EXPOSURE TO ORGANOPHOSPORUS FLAME RETARDANTS AND ALTERNATIVE PLASTICIZERS IN INTENSIVE CARE PATIENTS: ASSOCIATION WITH THE MEDICAL DEVICES

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Background

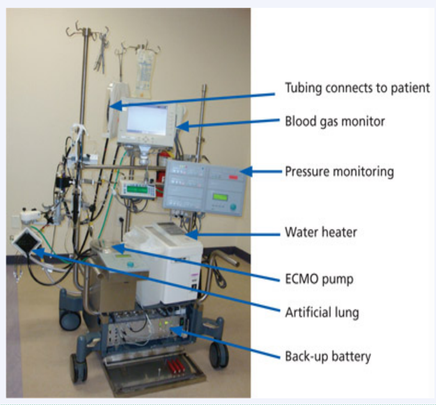
- Critically-ill patients treated in intensive care units (ICU) are potentially exposed to high levels of chemicals used as additives in plastic of indwelling devices which are employed extensively in these patients[1,2].
- Previous studies have shown that ICU patients had higher levels of phthalate esters (PEs), such as di(2-ethylhexyl) phthalate (DEHP), and bisphenol A (BPA) in serum and urine compared to healthy individuals[3,4].
- ICU patients could however be exposed to other plastic additives, such as organophosphorous flame retardants (PFRs) and alternative plasticizers (APs), yet no information is currently available in this regard.

Objectives

- We hypothesized that 1) adult patients who are admitted to the ICU are also exposed to PFRs and APs. We assessed this exposure by measuring the urinary levels of PFR and AP metabolites and 2) if the levels can be linked to the ICU-admission, the intensity of exposure and the type of plastic-containing medical devices.

Research design and methods

- Urine samples of adult ICU patients treated with a range of medical devices were analyzed for a suite of PFR metabolites and AP metabolites[5,6].
- PFR and AP metabolites were also measured in patients necessitating continuous venovenous hemofiltration (CVVH) and/or extracorporeal membrane oxygenation (ECMO).
- BPA and DEHP metabolites were previously measured in the same population, data are taken from Huygh et al[3].



Study population

- Urine samples (n=78) of adult ICU patients (n=23) were analyzed for a suite of PFR metabolites and AP metabolites. (see below the list of investigated compounds)
- Urine samples were obtained on admission in the Antwerp University Hospital (< 24h pre-operatively), and repeat samples were taken on days 1 to 4 during their stay in the ICU.
- Control population for the urine samples (n=22) were used from previously recruited persons in another study.

Parent PFR	Metabolites (target compounds) [5]	Abbreviation
Triphenylphosphate (TPHP)	4-hydroxyphenyl phenyl phosphate	4-HO-DPHP
	diphenyl phosphate	DPHP
	4-hydroxyphenyl diphenyl phosphate	4-HO-TPHP
	3-hydroxyphenyl diphenyl phosphate	3-HO-TPHP
2-ethylhexyldiphenyl phosphate (EHDPHP)	2-ethyl-5-hydroxyhexyl diphenyl phosphate	5-HO-EHDPHP
	2-ethylhexyl phenyl phosphate	EHPHP
Tris(2-chloroisopropyl) phosphate (TCIPP)	1-hydroxy-2-propyl bis(1-chloro-2-propyl) phosphate	BCIPHIPP
	bis(1-chloro-2-propyl) phosphate	BCIPP
Tris(chloroethyl) phosphate (TCEP)	tris(chloroethyl) phosphate	TCEP
Tris(2-butoxyethyl) phosphate (TBOEP)	bis(2-butoxyethyl) phosphate	BBOEP
	2-hydroxyethyl bis(2-butoxyethyl) phosphate	BBOEHEP
	bis(2-butoxyethyl) 3'-hydroxy-2-butoxyethyl phosphate	3-HO-TBOEP
tris(1,3-dichloro-2-propyl) phosphate (TDCIPP)	bis(1,3-dichloro-2-propyl) phosphate	BDCIPP
tri-n-butyl phosphate (TNBP)	di-n-butyl phosphate	DNBP

