Serum and Urinary Levels of Transforming Growth Factor Beta-1 in Children with Vesicoureteric Reflux

Thesis

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Abstract

Transforming growth factor beta-1 (TGF-β1) is a peptide of low molecular weight and has pleiotropic action. In the kidneys, it stimulates fibrogenesis through enhanced production of ECM proteins. The aim of this study is to measure the level of TGF-β1 in serum and urine of children with different grades of vesicoureteric reflux (VUR) and to assess its diagnostic significance in the diagnosis of VUR. It has been found that serum TGF-β1 level in children with VUR was significantly higher than that in control children. In addition, serum TGF-β1 level in children with grade IV-V VUR was significantly higher than that in children with grade III VUR, which in turn was significantly higher than that in children with grade II VUR. Thus, serum TGF-β1 level could be used in the diagnosis of the VUR. In addition, serum TGF-β1 level has also a prognostic value as it correlates well with the gradient of the VUR.

Key Words:
Transforming growth factor beta-1, Vesicoureteric reflux.

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List of Abbreviations

ACE	angiotensin-converting enzyme
BMI	Body mass index
CAKUT	congenital anomalies of the kidney and urinary tract
CBC	complete blood count
CIC	clean intermittent catheterization
CT	computed topography
DMSA	2,3-dimercaptosuccinic acid
DNA	deoxyribonucleic acid
E. coli	*Escherichia coli*
ECM	extracellular matrix
EGF	epidermal growth factor
ESRD	end-stage renal disease
FDA	Food and Drug Administration
G1	Gap 1
G2	Gap 2
HHT	hereditary hemorrhagic telangiectasia
HLA	human leucocyte antigen
IVP	intravenous pyelogram
mRNA	messenger ribonucleic acid
PDGF	platelet derived growth factor
RAS	renin angiotensin system
TGF	transforming growth factor
TGF-β	transforming growth factor-beta
TLC	Total leucocytic count
UPJ	ureteropelvic junction
UTI	urinary tract infection
VCUG	voiding cystourethrogram
VUR	vesicoureteral reflux

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INTRODUCTION

Vesicoureteric reflux (VUR), the retrograde flow of urine from the bladder toward the kidney, is common in young children. About 30% of children with urinary tract infections will be diagnosed with VUR after a voiding cystourethrogram. For most, VUR will resolve spontaneously; 20% to 30% will have further infections, but few will experience long-term renal sequelae ***(Williams et al., 2008)***.

High-grade VUR promotes intrarenal refluxes, recurrent urinary tract infections (UTI) and the development of renal nephropathy (RN) due to renal interstitial scar formation ***(Orellana et al., 2004)***.

The mechanism of scar formation is not fully elucidated. It implies excessive production and accumulation of proteins of the extracellular matrix (ECM). Infected urine reaching renal parenchyma causes local and systemic inflammatory reaction. This triggers immunological mechanisms that lead to increased expression of cytokines, adhesion molecules and growth factors, whose mutual interactions result in enhanced fibrogenesis and scar formation ***(Strutz and Neilson, 2003)***.

Transforming growth factor beta-1 (TGF β1) is a peptide of low molecular weight and has pleiotropic action. It stimulates the growth of cells of mesenchymal origin and inhibits proliferation of epithelial and hemopoietic cells. In the kidneys, it stimulates fibrogenesis through enhanced production of ECM proteins ***(Sales et al., 2006)***. Additionally, TGF β1 inhibits the synthesis of metalloproteinases (MMP) that degrade matrix proteins, and it stimulates the synthesis of tissue inhibitors of metalloproteinases (TIMP) ***(Zuk and Matlin, 2002)***.

Whether the determination of the urinary and serum levels of TGF β1 has a diagnostic significance in the diagnosis of VUR in children with UTI and whether theses levels correlate with VUR grade is still lacking prove and need further study ***(Sabasiñska et al., 2008)***.

AIM OF THE STUDY

The aim of this study is to measure the level of TGF β1 in serum and urine of children with different grades of vesicoureteric reflux and to assess the diagnostic significance of the level of TGF β1 in the diagnosis of VUR and whether theses levels correlate with VUR grade.