PRENATAL EXPOSURE TO DEXAMETHASONE ALTERS THE CYTOKINE PROFILE: IMPLICATIONS FOR PEPTIC DISEASE

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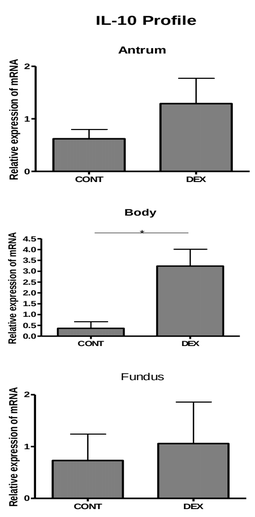
Introduction

Prenatal dexamethasone (DEX) exposure triggers several changes in nervous, autonomic and immune systems later in adulthood. As a result, we have shown that prenatal administration of DEX is associated with an increase vulnerability to peptic disease in adult life. In this study, we aim to clarify the impact of DEX-induced deregulation in the secretion of pro- (IL-1and IL-6) and anti-inflamatory (IL-10) cytokines, as well as COX-1 and COX-2 in the gastric mucosa.

Methods

Rat dams were exposed to the synthetic glucocorticoid dexamethasone (1mg/Kg) on days 18 and 19 of gestation. COX-1, COX-2 and cytokine (IL-1β, IL-6 and IL-10) expression was assessed, by quantitative RT-PCR, in different regions of the stomach mucosa (fundus, body and antrum) of adult rats exposed to DEX (n=5) and CONT (n=5) in the prenatal period.

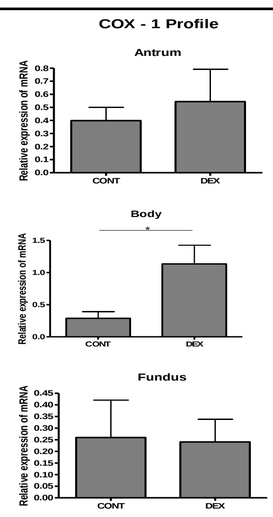
Results



Anti-inflamatory IL-10 Cytokine

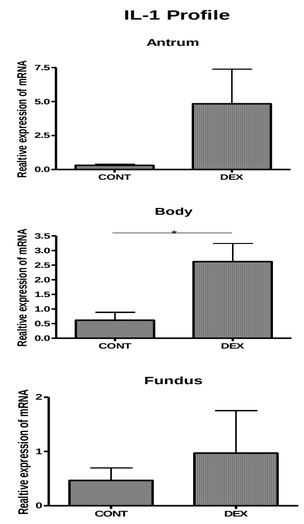
Anti-inflamatory cytokines play an important role in downregulation of inflammation and the prevention of neoplasic disorders. IL-10 are implicated in regulatory suppression of gastric inflammation.

In this study we observed a high significantly IL-10 expression in body of the stomach (p<0,05).



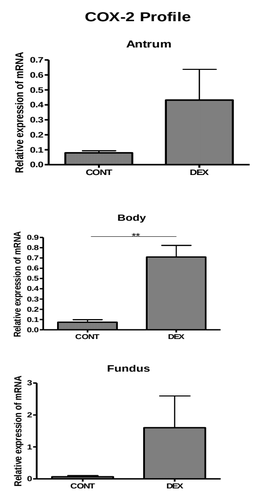
COX-1 (constitutive) isoform expression in Gastric Mucosa

COX-1 is constitutively expressed in the gastrointestinal tract in large quantities and has been suggested to maintain mucosal integrity through continous generation of prostaglandins. Our observations reveals a significantly alterations on COX -1 expression in DEX-treated rats (p<0,05) especially in body of gastric mucosa.



IL-1β profile in Gastric Mucosa

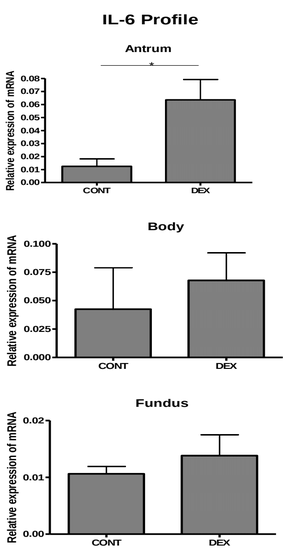
Relative expression of mRNA obtained by RT-PCR in the gastric mucosa of prenatal DEX-treated animals. IL-1 pro-inflamatory cytokine show a high significantly expression level in body region. P<0,05.



COX-2 (non-constitutive) isoform expression in Gastric Mucosa

Effect of DEX-treated animals on mRNA expression of COX-2 . Total RNA was extracted from gastric mucosa.

The results reveals that body gastric region is significantly sensitive (p<0,01) to COX-2 expression in DEX-treated animals. This may be implicated with pathophysiological reactions such inflammation.



Pro-inflamatory IL-6 Cytokine

Interleukin IL-6 mRNA changes significantly (p<0,05) in DEX animals in antrum region.

Interleukin-6 (IL-6) is proinflammatory cytokine that produces multifunctional effects. It is involved in the regulation of immune reactions, but it has also been shown to be associated with tumor progression including inhibition of cancer cells apoptosis.

Conclusion

These observations, which identify glucocorticoid-sensitive gastric regions (antrum and body) in female progeny, pave way for future studies designed to understand how early life events can predispose individuals for developing peptic disease in adult life, and may contribute for the study of future therapeutic approaches to this pathology.

References

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