EFFECTS OF STREPTOZOTOCIN-DIABETES AND INSULIN REPLACEMENT ON ANDROGEN AND ESTROGEN RECEPTOR CONCENTRATIONS IN THE EPIDIDYMIS OF WISTAR RATS

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SUMMARY

The present study was aimed at evaluating the effects of streptozotocin (STZ)-induced diabetes and insulin replacement on the androgen (AR) and estrogen receptor (ER) concentrations in the caput, corpus and cauda epididymides of prepubertal and adult Wistar rats. Prepubertal (40 days old) and adult (120 days old) male Wistar rats were made diabetic by single *intraperitoneal* (*i.p.*) injection of STZ (120 mg/kg and 60 mg/kg body weight, respectively). To one set of diabetic rats, insulin was administered daily at a dose of 3 U/100 g body weight, subcutaneously, in two equally divided doses at 8.00 AM and 6.00 PM. All the rats were killed on the 21st day of commencement of experimentation. The epididymis was dissected out and caput, corpus and cauda segments were separated, freed from spermatozoa and processed for AR and ER quantification. STZ-induced diabetes caused a marked decrease in both nuclear and cytosolic AR and ER concentrations in the caput, corpus and cauda epididymides. Insulin replacement circumvented the adverse effects of diabetes in a segment-specific manner. These findings emphasize the detrimental effects of diabetes and the importance of insulin in the maintenance of epididymal AR and ER concentrations in immature as well as adult rats.

Key words: Androgen receptor, diabetes, epididymis, estrogen receptor, insulin.

INTRODUCTION

Diabetes has adverse effects on male sexual and reproductive functions in adolescent boys and men, which include impotency, reduced libido and sterility (1, 2). Clinical as well as experimental studies reveal impairment of spermatogenesis and decrease in sperm count, motility, volume of seminal fluid and serum testosterone in the diabetics (3-5). Since streptozotocin (STZ)-induced diabetic rats exhibit several deficiencies in reproductive function, which resemble those recorded in diabetic human beings, they form an appropriate model to study reproductive dysfunction under diabetic condition (2).

The structure and function of the epididymis are mainly under androgenic control, and presence of androgen receptor (AR) in the epididymis is well-documented (6-8). Estrogen is another hormone, which can modify the growth and function of accessory sex organs including the epididymis through estrogen receptors (ERs). Recent studies have revealed the localization of ER-alpha in the stroma and ER-beta in the epithelium (9). The present study was designed to assess the impact of STZ-diabetes and insulin replacement on the epididymal AR and ER.

MATERIALS AND METHODS

Pre-pubertal (40 days old) and adult (120 days old) male albino rats of Wistar strain were used. The rats were maintained in a temperature-controlled room with a 12:12 h light:dark schedule and provided with standard rat pellet feed (Lipton India Ltd., Bangalore, India) and water *ad libitum*.

Experimental design

Rats in each of the age groups were divided into three groups: Group-I control (treated with the vehicle *i.e.*, citrate buffer pH 4.5), group-II diabetic (induced by single *i.p.* injection of streptozotocin at a dose of 120 mg/kg body weight for prepubertal and 60 mg/kg body weight for adult rats) and group-III insulin-treated diabetic rats (3 U/100 g body weight administered subcutaneously, daily in two equally divided doses at 8.00 AM and 6.00 PM 3 days after STZ treatment, for 20 days). The rats were decapitated on the 21st day and the epididymes were dissected out, cleared of fat pads and divided into caput, corpus and cauda regions identified according to Hamilton (10).

Preparation of nuclear and cytosolic fractions and binding assay

AR and ER in both the nuclear and the cytosoilc fractions of caput, corpus and cauda epididymides were quantified adopting the method of Teutsch *et al.* (11). The values are expressed as fmol/mg protein.

Statistical analysis

The data were analyzed by one-way analysis of variance (ANOVA) followed by SNK test to assess the significance between the control and experimental groups.

