

Effects of glucocorticoids on various organs and tissues: Focus on age-related differences

Abstract

Experimental data are described, showing that glucocorticoid-induced growth retardation may have quite complex mechanisms in various organs and tissues, with age-dependent differences of these mechanisms. It is expected that these data may contribute to clarification of the role of glucocorticoids as mediators of programming / imprinting and embedding phenomena in DOHaD paradigm.

Keywords: glucocorticoids, growth, ontogeny, organs and tissues

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Viktor I. Goudochnikov

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

Correspondence: Viktor I. Goudochnikov, member of LA-DOHaD / ISOAD, PhD in Biochemistry, Rua Tiradentes, 55, Apto.101, CEP 97050-730, Santa Maria – RS, Brazil, Tel +5555991310805

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Abbreviations: GC, glucocorticoids; hCG, human chorionic gonadotropin; 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

Today glucocorticoids (GC) are widely used in medicine, principally as anti-inflammatory and immunosuppressive drugs,¹ although they possess several adverse effects including somatic growth retardation in pediatric patients.² However, it is not clear yet, how these potent hormonal agents affect various tissues and organs in the developing human body. In order to approach better the understanding of this important issue, experimental models using laboratory animals and cells cultures are repeatedly employed. Here we describe our personal experience in this respect during approximately the last 35 years.

Experiments on cell cultures in vitro

We began our studies, comparing GC effects on hepatocytes in primary cultures obtained from fetal and prepubertal rats. It was shown that GC stimulated serum albumin production, as well as the biosynthesis of total RNA and proteins, without notable differences related to the age of the animals.^{3,4}

We also investigated GC influence on primary pituitary cell cultures obtained from neonatal, prepubertal and adult rats. It was demonstrated that GC stimulated growth hormone secretion, but inhibited DNA and total protein biosynthesis much more in cultured pituitary cells of neonatal rats, as compared with prepubertal and adult animals.^{5,6}

Later on we have performed several studies on cultured cell lines. In particular, it was shown that GC decreased cell proliferation, according to the number of mitotic events in cultures of MDBK (an adult bovine-derived kidney cell line) cells, as well as Monomac-6 (a human monocyte-derived cell line) cell number.⁷

Experiments with laboratory animals in vivo

At first, we demonstrated that administration of dexamethasone to neonatal rats resulted in irreversible (or only partially reversible) body growth retardation, in contrast to their action on prepubertal animals.⁸

Thus we have reproduced with GC the age-related difference of malnutrition-induced growth retardation shown already in the sixties of the last century by British researchers E.M. Widdowson and R.A. McCance.⁹

In addition, neonatal dexamethasone resulted in proportional inhibition of growth of several internal organs: lungs, liver and kidneys, whereas for heart the result was different, suggesting some tendency for its hypertrophy.¹⁰

Several experiments were performed on prepubertal rats treated with gonadotropin (hCG) or sex steroid hormones, in order to stimulate the growth of the organs of reproductive system: uterus, prostate and seminal vesicles. It was shown that GC inhibited their growth to a lesser degree than body growth.¹¹

Finally, we studied GC effects on the organs of immune and endocrine systems in rats of different age groups. It was demonstrated that GC inhibited the growth of thymus, spleen, adrenals and pituitary gland somewhat more efficiently in younger animals.¹² Moreover, this GC action appeared to be related to a decrease in the state of organ hydration.¹³

General discussion

Although we have already investigated several aspects of GC influence on body and organ growth in age-related mode, a lot of lacunae remain in our understanding of this important topic. Perhaps, the main problem is the lack of knowledge about the mechanisms of hormonal regulation of tissue and organ growth.²

In fact, biochemical procedures don't allow us to differentiate properly hyperplasia and hypertrophy in growing tissues composed of several tissue types. Previously we tried to apply the conceptual modeling of tissue streaming for cytoarchitectonics in pituitary and adrenal glands. The next step would be the elaboration of more detailed schemes involving stem and progenitor cells, together with their niches.¹⁴

In conclusion, there remain significant gaps in understanding GC action at the molecular, cellular, tissue and whole organism level, and these mechanisms vary during the course of development of individuals in species. We propose that advanced techniques of molecular and cell biology, histology, morphometry, etc. should be applied in near

future, in order to understand more clearly the mechanisms of GC-induced growth inhibition in various organs and tissues. It is hoped that experimental data described here may contribute to clarification of the role of GC in the phenomena of programming / imprinting and embedding in DOHaD paradigm.¹⁵

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Conflict of interest

The autor declares that conflicts of interest do not exist.

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