ACTA SCIENTIFIC CLINICAL CASE REPORTS

Volume 6 Issue 7 July 2025

Mini Review

Case Studies in Dohad Paradigm: Organs and Systems Probably Involved

Viktor I Goudochnikov*

Member of LA-DOHaD and ISOAD, PhD in Biochemistry, Santa Maria – RS, Brazil

***Corresponding Author:** Viktor I Goudochnikov, Member of LA-DOHaD and ISOAD, PhD in Biochemistry, Santa Maria – RS, Brazil.

Received: April 29, 2025

Published: June 16, 2025

Abstract

A mini-review is presented on the role of glucocorticoids (GC) and stress in programming/imprinting phenomena, as referred to DOHaD concept in various organs and systems. The conclustion is made about the necessity for elaboration of medico-biographical method, in order to reunite subsequently individual case reports on the basis of the onto- and phylopathogenic models.

Keywords: Case Reports; Glucocorticoids; Ontogeny; Stress

Abbreviations

GC: Glucocorticoids; ISOAD: International Society on Aging and Disease; LA-DOHaD: Latin-American chapter of International Society for Developmental Origins of Health and Disease; PhD: Philosophy Doctor.

Introduction

It is well known that clinical assays are much more difficult to organize and perform in special groups of patients including pregnant women, children and elderly persons. The main reason of such situation is bioethical barrier that greatly diminishes the possibilities of invasive procedures in such special groups of patients. In numerous projects the only solution is to use experimental models on laboratory animals, but here again another problem emerges, that of interspecies differences.

Therefore, in many areas of medicine the case studies and reports are especially important for these vulnerable groups of patients. Earlier we have devoted much of our research attention to the area of DOHaD – developmental origins of health and disease [1,2]. In fact, we tried to assess where this paradigm may be more useful, considering that medicine subdiscplines are separated according to anatomical organs and systems: cardiovascular, respiratory, gastro-intestinal, etc. That's why the aim of this mini-review will be to re-evaluate the current state of DOHaD concept, as referred to pathogenic mechanisms in different organs and systems.

The main focus is on glucocorticoids (GC), principal stress hormones and used also mainly as anti-inflammatory and immunosupressive agentes. We shall cite preferably our own articles published in open access journals and mirrored on ResearchGate and Academia websites, where interested readers can easily find the references to original publications of many other authors.

Some historical aspects of dohad concept

The grreat impulse to this area was given at the end of eighties of the last century when English epidemiologist David J.P. Barker and his colleagues from Southampton University began to study the long-term consequences of intrauterine growth restriction revealed by lower birthweight.

Today, approximately 35 years later we are able to discuss, which organs and systems are probably involved in pathogenic mechanisms of programming/imprinting and embedding phenomena, when adverse events in prenatal and early postnatal ontogeny may provoke these long-term consequences. It is important that at pre-

sent GC (both endo- and exogenous) are considered as principal candidates for the role of mediators in the phenomena mentioned above [3].

Cardiovascular disorders

In accord to general conclusions of David Barker and many other researchers, systemic arterial hypertension, some other cardiovascular diseases and diabetes mellitus type 2 are the main consequences of programming/imprinting phenomena. And it appears that in perinatal period GC may result in premature inhibition of body and organ growth as one of the main pathogenic mechanisms.

Earlier we have shown much higher sensitivity of neonatal rats to growth-inhibitory influence of GC, as compared to prepubertal animals [4]. Moreover, we demonstrated also that in younger rats inhibitory effects of GC on target organs of immune and endocrine systems were more evident, in comparison with older animals [5]. Finally, in primary pituitary cultures the inhibitory action of GC on DNA and total protein synthesis (i.e. the parameters strongly related to cellular growth and proliferation) was much more expressive in cells of neonatal rats, as compared to prepubertal and adult animals [6]. Therefore, it is not surprising that in many articles related to DOHaD paradigm the programming/imprinting phenomenaare explained via GC-induced premature inhibition of growth in perinatal period.

Since systemic arterial hypertension is considered at present as principal risk factor for other cardiovascular disorders, we have focused our attention on this pathologic entity. And in fact, several authors suggest that inhibition of kidney growth in perinatal period may provoke oligonephrony, with subsequente increase in blood pressure and overload of glomerular filtration, together with more rapid progression to renal insufficiency in later ontogeny [7].

What for the heart, it appears that perinatal growth inhibition results in higher risk of subsequent cardiac hypertrophy that finally may increase the risk of heart insufficiency. In parallel, the decrease in angiogenesis may provoke the disbalance of higher myocardial mass with insufficient supply of hemoperfusion via coronary vessels. Finally, the decrease in elastin content in aorta and other great arteries and its substitution by collagen fibers appear to provoke higher tendency to systemic arterial hypertension also [7].

Disorders in other organs and systems

Higher risk of diabetes mellitus type 2 may be explained by inhibition of growth in endocrine part of the pancreas in perinatal period, with subsequent overload of insulin-producing islet cells during later ontogeny [8]. On the other hand, growth inhibition in perinatal lungs may result in larger alveolar size and therefore in lower efficiency of air-blood exchange, because of lower surface area for it in subsequent ontogeny [9].

