for a prolonged period of time. ETT biofilm could be a likely source of recurrent infection.

Nephrology

USING NONSTEROIDAL ANTIINFLAMMATORY DRUGS IN VOLUME-DEPLETED CHILDREN CAN PRECIPITATE ACUTE RENAL FAILURE

Submitted by John Cheri Mathews

Cheri Mathews John, Vivek Saroha, Caroline Jones

Royal Liverpool Children's Hospital, Liverpool, United Kingdom

INTRODUCTION: Nonsteroidal antiinflammatory drugs (NSAIDs) are ever increasing in popularity in hospital medicine and general practice and are readily available over-the-counter.

OBJECTIVE: Our goal was to illustrate the need to be aware of the effect of NSAIDs on dehydrated patients.

PATHOGENESIS: The risk of renal toxicity is increased in situations in which there is a stimulation of the renin-angiotensin system such as volume depletion. In these conditions, circulating vasoconstrictors are released, maintaining vascular resistance and blood pressure at the potential expense of regional organ blood flow. To maintain renal blood flow, counter-regulatory renal prostaglandins are released that counteract vasoconstrictors and normalize renal blood flow. NSAIDs blunt this counter-regulatory response and intensify the renal vasoconstriction, which leads to acute renal failure. In Table 1 we report 4 children with mild dehydration who developed acute renal failure after the use of therapeutic doses of NSAIDs in a children's hospital.

TABLE 1. Acute Renal Failure in 4 Children After Use of NSAIDs

	Patient No.			
	1	2	3	4
Age, y	13	7	14	13
Gender	Male	Male	Male	Female
Underlying pathology	Craniopharyngioma diabetes insipidus	Juvenile idiopathic arthritis; fasted for surgery	Juvenile idiopathic arthritis with vomiting	Relapse of Crohn disease
NSAID	Diclofenac sodium	Indomethacin diclofenac sodium	Diclofenac sodium	Diclofenac sodium
Highest urea level, mmol urea/L	10.7	12.9	10.7	22
Highest creatinine level, μmol/L	226	146	376	629
Normalization, d	5	3	3	Permanent impairment

CONCLUSIONS: We recommend that NSAIDs should be avoided in children with actual or potential intravascular volume depletion. Although we have not proven cause and effect, additional research is needed to define the true risk of the potential renal complications of using NSAIDs in patients who are at risk of dehydration.

NOTE: The cases of the 4 children described in this report have been published elsewhere (John CM, Shukla R, Jones CA. Using NSAID in volume depleted children can precipitate acute renal failure. *Arch Dis Child.* 2007;92:524–526).

ROLES OF SCAP (STEROL REGULATORY ELEMENT–BINDING PROTEIN CLEAVAGE-ACTIVATING PROTEIN) IN THE MECHANISM FOR MESANGIAL FOAM-CELL FORMATION UNDER INFLAMMATORY STRESS

Submitted by Qiu Li

Qiu Li[a], Xiong Zhong Ruan[b]

[a]*Division of Nephrology and Immunology, Affiliated Children's Hospital, Chongqing Medical University, Chongqing, China;* [b]*Centre for Nephrology, Royal Free and University College Medical School, Royal Free Campus, London, United Kingdom*

INTRODUCTION: Our previous studies have demonstrated that lipid abnormalities play a significant role in glomerulosclerosis. Inflammatory cytokines promote lipid accumulation in human mesangial cells (HMCLs) by disrupting low-density lipoprotein receptor (LDLr) feedback regulation. The sterol regulatory element–binding protein (SREBP) cleavage-activating protein (SCAP) carries SREBP from endoplasmic reticulum (ER) to Golgi, where it is known to cleave SREBP, thereby enhancing LDLr gene expression and cholesterol uptake when cells need cholesterol.

OBJECTIVE: We aimed to investigate whether inflammatory mediators interfere with SCAP translocation and its biological consequence.

METHODS: HMCLs were used in all experiments. Total cellular RNA was isolated from these cells for detecting LDLr, SREBP-2, and SCAP messenger RNA levels with real-time quantitative polymerase chain reaction. LDLr protein expression was measured by Western blot. Translocation of the SCAP-SREBP complex from the ER to Golgi was investigated by confocal microscopy.

RESULTS: In the absence of exposure to interleukin 1β, a high concentration of LDL retained SCAP in the ER, a low LDLr promoter activity, messenger RNA synthesis, and protein expression were found, respectively. However, exposure to interleukin 1β caused overexpression of SCAP and enhanced its translocation from the ER to Golgi. This disrupted normal feedback regulation and resulted in inappropriately increased LDL uptake with transformation of HMCLs into foam cells. Overexpression of SCAP in HMCLs resulted in an increased translocation of SCAP from the ER to Golgi, and high concentrations of LDL were unable to suppress SREBP-2 and LDLr gene expression.

CONCLUSIONS: These data suggest that inflammatory mediators promote abnormal translocation of SCAP from the ER to Golgi and play an important role in lipid accumulation in HMCLs.

USING NONSTEROIDAL ANTIINFLAMMATORY DRUGS IN VOLUME-DEPLETED CHILDREN CAN PRECIPITATE ACUTE RENAL FAILURE

Cheri Mathews John, Vivek Saroha and Caroline Jones

Pediatrics 2008;121;S142
DOI: 10.1542/peds.2007-2022PPPPP

PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

USING NONSTEROIDAL ANTIINFLAMMATORY DRUGS IN VOLUME-DEPLETED CHILDREN CAN PRECIPITATE ACUTE RENAL FAILURE

Cheri Mathews John, Vivek Saroha and Caroline Jones

Pediatrics 2008;121;S142
DOI: 10.1542/peds.2007-2022PPPPP