Parent AP	Metabolites (target compounds) [6]	Abbreviation
di(2-ethylhexyl) terephthalate (DEHTP)	mono(2-ethylhexyl) terephthalate	MEHTP
	mono(2-ethyl-5-hydroxyhexyl) terephthalate	5-OH-MEHTP
di-2-ethylhexyl adipate (DEHA)	mono(2-ethylhexyl) adipate	MEHA
	mono(2-ethyl-5-oxohexyl) adipate	oxo-MEHA
	mono(2-ethyl-5-hydroxyhexyl) adipate	OH-MEHA
di(isononyl)cyclohexane-1,2-dicarboxylate (DINCH)	cyclohexane-1,2-dicarboxylic mono isononyl ester	MINCH
	cyclohexane-1,2-dicarboxylic mono hydroxyisononyl ester	OH-MINCH
	cyclohexane-1,2-dicarboxylic monocarboxy isooctyl ester	Cx-MINCH
di(2-propylheptyl) phthalate (DPHP)	mono(2-propyl-6-hydroxyheptyl) phthalate	OH-MPHP
	mono(2-propyl-6-carboxyhexyl) phthalate	Cx-MPHxP
	mono(2-propyl-6-oxoheptyl) phthalate	oxo-MPHP

Demographics of the ICU patients

Variable		Mean (SD)
Gender (male/female)		13/10
Age (years)		57 (16.8)
Total population		23
	General ICU, no device	15 (65%)
	Of whom with preoperative inclusion	8 (35%)
Patients with devices:		
	ICU + CVVH	5 (22%)
	ICU + ECMO	1 (4%)
	ICU + CVVH + ECMO	2 (8%)

Other chemicals [3,4]	Abbreviation
Bisphenol A	BPA
Mono(2-ethyl-5-carboxypentyl)phthalate	5Cx-MEPP
Mono(2-ethyl-5-hydroxyhexyl)phthalate	5OH-MEPP
Mono(2-ethyl-5-oxohexyl)phthalate	5oxo-MEHP
Mono(2-ethylhexyl)phthalate	MEHP
Mono-iso-butyl-phthalate	MiBP
Di(2-ethylhexyl)phthalate	DEHP
Triclosan	TCS

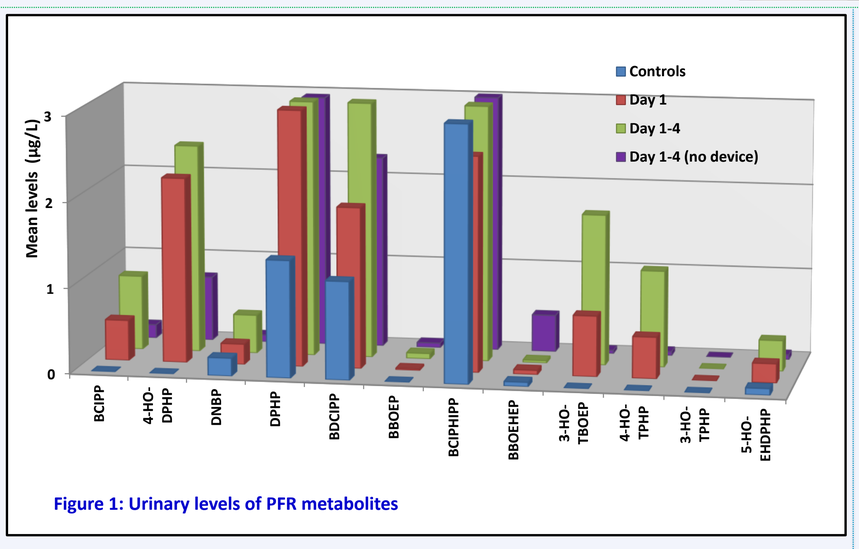


Figure 1: Urinary levels of PFR metabolites

- Levels of some PFR metabolites (deriving from TPHP, TCDIPP and TCIPP) were higher after admission to the ICU and stayed higher compared to the controls.
- Levels of PFR metabolites were lower than AP or DEHP metabolites.

