METHODS OF ARTIFICIAL FEEDING OF RAT PUPS: BASIC MODELS

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Abstract. *The neonatal period is considered one of the most critical stages of organismal development, during which the type of nutrition significantly influences the morphological and functional maturation of the digestive system. In particular, the structural development of the small intestine, differentiation of enterocytes, enzymatic activity, and formation of local immune defense mechanisms are closely associated with feeding patterns. Breast milk contains biologically active substances, immunoglobulins, and growth factors that create physiologically optimal conditions for neonatal development. In contrast, artificial feeding may lead to various morphological and functional alterations in the intestine due to the absence or insufficiency of these natural components.*

This article presents an analysis of the main experimental models of artificial feeding in neonatal rats, their methodological characteristics, and their effects on intestinal development. The reviewed studies included the "pup-in-a-cup" artificial rearing system, gastric tube feeding methods, and the use of milk substitute formulas such as RMS-2A and RMS-2B. Artificial feeding conditions were associated with significant changes in villus length, crypt depth, enterocyte ultrastructure, and disaccharidase enzyme activity in neonatal rats.

According to the literature, high intestinal lactase activity in suckling rats is maintained during the first two weeks after birth. In artificially reared animals, a decrease in jejunal and ileal lactase activity was observed, whereas sucrase activity increased prematurely. Furthermore, artificial feeding was characterized by prolonged persistence of immature enterocyte features, including supranuclear vacuoles, apical tubular systems, and pinocytotic vesicles. Morphometric analyses also demonstrated increased crypt depth and remodeling of the intestinal mucosa.

In artificial rearing systems, the infusion rate and duration of milk formula administration were adjusted individually to approximate physiological feeding conditions. Studies demonstrated that neonatal rats fed with RMS-2A and RMS-2B formulas showed growth rates comparable to naturally suckled animals. In addition, maintenance of sterility, cooled feeding systems, and pathogen-free housing conditions were considered essential factors for preventing infectious complications and edema syndrome.

Thus, experimental models of artificial feeding in neonatal rats represent effective platforms for investigating intestinal development, enzymatic maturation, and morphofunctional alterations. These models have important scientific value for fundamental and applied research in neonatology, gastroenterology, and experimental morphology.

Keywords: *neonatal rats, artificial feeding, pup-in-a-cup, small intestine, morphology, lactase, enterocyte, experimental model.*

МЕТОДЫ ИСКУССТВЕННОГО ВСКАРМЛИВАНИЯ КРЫСЯТ: ОСНОВНЫЕ МОДЕЛИ

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Аннотация. *Неонатальный период считается одним из наиболее важных этапов развития организма, в течение которого тип питания существенно влияет на морфологическое и функциональное созревание пищеварительной системы. В частности, структурное развитие тонкой кишки, дифференциация энтероцитов, ферментативная активность и формирование местных механизмов иммунной защиты тесно связаны с режимом питания. Грудное молоко содержит биологически активные вещества, иммуноглобулины и факторы роста, которые создают физиологически оптимальные условия для развития новорожденного. Напротив, искусственное вскармливание может привести к различным морфологическим и функциональным изменениям в кишечнике из-за отсутствия или недостаточности этих природных компонентов.*

В данной статье представлен анализ основных экспериментальных моделей искусственного вскармливания у новорожденных крыс, их методологических характеристик и влияния на развитие кишечника. Рассмотренные исследования включали систему искусственного вскармливания «щенок в чашке», методы зондового питания и использование заменителей молока, таких как RMS-2A и RMS-2B. Искусственное вскармливание было связано со значительными изменениями длины ворсинок, глубины крипт, ультраструктуры энтероцитов и активности дисахаридазных ферментов у новорожденных крыс.

Согласно литературным данным, высокая активность кишечной лактазы у крысят сохраняется в течение первых двух недель после рождения. У животных, выращенных искусственным путем,

наблюдалось снижение активности лактазы в тощей и подвздошной кишке, в то время как активность сахаразы преждевременно возрастала. Кроме того, искусственное вскармливание характеризовалось длительным сохранением признаков незрелых энтероцитов, включая супрануклеарные вакуоли, апикальные канальцевые системы и пиноцитозные везикулы. Морфометрический анализ также продемонстрировал увеличение глубины крипт и ремоделирование слизистой оболочки кишечника.

В системах искусственного вскармливания скорость инфузии и продолжительность введения молочной смеси регулировались индивидуально для приближения к физиологическим условиям кормления. Исследования показали, что у новорожденных крыс, получавших смеси RMS-2A и RMS-2B, темпы роста были сопоставимы с темпами роста животных, находящихся на естественном вскармливании. Кроме того, поддержание стерильности, системы охлаждения для кормления и условия содержания, свободные от патогенов, рассматривались как важные факторы предотвращения инфекционных осложнений и отечного синдрома.

Таким образом, экспериментальные модели искусственного вскармливания у новорожденных крыс представляют собой эффективные платформы для исследования развития кишечника, ферментативного созревания и морфофункциональных изменений. Эти модели имеют важное научное значение для фундаментальных и прикладных исследований в неонатологии, гастроэнтерологии и экспериментальной морфологии.

