenesis. However, in the absence of fertilization, corpus luteum undergoes luteolysis, a process where luteal cells regress and involute into corpus albican [3].

Over the years, attempt to evaluate estrous cycle using relativity of luteogenesis and luteolysis have been largely unsuccessful [4,5]. For example, estrous frequency and regularity, estrous cycle length, estrous phase interval and diestrus index do not provide detailed information about relative durations of folliculogenesis, luteogenesis and luteolysis. The present study demonstrated the relevance of estrous cycle ratio as a predictor of luteogenesis and luteolysis intervals.

Our ECR analysis shows an average value of 0.81 with a nadir of 0.5 and a zenith of 1.5. Increase or decrease in ECR indicates acyclicity. For example, during pregnancy, the presence of hormonal support in form of chorionic gonadotropin facilitates the persistence of luteal cells and delays regression of corpus luteum. High level of progesterone secreted by luteal cells result in feedback inhibition of follicle stimulating hormone, culminating in delay in the initiation of new folliculogenesis. Therefore, as luteal cells persist, a decrease in estrous cycle ratio occurs.

Increase in estrous cycle ratio may signify prolongation of follicular phase length and delay in ovulation. For example, in anovulatory cycle, folliculogenesis occur without substantive luteinization. This results in prolongation of luteogenesis. In many experimental models of anovulatory cycles, a decrease in LH secretion brings about a delay in ovulation and phase transition. In many experimental models of anovulatory cycles, in addition to inadequate luteinization, decrease in expression of kissipeptin has also been documented [6].

While the famous estrous phase interval looks at the average duration of each estrous phase, estrous cycle length examines the average number of days it takes to complete a cycle and diestrus index examines the relation of diestrus phase to other phases [7-15]. However, estrous cycle ratio is a better predictor of the cyclical phenomenon which takes place in ovarian parenchyma during puberty [16-23].

In conclusion, the study has demonstrated the relevance of estrous cycle ratio as a reproductive index in murine studies.

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