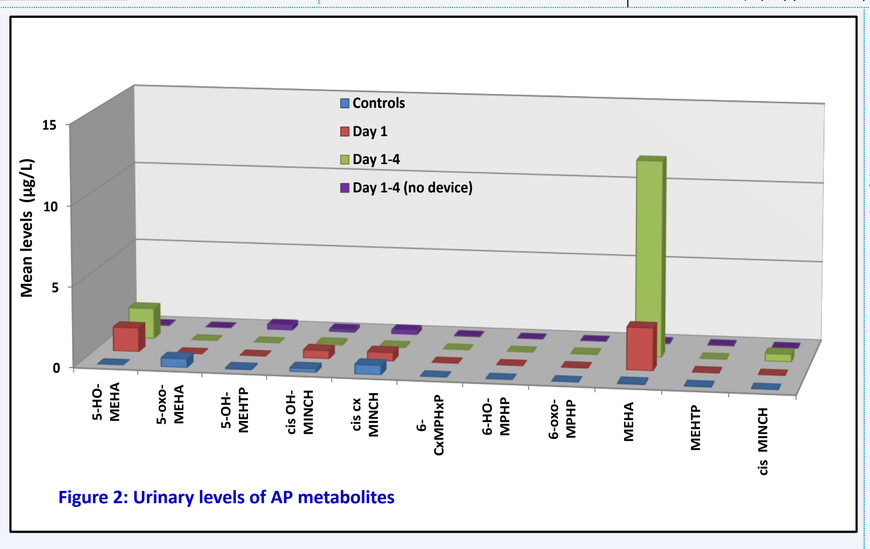


Figure 2: Urinary levels of AP metabolites

- Only DEHA metabolites were higher after admission to the ICU compared to controls.
- Levels of AP metabolites were lower levels of DEHP metabolites.

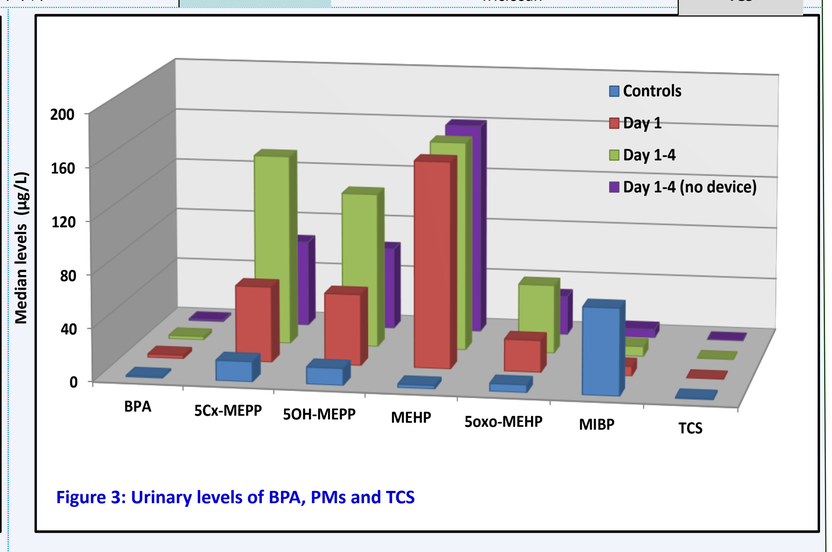


Figure 3: Urinary levels of BPA, PMs and TCS

- One day after admission in the ICU, the levels of BPA and PMs were significantly ($p < 0.001$) higher than in the controls.
- Levels of DEHP metabolites were higher on day 1 than in controls, and levelled off to day 4.

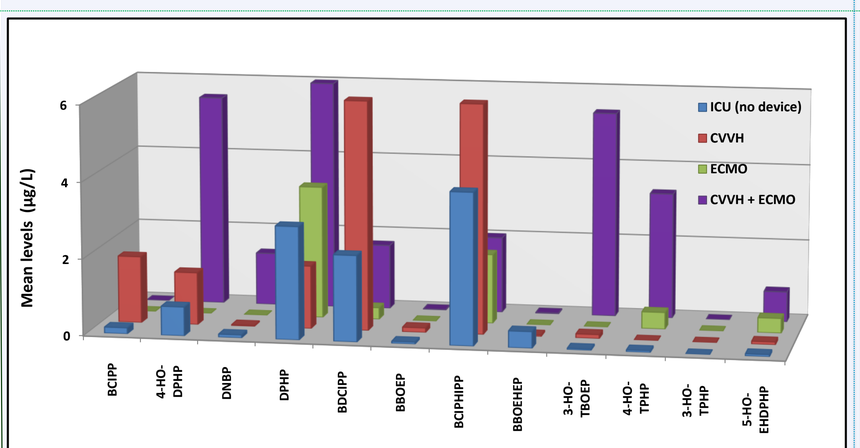


Figure 4: Urinary levels of PFR metabolites according to the type of devices

- While there are no obvious trends, the concentrations of some PFR metabolites in urine of CVVH and ECMO patients had a higher tendency than in other ICU patients.

