

Knowledge and Awareness of Anesthesiologists about Di(2-EthylHexyl) Phthalate in Turkey: A Survey Study

Türkiyede anestezi hekimlerinin Di (2-ETİLHEKSİL) fitalat hakkında bilgi ve farkındalığı; Anket Çalışması

 İsmail BOZKURT¹,  Aydın TAŞDÖĞEN²,  Nilay BOZTAŞ²,  Esma ADIYAMAN³,  Volkan HANCI²

¹Anesthesiology and Reanimation, Tekirdag City Hospital, Tekirdag, Türkiye

²Dokuz Eylül University, Anesthesiology and Intensive Care, Izmir, Türkiye

³Anesthesiology and Reanimation, Bozyaka Training and Research Hospital, Izmir, Türkiye

ABSTRACT

Objective: This study aims to evaluate the knowledge and experiences of anesthesiologists in Turkey about the presence and hazards of DEHP and increase their awarenesses.

Materials and Methods: The questionnaire study consisting of web based 20 survey questions about DEHP is sent to anesthesiologists in Turkey via electronic mail. Participants were asked questions about whether they heard the name of the DEHP, whether they knew the harmful effects that the DEHP could cause, and whether it was the effect of DEHP in the selection of the operating room and intensive care medical supplies.

Results: We determined that 70% of anesthesiologists have never heard of 'the name or notion of DEHP. The study also demonstrates that 90-95% of them do not know whether the medical supplies that they use contain DEHP and they suffer from lack of knowledge about the purchase and selection of medical supplies.

Conclusion: According to the data of this research, the majority of the anesthesiologists in Turkey have insufficient information about DEHP. In order to prevent this threat, there is a need for multidisciplinary working from industrial organizations to health institutions.

Keywords: Anesthesiologist, Diethylhexyl Phthalate, Surveys and Questionnaires.

ÖZ

Amaç: Bu çalışmanın amacı Türkiye'deki anestezi uzmanlarının Di(2-EthylHexyl) Fitalatın (DEHP) varlığı ve zararları hakkındaki bilgi ve deneyimlerini değerlendirmek ve farkındalıklarını artırmaktır.

Nilay BOZTAŞ

Dokuz Eylül University,
Anesthesiology and Intensive Care,
Izmir, Türkiye

E-posta: nilayboztas@hotmail.com

 <https://orcid.org/0000-0001-9341-754X>

Gereç ve Yöntem: DEHP hakkında web tabanlı 20 anket sorusundan oluşan anket çalışması Türkiye'deki anestezi uzmanlarına elektronik posta yoluyla gönderilmiştir. Katılımcılara DEHP'nin adını duyup duymadıkları, DEHP'nin neden olabileceği zararlı etkileri bilip bilmedikleri, ameliyathane ve yoğun bakım tıbbi malzeme seçiminde DEHP'nin etkisinin olup olmadığı ile ilgili sorular sorulmuştur.

Bulgular: Anestezi uzmanlarının %70'inin DEHP'nin adını veya kavramını hiç duymadığını belirledik. Çalışma ayrıca, %90-95'inin kullandıkları tıbbi malzemelerin DEHP içerip içermediğini bilmediğini ve tıbbi malzemelerin satın alınması ve seçimi konusunda bilgi eksikliği yaşadıklarını göstermektedir.

Sonuç: Bu araştırmanın verilerine göre, Türkiye'deki anestezi uzmanlarının çoğunluğu DEHP hakkında yeterli bilgiye sahip değildir. Bu tehdidin önlenmesi için sanayi kuruluşlarından sağlık kurumlarına kadar multidisipliner bir çalışmaya ihtiyaç vardır.

Anahtar Kelimeler: Anestezi uzmanı, Dietilheksil Ftalat, Anket ve soruları.

INTRODUCTION

While the rapid development of industry has brought many conveniences for life, it has caused organisms to be exposed to new synthetic chemical materials. A report published by the European Union Commission in 2002 found 60 materials with damage to “environmental and human health” clearly shown among hundreds of chemical materials. Phthalates are among these materials causing damage to human health (1). Phthalates have many industrial uses (2-3). Phthalates are commonly used to add softness and flexibility to naturally hard and brittle plastic items. Among phthalates, di-(2ethylhexyl) phthalate (DEHP) is the most commonly used and annual production is reported to be nearly two million tons (4-6).

