Hyposecretion of the adrenal androgen dehydroepiandrosterone sulfate and its relation to clinical variables in inflammatory arthritis

ABSTRACT

The presence of hypothalamic–pituitary–adrenal underactivity in rheumatoid arthritis (RA) has implications for the pathogenesis and treatment. Among the participants in this study, 54 were women. The study examined the secretion of adrenal androgen dehydroepiandrosterone sulfate (DHEAS) and its correlation with clinical variables in RA, Spa, and UCI. The number of patients who had taken glucocorticoids before was 12, with 14% having done so. Controls included both age-matched women (134) and men (149). Fasting blood samples were obtained to determine the ESR, serum DHEAS and insulin, and plasma glucose. Insulin resistance was estimated using the homeostasis-model assessment (HOMAIR). The DHEAS levels were found to be lower in women and men with inflammatory arthritis (IA) compared to controls (P 0.001) than in men and women (DHEARS). The control of previous glucocorticoid usage, current treatment with nonsteroidal anti-inflammatory drugs, duration of disease, and HOMAIR resulted in significant differences in DHEAS levels between patients and controls (P = 0.050) and men (p = 0.133). Our conclusion was that low levels of DHEAS are frequently observed in IA, and this may not be fully accounted for by disease parameters in women. The role of hypoadrenalism in the pathophysiology of IAA warrants further attention. DheA replacement may be recommended in many patients with II, even in those not taking glucocorticoids.

INTRODUCTION

Retinoic acid receptors (RAR-, -Aceast■ne, and Serrano) are transcription factors that regulate various endocrine metabolic pathways. In contrast, anti-estrogens like tamoxifen or raloxiferon have been shown to possess anticancer activity in both estrogen receptor positive and negative breast tumor cells, when ligands are targeted specifically for these RAR isoforms. Hence, such molecules could form a new class of drugs targeting breast cancer; because both agonists and antagonists of RAR can exhibit anti-tumor activity against breast or prostate cancer as well as lung cancer or leukemia respectively, the development of both types of ligands may have important biomedical applications. Our recent work has shown that antagonists can be discovered logically using a model of the antagonist-bound conformation of their receptors. We aim to identify novel molecular structures that have RAR agonist activity, as several retinoid and non-retinol ligands have been described, which activate one or fewer Rar isoforms simultaneously. Several compounds, including the all-trans retinoic acid (all-tran RA), have been clinically tested and exhibit unacceptable side effects, such as skin dryness, cheilitis, hypertriglyceridemia, and conjunctivitis (Fig. 1a). However, the compounds examined so far belong to a small series of related structures. With the increasing evidence, it seems likely that the RAR- isoform, which is under the transcriptional control of RARN-, suppresses cell growth and tumorigenicity, suggesting potential therapeutic properties. New molecules with both receptors on the epitope and an active RRNA antagonist may therefore present more favorable toxicity than pan-agonists. Using a flexible virtual screening algorithm (Molsoft ICM, virtual library screening module), we quickly docked hundreds of thousands of different flexible compound structures into the ligand binding pocket of RAR and identified two novel RER- selective agonists. The ligands that exhibit unique structural and chemical traits could be utilized to create novel compounds

for cancer prevention and treatment.

CONCLUSION

The relationship between water fluoride levels and the occurrence of Down's syndrome is not well-established. Nevertheless, the reviews provided are of low quality and additional high-quality research is required. Research on the connection between Down's syndrome and water fluoride levels should be further explored to determine how much water contains fluoridation and balance it with other confounding factors, such as maternal age, the frequency of termination of pregnancies in which the child is diagnosed with Down’s Syndrome, and exposure to alternative sources of fluoralide. The decision to select study areas at random and blind the fluoridation status of mothers should be made when identifying cases, and the denominator chosen to measure the risk of a Down's syndrome birth should relate to the total number of births rather than the population of the study area. The objective of case ascertainment should be as comprehensive as possible and consistent with all populations studies.