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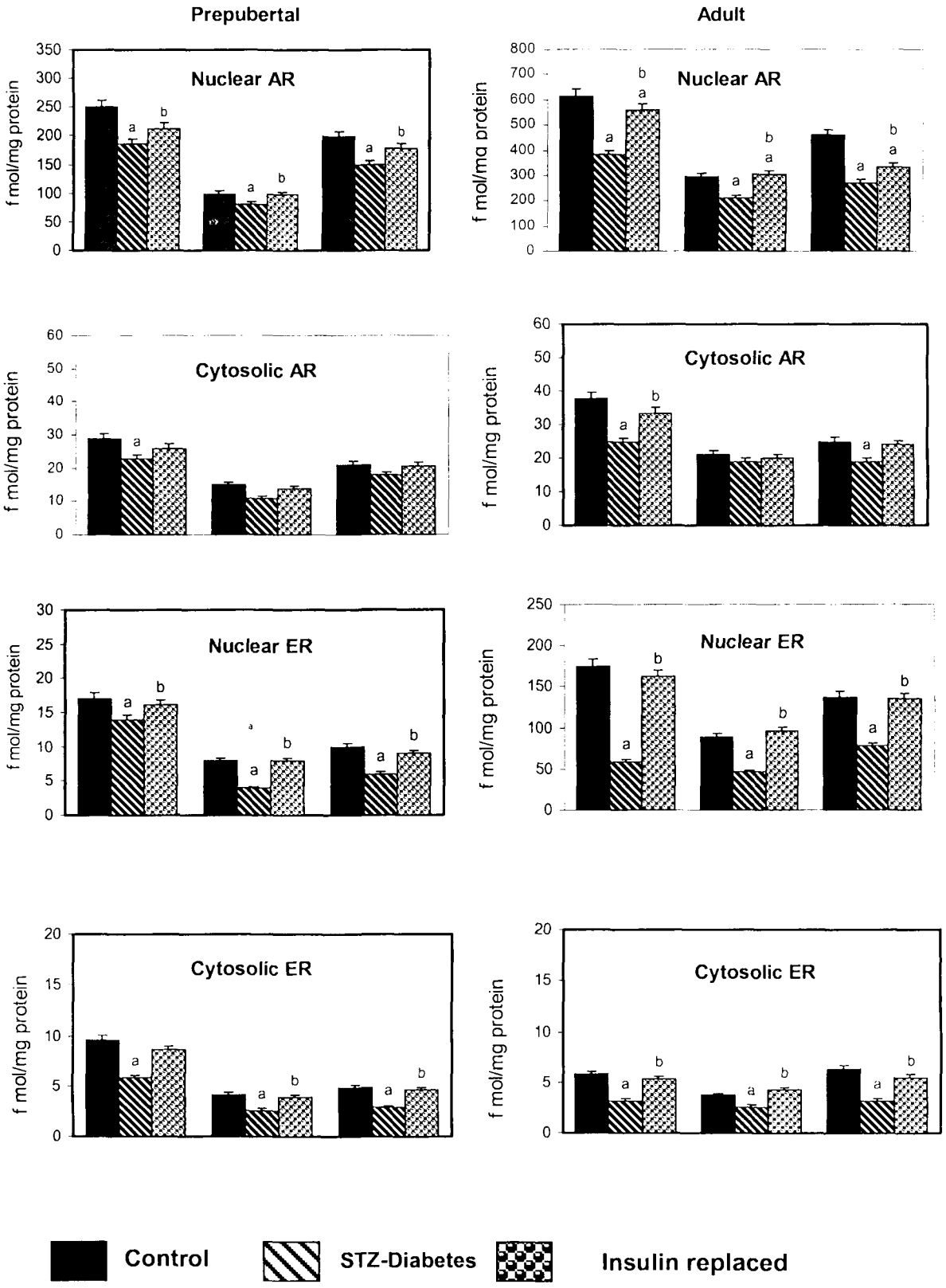

Fig 1. Effects of streptozotocin-diabetes and insulin replacement on the androgen and estrogen receptor concentrations in caput, corpus and cauda epididymides of prepubertal and adult rats. Each bar represents mean + SEM of 5 values. Significance at $p<0.05$. a - compared with control; b - compared with STZ diabetes

RESULTS

Induction of diabetes caused a marked reduction in the nuclear AR concentration in all the three epididymal segments of both prepubertal and adult rats. Insulin replacement circumvented this change only partially in the caput and cauda regions. The cytosolic AR concentration decreased only in the caput region of prepubertal rats and the caput and cauda regions of adult rats. On the other hand, ER concentration in both the nuclear and cytosolic fractions decreased in STZ-diabetic rats irrespective of the segment and the age group, whereas insulin replacement restored it to the control level (Fig-1).

DISCUSSION

AR and ER are known to be regulated in a homologous manner, *i.e.*, decrease in testosterone and dihydrotestosterone (DHT) tend to diminish AR concentration, whereas increase in testosterone and DHT upregulate the AR concentration in rat epididymis (12). AR concentration in the accessory sex organs is influenced, apart from androgen, by estradiol, growth hormone and prolactin (12). Studies from our laboratory have shown reduced titers of serum as well as intra-testicular testosterone and estradiol in STZ-diabetic rats (13). Even though AR and ER concentrations recorded a parallel decrease in the epididymal segments of STZ–diabetic rats, the magnitude of decrease varied in a segment-specific manner. It is, therefore, suggested that the diabetes-induced impairment of the availability of testosterone at epididymis and its conversion to DHT or estradiol may be responsible for the decrease in AR and ER concentration recorded in this study. It is concluded that diabetes has adverse effect on cytosolic and nuclear AR and ER of epididymis, and insulin replacement partially circumvents this adverse effect.

ACKNOWLEDGMENTS

The research grant to Dr. K. Balasubramanian [No. F.3-28/ 2001 (SR-II) dated March, 2001] from the University Grants Commission (UGC), New Delhi, the funds under SAP-DRS (Phase-II) to the Department of Endocrinology from UGC, and the support under the FIST Programme to the Department of Endocrinology from the Department of Science and Technology (DST), Government of India, New Delhi, are gratefully acknowledged.

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