Ключевые слова: *новорожденные крысы, искусственное вскармливание, щенок в чашке, тонкий кишечник, морфология, лактаза, энтероцит, экспериментальная модель.*

KALAMUSH BOLALARINI SUN'IY OZIQLANTIRISH USULLARI: ASOSIY MODELLARI

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Annotatsiya. *Yangi tug'ilgan chaqaloqlar davri organizm rivojlanishining eng muhim bosqichlaridan biri hisoblanadi, bu davrda ovqatlanish turi ovqat hazm qilish tizimining morfologik va funktsional yetukligiga sezilarli darajada ta'sir qiladi. Xususan, ingichka ichakning strukturaviy rivojlanishi, enterotsitlarning differentsiatsiyasi, fermentativ faollik va mahalliy immunitet himoya mexanizmlarining shakllanishi ovqatlanish shakllari bilan chambarchas bog'liq. Ona sutida biologik faol moddalar, immunoglobulinlar va yangi tug'ilgan chaqaloqlarning rivojlanishi uchun fiziologik jihatdan optimal sharoitlarni yaratadigan o'sish omillari mavjud. Aksincha, sun'iy oziqlantirish ushbu tabiiy komponentlarning yo'qligi yoki yetishmasligi tufayli ichakda turli morfologik va funktsional o'zgarishlarga olib kelishi mumkin.*

Ushbu maqolada yangi tug'ilgan kalamushlarda sun'iy oziqlantirishning asosiy eksperimental modellari, ularning metodologik xususiyatlari va ichak rivojlanishiga ta'siri tahlili keltirilgan. Ko'rib chiqilgan tadqiqotlar "kubokdagi kuchukcha" sun'iy o'stirish tizimi, oshqozon naychasi bilan oziqlantirish usullari va RMS-2A va RMS-2B kabi sut o'rnini bosuvchi formulalardan foydalanishni o'z ichiga olgan. Sun'iy oziqlantirish sharoitlari yangi tug'ilgan kalamushlarda villus uzunligi, kript chuqurligi, enterotsit ultrastrukturasi va disaxaridaza fermenti faolligida sezilarli o'zgarishlar bilan bog'liq edi.

Adabiyotlarga ko'ra, emizikli kalamushlarda yuqori ichak laktaza faolligi tug'ilgandan keyingi dastlabki ikki hafta davomida saqlanib qoladi. Sun'iy ravishda boqilgan hayvonlarda jejunal va ileal laktaza faolligining pasayishi kuzatilgan, saxaroza faolligi esa muddatidan oldin oshgan. Bundan tashqari, sun'iy oziqlantirish yetilmagan enterotsit xususiyatlarining, jumladan, supranuklear vakuolalar, apikal naycha tizimlari va pinotsitotik vesikulalarning uzoq vaqt saqlanib qolishi bilan tavsiflangan. Morfometrik tahlillar shuningdek, kript chuqurligining oshganligini va ichak shilliq qavatining qayta tuzilishini ko'rsatdi.

Sun'iy boqish tizimlarida sut aralashmasini yuborish tezligi va davomiyligi taxminiy fiziologik oziqlantirish sharoitlariga individual ravishda sozlangan. Tadqiqotlar shuni ko'rsatdiki, RMS-2A va RMS-2B formulalari bilan oziqlangan yangi tug'ilgan kalamushlar tabiiy ravishda emizikli hayvonlarga o'xshash o'sish sur'atlarini ko'rsatdi. Bundan tashqari, sterillikni saqlash, sovutilgan oziqlantirish tizimlari va patogensiz yashash sharoitlari yuqumli asoratlar va shish sindromining oldini olish uchun muhim omillar deb hisoblangan.

Shunday qilib, yangi tug'ilgan kalamushlarda sun'iy oziqlantirishning eksperimental modellari ichak rivojlanishi, fermentativ yetilish va morfofunktsional o'zgarishlarni o'rganish uchun samarali platformalarni ifodalaydi. Ushbu modellar neonatologiya, gastroenterologiya va eksperimental morfologiyada fundamental va amaliy tadqiqotlar uchun muhim ilmiy qiymatga ega.

Kalit so'zlar: *yangi tug'ilgan kalamushlar, sun'iy oziqlantirish, chashka ichidagi kuchukcha, ingichka ichak, morfologiya, laktaza, enterotsit, eksperimental model.*

Introduction. The neonatal period is one of the most rapid stages of development of the organism, and it is during this period that the type of nutrition has a significant impact on the structural and functional maturation of the digestive system, in particular the small intestine. Biologically active substances, immunoglobulins and various growth factors contained in breast milk ensure the normal development of the intestinal epithelium and support the maturation process of enterocytes. Artificial feeding, due to the lack of these natural components, can cause the development of morphological and functional changes in the intestinal mucosa [1].

The neonatal rat artificial feeding model is currently one of the widely used methods in neonatology, gastroenterology and experimental morphology. This model is used to study the differentiation of enterocytes, the activity of disaccharidase enzymes, the formation of intestinal microbiota and local immune defense mechanisms. Therefore, the improvement of experimental models of artificial feeding and the assessment of their morphofunctional effects are of urgent scientific importance [1,2].

