Reply 'Energy drinks and risk of non alcoholic steatohepatitis'

[1,2]**Nobili V, MD;** nobili66@yahoo.it

[1,]**Mosca A, MD;** antonella.mosca@opbg.net

[3,4,]**Scorletti E, MD;** e.scorletti@soton.ac.uk

[3,4]**Byrne CD, MD;** C.D.Byrne@soton.ac.uk

1. Hepatometabolic Unit – Bambino Gesù Children's Hospital – Rome, Italy
2. Department of Pediatric – University "La Sapienza" - Rome, Italy
3. Human Development and Health Academic Unit, Faculty of Medicine, University of Southampton, Southampton, United Kingdom
4. NIHR Southampton Biomedical Research Centre, University Hospital Southampton NHS Foundation Trust and University of Southampton, Southampton, United Kingdom

Corresponding author:

Prof. Valerio Nobili, MD

Department of Pediatric – University "La Sapienza" , and Hepatometabolic Disease Unit, Bambino Gesù Children's Hospital IRCCS (Instituto di Ricovero e

Cura a Carattere Scientifico), P.le S. Onofrio, 4 – 00165 Rome, Italy. Tel.: +39 06 68592192.

Funding: This study did not receive funding.

Conflict of interest: The authors have no conflicts of interest to declare.

Author contributions: AM and SE were all manuscript drafting, NV and BCD have revised the final manuscript.

Keywords: energy drinks, niacin, non-alcoholic steatohepatitis, children

Word count: 310

Number of tables: 1; **number of figures**: 0

Dear Editor,

We read with interest the letter by Buchanan et al referring to our paper entitled "Serum uric acid concentrations and fructose consumption are independently associated with NASH in children and adolescents" (1,2). In their letter, the authors report the case of a 17-year-old-boy story who developed NASH due to his unhealthy lifestyle and his consumption of energy drinks (EDs). Buchanan et al also highlight that other components of the diet, such as niacin, xanthine, taurine and B vitamins, could contribute to liver damage (1).

With respect to niacin consumption, a case of fulminant hepatitis requiring liver transplantation was reported in a 36-year-old-man in 2014. The patient consumed three cans per day of EDs for 1 year (about 120 mg/daily of niacin) (3,4). We have now re-analysed our data and examined the numbers of children consuming energy drinks. In our predominantly young children, only 12/271 children admitted to consuming energy drinks; and, of these children, 9/12 were male. The data comparing the characteristics of subjects consuming, and not consuming energy drinks, are shown in the Table. Consumers of energy drinks were older than subjects who did not consume energy drinks. There were significant differences in BMI (>97th percentile) between the two groups (p=0.001). There was a borderline non significant increase in uric acid concentration in subjects consuming energy drinks, but it is noteworthy that fructose consumption was very similar between the groups. There were borderline significant increases in steatosis, inflammation, and NAS, in the group consuming energy drinks. The unadjusted odds ratio (95% CIs) for NASH in the group consuming energy drinks was [OR=3.51 (1.03-11.97); p=0.033]. In summary, we agree with Buchanan et al and suggest that larger case control studies are now urgently needed to begin to test the independence of the association between energy drink consumption and liver damage, and to assess the importance of this potential risk factor.

Reference

1. Buchanan R (J Hepatol, 2017)
2. Mosca A, Nobili V, De Vito R, Crudele A, Scorletti E, Villani A, et al. Serum uric acid concentrations and fructose consumption are independently associated with NASH in children and adolescents. J Hepatol 2017;66:1031–6.
3. Huang B, Kunkel D, Kabany ME. Acute Liver Failure Following One Year of Daily Consumption of a Sugar-Free Energy Drink. ACG Case Rep J. 2014 Jul 8;1(4):214-6.
4. WHO: www.apps.who.int/iris/bitstream/10665/149782/1/9789241549028_eng.pdf. Guideline: sugars intake for adults and children: draft guidelines on free sugars released for public consultation, WHO, 2014.

Table: Characteristics of children consuming and not consuming energy drinks with NAFLD

	Energy Drink consumers (n=12, 9 Male)	Non consumers of energy drinks (n=259, 146 Male)	*p*
Age (years)	17.3(1.98)	10.88 (2.44)	0.001
Weight (median; IQR)	115 (78-134)	56 (38-107)	0.001
BMI, Kg/m^2 (mean±SD)	33.98 (5.73)	25.99 (4.47)	0.001
Waist circumference, cm (mean±SD)	100 (17.10)	85.8 (10.43)	*0.01*
AST, UI/L (median; IQR)	29(15-95)	49 (26-104)	*0.001*
ALT, UI/L (median; IQR)	35 (23-102)	45 (24-121)	*0.05*
Uric Acid, mg/dl (median; IQR)	6.8 (4.5-7.9)	5.5 (2.1-9.6)	0.06
Total Cholesterol, mg/dl (median; IQR)	152 (109-210)	161 (85-257)	0.34
LDL Cholesterol, mg/dl (median; IQR)	94 (68-153)	90 (53-141)	0.29
HDL cholesterol, mg/dl (median; IQR)	39 (28-60)	44 (38-82)	0.70
Triglycerides, mg/dl (median; IQR)	117 (68-174)	91 (44-171)	0.13
Fasting plasma glucose, mg/dl (median; IQR)	84 (65-110)	82 (52-87)	0.65
Fasting plasma gluc-120'(median; IQR)	121 (99-151)	112 (66-138)	0.52
Fasting Insulin, mU/L (median; IQR)	23 (9-44)	13 (9-74)	0.001
Insulin -120 minute mU/L (median; IQR)	118 (43-138)	100 (57-140)	0.40
HOMA-IR(mean±SD)	3.7 (2.1)	2.8 (1.88)	0.041
SBP, mmHg (mean±SD)	119 (8.65)	111(13.14)	0.10
DBP, mmHg (mean±SD)	65.7 (8.92)	67 (9.27)	0.49
Fructose, grammes/day (median; IQR)	57 (33-105)	60 (34-98)	0.77
Steatosis (mean±SD)	1.41 (0.75)	1.92 (0.76)	0.05
Inflammation (mean±SD)	1.92 (0.27)	1.26 (0.54)	0.06
Ballooning (mean±SD)	0.66 (0.47)	0.74 (0.77)	0.66
Fibrosis (mean±SD)	1.1 (0.41)	0.87 (0.72)	0.24
NAS (mean±SD)	5.01 (1.32)	3.82 (1.08)	0.05

BMI = body mass index; AST = aspartate aminotransferase; ALT = alanine aminotransferase; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; HOMA-IR = homeostasis model assessment of insulin resistance; SBP = systolic blood pressure; DBP = systolic blood pressure. Differences were considered statistically significant at $p \leq 0.05$