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Glucocorticoids, a general introduction

Although the name glucocorticoids (GCs) refers to a class of steroid hormones produced by the adrenal cortex, the name is commonly used to indicate synthetic analogues of these molecules such as prednisolone. The endogenous glucocorticoid cortisol, is part of many different processes in the body, ranging from glucose metabolism to memory consolidation. And indeed cortisol also affects immunological processes such as regulation of delayed type hypersensitivity[1] or modulating the Th1/Th2 balance[2]. However, clinically GCs are used for the general suppression of inflammation. At supraphysiological concentrations, GCs can inhibit various aspects of both the innate and adaptive immune response[3]. Hence they are used for the treatment of allergies, auto-immune diseases and other inflammatory conditions. In general their effect is swift and powerful, unparalleled by other immunosuppressants. Combined with molecular properties that allow for different routes of administration, unhindered passage through the body and the low cost of production, make GCs a very attractive drug. Unfortunately, a proportion of patients becomes refractory to treatment and over time require an increasing dose[4]. Additionally, effects of treatment are not limited to suppression of inflammation alone but coincide with a wide range of adverse effects. The incidence of adverse effects increases along with the dose and prolonged exposure[5]. This can develop into serious complications, resulting in discontinuation of the treatment or worse. And so, taken together, GCs are both bitter and sweet. Considering the limited repertoire of anti-inflammatory drugs to our disposal, GCs cannot simply be disposed of. Smarter and improved versions of this drug need to be developed. But so far this has not proven to be an easy task[6]. Their potency may be explained by evolutionary development as an integral part of the human body. But this is also their weakness since the underlying mechanisms that regulate immunosuppression do not

differ from those that cause adverse effects. Separating the two may not be possible and indeed, so far, no safe GC has been developed. It did, however, yield a myriad of information on how GCs work, changing insights and maybe one day, resulting in the development of a safe GC.

References

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