Viazzi et al. Italian Journal of Pediatrics 2015, 41(Suppl 2):A76
http://www.ijponline.net/content/41/S2/A76

ITALIAN JOURNAL OF PEDIATRICS

MEETING ABSTRACT Open Access

Sugar, fructose, uric acid and hypertension in children and adolescents

Francesca Viazzi[1*], Simonetta Genovesi[2], Maria Amalia Ambruzzi[3], Marco Giussani[4]

From 71st Congress of the Italian Society of Pediatrics. Joint National Meeting SIP, SIMGePeD, Study Group on Pediatric Ultrasound, SUP Study Group on Hypertension
Rome, Italy. 4-6 June 2015

Fructose consumption has been increasing over recent decades and is believed to play a role in the rising epidemic of metabolic disorders and hypertension (HT) in children [1,2]. This theory is supported by epidemiological and experimental studies in animals and humans.

High-fructose diets upregulate sodium and chloride transporters, resulting in salt overload that increases blood pressure (BP) [3]. Moreover, excess fructose has also been found to deregulate vasoconstrictors and vasodilators, and over-stimulate the sympathetic nervous system. Metabolism of fructose is mediated by fructokinase, which uses ATP as a phosphate donor. Unlike glucose, there is no feedback mechanism regulating fructokinase. As a result, AMP is continuously involved in the production of uric acid (UA) [4]. In adolescents in the US, serum UA was showed to increase from the lowest to the highest category of fructose-sweetened beverage intake and this increment was paralleled by an increase in BP, even independently of body mass index [5]. These data suggest pathways other than obesity relating soft drinks to the development of HT.

Epidemiological studies demonstrate an association between serum UA and both prevalence and new onset of essential HT in adolescents [6]. Recently, UA showed a strong independent relationship with BP values across different BP categories, from normal BP up to pre-and finally to established HT in children at relatively high cardiovascular risk [7].

Animal models support a two-phase mechanism for the development of hyperuricemic HT. Initially, UA induces vasoconstriction by activation of the renin-angiotensin system and reduction of nitric oxide. Over time, UA uptake into vascular smooth muscle cells (VSMC) causes cellular proliferation and arteriolosclerosis that impair pressure natriuresis, causing sodium-sensitive HT [8]. Increased UA causes endothelial dysfunction by inflicting oxidative stress once inside cells. UA internalization is mediated by URAT-1, and stimulates production of growth factors and chemokines in human VSMC [9] and increases ROS activating NADPH-oxidase, leading to apoptosis in human tubular cells [10]. These actions may, at least in part, explain the association between increased serum UA levels and initial cardiovascular and renal damage described in adolescents with obesity or HT [11,12].

Interestingly, in both animal and human studies, allopurinol attenuates the development of fructose-induced HT by lowering UA. Indeed, lowering UA with either allopurinol or probenecid reduces BP in adolescents with HT or pre-HT [13,14]. While larger studies are needed, fructose assumption and serum UA are emerging as potentially modifiable risk factors for the prevention and treatment of HT in children.

Authors' details
[1]University of Genoa, Department of Internal Medicine, IRCCS, AUO San Martino-IST, Genova, Italy. [2]Department of Health Sciences, University of Milano-Bicocca and Nephrology Unit, San Gerardo Hospital, Monza, Italy. [3]Ospedale Pediatrico IRCCS Bambino Gesù, Rome, Italy. [4]Family Pediatrician, Milan, Italy.

Published: 30 September 2015

References

1. Choi JW, Ford ES, Gao X, Choi HK: **Sugar-sweetened soft drinks, diet soft drinks, and serum uric acid level: the Third National Health and Nutrition Examination Survey.** *Arthritis Rheum* 2008, **59(1)**:109-116.
2. Grimes CA, Riddell LJ, Campbell KJ, Nowson CA: **Dietary salt intake, sugar-sweetened beverage consumption, and obesity risk.** *Pediatrics* 2013, **131(1)**:14-21.

* Correspondence: francesca.viazzi@unige.it
[1]University of Genoa, Department of Internal Medicine, IRCCS, AUO San Martino-IST, Genova, Italy
Full list of author information is available at the end of the article

3. Singh AK, Amlal H, Haas PJ, Dringenberg U, Fussell S, Barone SL, *et al*: **Fructose-induced hypertension: essential role of chloride and fructose absorbing transporters PAT1 and GLUT5.** *Kidney Int* 2008, **74(4)**:438-447.
4. Stirpe F, Della Corte E, Bonetti E, Abbondanza A, Abbati A, De Stefano F: **Fructose-induced hyperuricaemia.** *Lancet* 1970, **2(7686)**:1310-1311.
5. Nguyen S, Choi HK, Lustig RH, Hsu CY: **Sugar-sweetened beverages, serum uric acid, and blood pressure in adolescents.** *J Pediatr* 2009, **154(6)**:807-813.
6. Feig DI: **Uric acid and hypertension.** *Semin Nephrol* 2011, **31(5)**:441-446.
7. Viazzi F, Antolini L, Giussani M, Brambilla P, Galbiati S, Mastriani S, *et al*: **Serum uric acid and blood pressure in children at cardiovascular risk.** *Pediatrics* 2013, **132(1)**:e93-e99.
8. Feig DI, Madero M, Jalal DI, Sanchez-Lozada LG, Johnson RJ: **Uric acid and the origins of hypertension.** *J Pediatr* 2013, **162(5)**:896-902.
9. Kang DH, Han L, Ouyang X, Kahn AM, Kanellis J, Li P, *et al*: **Uric acid causes vascular smooth muscle cell proliferation by entering cells via a functional urate transporter.** *Am J Nephrol* 2005, **25(5)**:425-433.
10. Verzola D, Ratto E, Villaggio B, Parodi EL, Pontremoli R, Garibotto G, *et al*: **Uric acid promotes apoptosis in human proximal tubule cells by oxidative stress and the activation of NADPH oxidase NOX 4.** *PLoS One* 2014, **9(12)**:e115210.
11. Pacifico L, Cantisani V, Anania C, Bonaiuto E, Martino F, Pascone R, *et al*: **Serum uric acid and its association with metabolic syndrome and carotid atherosclerosis in obese children.** *Eur J Endocrinol* 2009, **160(1)**:45-52.
12. Tomczak J, Wasilewska A, Milewski R: **Urine NGAL and KIM-1 in children and adolescents with hyperuricemia.** *Pediatr Nephrol* 2013, **28(9)**:1863-1869.
13. Feig DI, Soletsky B, Johnson RJ: **Effect of allopurinol on blood pressure of adolescents with newly diagnosed essential hypertension: a randomized trial.** *JAMA* 2008, **300(8)**:924-932.
14. Soletsky B, Feig DI: **Uric acid reduction rectifies prehypertension in obese adolescents.** *Hypertension* 2012, **60(5)**:1148-1156.

doi:10.1186/1824-7288-41-S2-A76
Cite this article as: Viazzi *et al.*: **Sugar, fructose, uric acid and hypertension in children and adolescents.** *Italian Journal of Pediatrics* 2015 **41**(Suppl 2):A76.