Since GC are strategically located on the crossroads of principal bioregulatory systems: nervous, endocrine and immune [10], their influence on these three systems is especially important. Earlier we have shown that neonatal GC treatment in rats results in thymus atrophy that persists, at least till prepubertal period [11]. On the other hand, the decrease in head circumference in human infants may indicate inhibitory action of perinatal GC on brain growth [12]. Finally, it is well known already that prenatal GC impact may result in postnatal hyperactivity of hypothalamo-pituitary-adrenal axis, probably because of the altered setpoint in its neuroendocrine regulation, especially in paraventricular nucleus and hippocampus [3].

Limitations of current theoretical models

Of course, GC-induced growth inhibition in perinatal period is not a unique mechanism of programming/imprinting phenomena. For example, in some papers it is repeatedly outlined that in principle, these phenomena may occur without significant decrease in birthweight. Moreover, the long-term consequences of these phenomena appear to be much more expressed when there occurs compensatory catch-up growth in early postnatal ontogeny.

Even molecular mechanisms of GC-induced growth inhibition are not clearly understood till the present time [13], beginning from their effects on stem and progenitor cells [14] and continuing to cellular flows or tissue streaming even in rather well characterized organs like the liver [8].

Especially subestimated may be considered the gastro-intestinal area of DOHaD concept. In many aspects this area is widely open for future research. And this is particularly important, if to remember the essential role of intestinal microbiome and bacterial endotoxins in programming/imprinting phenomena, another area in rapid expansion during the last years [15]. The role of GC and stress in programming/imprinting phenomena, as referred to musculo-skeletal and reproductive systems, as well as skin is also not clear yet.

Final Remarks

In conclusion, case reports must be channeled to studies on several organs including heart, kindeys and lungs, as well as to principal bioregulatory systems: nervous, endocrine and immune. The main challenge is to follow long-term consequences of perinatal events along postnatal development till adult state and continuing through intermediate age categories even to senescence. In order to realize this great endeavor, we propose to begin the elaboration of medico-biographical method that will necessitate also parallel increase in the power of information technologies.

Bibliography

1. Goudochnikov VI. "Translational and some other aspects of DOHaD concept: A polemic overview related to endocrinology and public health". *Endocrinology and Metabolism International Journal* 11 (2023): 4-7.

2. Goudochnikov VI. "The necessity of regional DOHaD centers based on programming/imprinting and embedding-like phenomena". *Advances in Health and Behavior* 2 (2019): 30-33.

3. Goudochnikov VI. "Central positions of glucocorticoids and stress in the phenomena of hormonal and metabolic programming / imprinting". *Journal of Endocrinological Science* 5 (2023): 1-7.

4. Goudochnikov VI. "[Pathogeny of glucocorticoid-induced growth retardation evaluated in experimental studies using laboratory animals and cell cultures as the models]". *NewsLab (São Paulo)* 22 (1997): 90-100 (in Portuguese).

5. Pettenon R., *et al*. "[Comparison of glucocorticoid effects on target organs in rats of different ages]". *Revista Contexto and Saude (Ijui)* 2 (2002): 105-113.

6. Gudoshnikov VI and Fedotov VP. "The hightened sensitivity of hypophyseal cells of neonatal rats to corticosteroids]". *Neuroscience and Behavioral Physiology (New York)* 23 (1993): 107-111.

7. Goudochnikov VI., *et al*. "The role of stress and its hormonal mediators in the ontopathogeny of cardiovascular disorders". *MedPress Cardiology and Vascular Medicine* 2 (2022): Article 04001.

8. Goudochnikov VI. "Hormonal programming / imprinting phenomena as related to the liver and pancreas". *Journal of Endocrinology and Thyroid Research* 7 (2023): Article 555707.

9. Goudochnikov VI. "The role of various factors in the ontopathogeny of respiratory disorders: Focusing on glucocorticoids". *EC Pulmonology and Respiratory Medicine* 8 (2019): 618-620.

10. Goudochnikov VI. "The contribution of stress and its mediators to the ontopathogeny of infections: A focus on the interactions of cytokines and glucocorticoids". *Advances in Gerontology (St. Petersburg)* 7 (2017): 25-28.

11. Dalmora SL., *et al*. "Prepubertal lymphocytopenia and thymus suppression accompany growth inhibition induced by neonatal glucocorticoid treatment". *Revista Argentina de Endocrinologia y Metabolismo* 31 (1994): 36.

12. Goudochnikov VI. "The role of stress and glucocorticoids in pathogeny of age-related neuropsychiatric disorders". *Journal of Geriatric Medicine and Gerontology* 4 (2018): Article 054.

13. Goudochnikov VI. "Glucocorticoid-induced growth inhibition: An update". *Open Access Journal of Endocrinology* 6 (2022): Article 000165.

14. Goudochnikov VI. "Broadening endocrinology as related to progenitor and stem cells: Some historical aspects". *Advances in Endocrinology and Hormone Research* 1 (2024): 1-9.

15. Goudochnikov VI. "[Phenomena of programming / imprinting in neuroimmunology: The role of endotoxins and microbiome in deevelopment and aging]". In: Proceedings of MOIP: Collection of Articles from the Gerontology Section. Toronto: Longevity Books (2025): 86-90.