According to the literature, intestinal lactase activity in suckling rats remains high for the first two weeks after birth. When 12-day-old rats were fed natural rat milk or various artificial mixtures, it was found that by day 16, the small intestine weight was almost the same in all groups, except for animals fed a chemically modified formula [1]. Also, although the length of the villi was similar in the naturally and artificially fed groups, a significant increase in the depth of the crypts was observed in the artificially fed rats [1]. Morphological studies revealed that the ileal enterocytes retained the characteristics of immature cells - supranuclear vacuoles, apical tubular systems and pinocytotic vesicles [1]. While artificially fed groups fed natural rat milk had high jejunal lactase activity, a significant decrease in lactase activity was noted in groups fed glucose or lactose-based artificial formulas [1]. All artificially fed groups showed a premature increase in sucrase enzyme activity [1].

In artificial feeding systems, the infusion rate of milk replacer formulas was adjusted to approximate the growth rates of rat pups to those of naturally breastfed rats [2]. The studies used RMS-2A and RMS-2B formulas, and feeding was carried out by pump at regular intervals. Rat pups fed RMS-2A were fed for 10 minutes every hour, while animals receiving RMS-2B were fed for 10 minutes/hour for up to 13 days and then for 20 minutes/hour [2]. This approach allowed to bring the feeding volume closer to physiological norms and reduce metabolic stress.

15-minute/hour and continuous feeding regimes have also been reported in the literature [10,11]. Studies on the volume of milk consumed by neonatal rats of different ages have shown that approximately 3.0–3.8 ml of milk is consumed at 4–5 days of age and 6.8 ml at 9–11 days of age [12,13].

A number of preventive measures have been used by researchers to prevent edema syndrome and infectious complications in artificial feeding systems [14,15]. In particular, it has been recommended to store syringes filled with milk in refrigerated conditions, use pregnant rats raised in a pathogen-free environment, and keep experimental animals separate from other colonies [6–10]. In addition, it has been noted that using only healthy and active neonatal rats for experiments increases the reliability of experimental results [2].

Materials and methods. This article is a review of the scientific literature. For the study, experimental articles on artificial feeding of neonatal rats, scientific sources from PubMed, ScienceDirect and Springer databases were studied.

During the analysis, attention was paid to the following criteria:

- artificial feeding method;
- composition of milk formula;
- feeding frequency;
- enteral feeding technique;
- morphological changes in the intestine.

The main experimental models were:

1. Pipette feeding model;
2. Gastric tube feeding model;
3. Automated enteral infusion model;
4. Milk replacer formula feeding model.

Results. The literature analysis showed that several main methods are used in artificial feeding of neonatal rats.

1. Pipette feeding model

This method is one of the simplest models, in which newborn rats are given formula milk through a special pipette. Although the method is technically convenient, it is difficult to precisely control the amount of food.

Advantages:

- inexpensive and simple;
- does not require special equipment.

Disadvantages:

- there is a risk of aspiration;
- it is difficult to standardize the dose of food.

2. Gastric tube feeding model

This model is most often used in neonatal gastroenterological studies. Milk is delivered to the stomach using a polyethylene catheter.

Advantages:

- precise control of the amount of food;

• compatibility with long-term experiments.

Disadvantages:

• possibility of mechanical damage;

• may increase stress responses.

Patel et al. recommended this model as a standard method for neonatal feeding studies.

3. Automated enteral infusion model

In this model, milk is continuously administered through a special infusion pump. The method gives results close to physiological nutrition.

Advantages:

• brings the feeding rhythm closer to the physiological state;

• reduces metabolic stress.

Disadvantages:

• requires expensive equipment;

• high technical complexity.

4. Milk replacer formulas

The following formulas are widely used in experimental studies:

• Esbilac puppy milk replacer;

• Rodent milk substitute;

• Goat milk-based formulas;

• Modified formulas based on Cabrita.

Studies have shown that artificial formulas have a weaker effect on enterocyte proliferation and villus development than breast milk.

Discussion. The neonatal rat artificial feeding model is an important experimental platform for studying the development of the digestive system. According to studies by Yeh and Holt, artificial formulas lead to a decrease in the activity of the lactase enzyme, which affects the functional maturation of the intestine.

Studies by Berseth have shown that breast milk stimulates enterocyte proliferation and better development of villi. It has also been found that the automated enteral feeding model gives results that are closer to the physiological development of the intestine.

The main limitation of artificial feeding models is that they do not completely replicate the bioactive components contained in natural breast milk. Therefore, it is important to develop formulas enriched with biologically active additives in future studies.

Conclusion. There are several experimental models of artificial feeding of neonatal rats, which are widely used in the study of intestinal development. The gastric tube and automated enteral infusion models are considered the most effective methods. Artificial feeding has a significant effect on intestinal morphology and enzymatic activity. These models are of great scientific importance for studies of neonatal gastroenterology and experimental morphology.

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