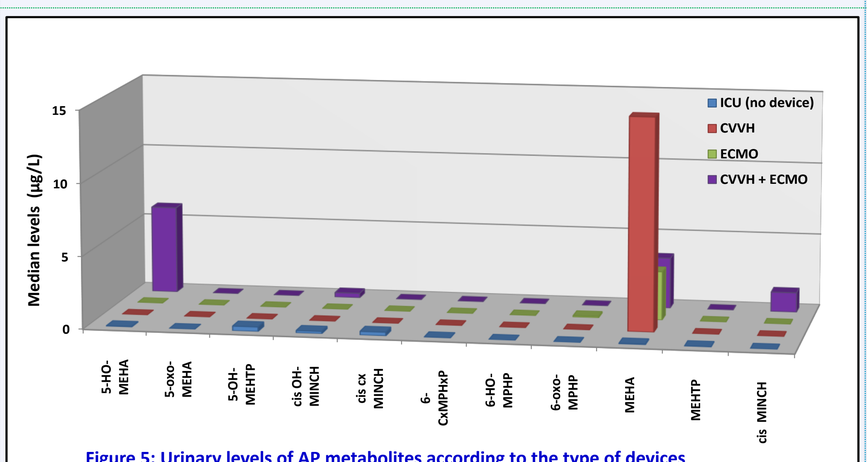


Figure 5: Urinary levels of AP metabolites according to the type of devices

- The concentrations of DEHA metabolites in urine of CVVH and ECMO patients were higher than in other ICU patients.
- Metabolites of other APs were in most urine samples not detected.

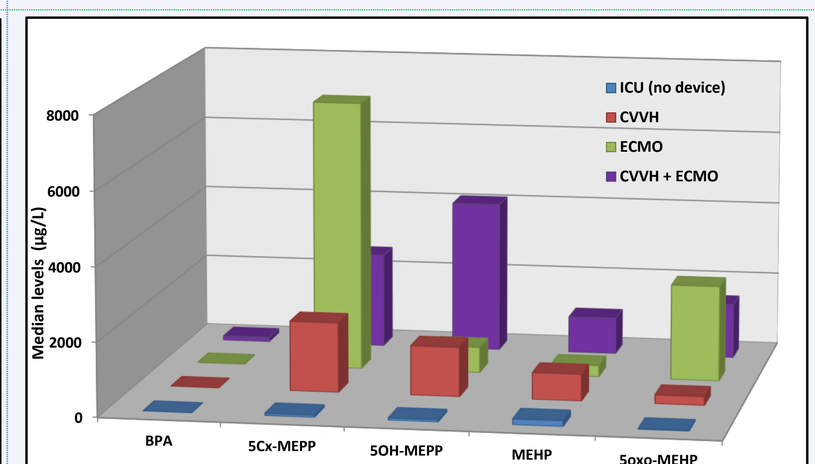


Figure 6: Urinary levels of BPA and PMs according to the type of devices

- In the urine samples from those CVVH patients, the PM levels were significantly elevated, except for BPA.
- In patients with ECMO support, urine had significantly increased PMs.

Conclusions

- This is the first report on PFR and AP metabolites in adult ICU patients.
- Patients with specialized treatments such as CVVH, ECMO or both had higher levels of some PFR and AP metabolites compared with the controls or with other ICU patients.
- Levels of PFR and AP metabolites were much lower that the levels of DEHP metabolites. This indicates that despite the continuously tightening regulations, DEHP are still present in medical devices.
- Because patient safety is a concern in the ICU, further research into the (possibly toxic and clinical) effects of chemicals released from medical devices should be urgently undertaken.

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