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Commentary

Pharmacotherapy of Pulmonary and Other Disorders: The Importance of Age-Related Considerations Focusing on Corticosteroids

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Abstract

This short commentary aims at describing some problems of pharmacotherapy, especially with glucocorticoids (GC), in early and late human ontogeny, outlining the necessity of more intense cooperation between health professionals, in order to make more adequate the utilization of pharmacokinetic data in DOHaD paradigm.

Keywords: *Glucocorticoids; Ontogeny; Pharmacokinetics*

The onset of this story occured in the first decade of current century when the author of this commentary was a teacher of pharmacology at the University of Ijui (Unijui) in the South of Brazil. Short educational inquiry has clearly shown that general textbooks on pharmacology used for preparing lessons on several courses of health area had incomplete information specifically on pharmacokinetics [1]. Moreover, only students of pharmacy course had pharmacokinetics in their curriculum. It appears also that future physicians are also largely devoid of adequate knowledge of this discipline till the present time. As a matter of fact, true pharmacokinetics is rather complex discipline, full of data with advanced mathematics, therefore even simplified versions of lessons were not so easy for understanding by students of Pharmacy course.

Why this peculiarity is so important? At least some pulmonary disorders are age-related. Really, morbidity due to pneumonia is concentrated at the beginning and in the end of human life, whereas mortality from this disease is characteristic mainly for elderly patients [2]. Therefore, it is critically necessary to pay higher attention for age-related pharmacology and especially, to pharmacokinetics during neonatal and senescent phases of human ontogeny, since biochemical pathways of drug metabolism are not yet fully mature in neonates, whereas elderly patients may have subclinical renal problems that nevertheless can affect the capacity of drug metabolite elimination with urine.

However, for corticosteroids and principally, glucocorticoids (GC) used in various subfields of clinics including pulmonology and respiratory medicine, there exists one more peculiarity. Indeed, especially in the paradigm of developmental origins of health and disease (DOHaD) both endo- and exogenous GC are considered at present as strong candidates for the role of mediators of the phenomena of programming/imprinting and embedding [3,4] in conceptual models of phylo- and ontopathogeny [5]. Particularly problematic in this regard appears to be world-wide GC utillization for acceleration of lung maturation in perinatal period [6], since this process may be accompanied by certain disruption of alveolar formation in the lungs, with long-term consequences at least till adult state and perhaps even in senescence [7].

It is important to outline here that this problem may be more serious than was previously thought, because of the tendency of GC to provoke inadequate adaptation to pregnancy and even lactation in the offspring of pregnant women treated with synthetic corticosteroids, i.e. in at least the intergenerational mode [8].

Of course, nobody can imagine modern medicine without widespread use of GC as potent anti-inflammatory and immunosuppressive agents [9,10] and for the treament of COVID-19 [11]. However, we insist on the necessity of better understanding of GC efects, especially in preclinical studies on experimental models of laboratory animals and cell cultures. In fact, after more than 30 years of our participation in this research, we have recognized finally that GC capacity to act as mediators of programming/imprinting may be related to their inhibitory action on somatic and organ growth [12,13], especially in perinatal period, thus corroborating long-known data of Widdowson and McCance on similar action of malnutrition in early ontogeny [14].

On the other hand, embedding phenomena provoked by GC in cumulative mode, may occur not only in childhood and adolescence, but also later on, e.g. in premenopausal period, thus turning out the pregnancy in this late fertile period more problematic both for the mother and her offspring [15].

In conclusion, the use of pharmacotherapy, especially with GC in age-related mode should be accompanied by intense collaboration between several health professionals (and first of all, physician, nurse and pharmacist), in order to preclude adverse drug reactions in short- and particularly, long-term manner.

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