Common use of phthalates has caused increased contact with humans and animals. Phthalates may be transmitted to humans via oral, dermal or inhalation routes. Phthalate esters and metabolites may be easily identified in items, care products, in urine, breastmilk and amniotic fluid. Additionally, phthalates may pass the placenta and may cause fetal effects in proportion to the mother's exposure. At the end of DEHP metabolism, the more

toxic MEHP (mono-ethyl hexyl phthalate) forms (7-12). Commonly used in practice in the health system and with high degree of lipophilia, DEHP may easily pass into body solutions (13). DEHP used in health applications may negatively affect human health. DEHP is assessed as a chemical material causing endocrine disorders in children (14). The FDA (Food and Drug Administration) and European Union Commission have made a range of recommendations to avoid this toxic material and to reduce its use. Especially in some countries like Canada, the use of plastic bags and medical material like teats containing phthalate, etc, have been banned.

The Republic of Turkey Ministry of Health recommended special precautions to protect children under the age of 3, especially, from phthalates. In 2011, a warning device regulation about the reduction or elimination of phthalates in medical material was published (15-17).

Surgeries and intensive care units are the health area where phthalates are most commonly used. The physician group working most in these areas and using most phthalate material are anesthesiologists. As a result, the physician group who should be most sensitive to the toxic effects of

DEHP and MEHP are anesthesiologists. In our study, we aimed to evaluate the knowledge of Anesthesia and Reanimation physicians about DEHP and to increase awareness on this issue.

MATERIAL AND METHODS

Our study was planned as a survey study after receiving permission from “Dokuz Eylül University Non-Interventional Ethics Committee”. Ethical approval for this study (Ethical Committee No 855) was provided Ethical Committee Dokuz Eylül University Non-Interventional Ethics Committee, İzmir, Türkiye (Chairperson Prof B. Onvural) on 20th November 2015.

A web-based survey comprising 4 sections of 20 questions (App. 1) was sent to lecturers, specialists and specialist students (2343 people in total) employed in Anesthesiology and Reanimation Departments in Türkiye 3 times at 1-month intervals from 23.12.2015. It was stated that participation was not mandatory. Our study did not include those with invalid e-mail addresses and responses sent after 01.03.2016.

The participants answered a total of 20 questions in 4 groups (A-D). The A section of the survey comprised 6 questions collecting data related to demographics and place of employment.

B section included 6 questions about whether they had heard the name DEHP and about products containing DEHP.

C section included 2 questions about the effect of presence of DEHP on the selection of medical material used in surgery and intensive care. The D section included 6 questions collecting data about the possible harmful effects of DEHP and legal regulations.

Data Analysis

Data obtained in response to questions on the survey were analyzed with Statistical Package for the Social Sciences (SPSS Inc, Chicago, IL, USA) 15.0 version program for Windows. Data indicating frequency are shown as frequency (n) and percentage

(%). Continuous variables are shown as mean \pm standard deviation (mean \pm SD). Comparison of frequency data used the chi square statistical method.

After determining the normality of distribution patterns of data with continuous values, the Kruskal Wallis, Mann Whitney U, Student t test and ANOVA test were used in accordance with distribution pattern and number of groups. Significance was accepted as $p < 0.05$.

RESULTS

Of the 2343 anesthesiologists that the survey questions were sent to, the data from 270 (11.52%) anesthesiologists who responded to the survey in time were assessed. Of the 270 participants answering the survey, 149 (55.2%) were female, 121 (44.8%) were male and the mean age was identified as 38.12 ± 9.59 years. It was identified that research assistants ($n=104$) and specialist doctors ($n=97$) provided most responses to our survey. The mean professional experience duration of those answering the survey was 10.56 ± 9.44 years.

The mean professional experience duration of research assistants was identified as 2.35 ± 1.13 years, specialists 11.80 ± 6.46 years of teaching assistants 21.33 ± 9.27 years and lecturers 21.00 ± 7.57 years of. Thus, it was identified that teaching assistants and lecturers were more experienced than others ($p=0.0001$).

Survey responses were mostly obtained identified to the Marmara ($n=99$), Aegean ($n=86$), and Central Anatolian ($n=52$) regions. The majority of anesthesiologists completed the survey lived in metropolitan areas ($n=202$). Of participants, 88.9% ($n=240$) worked in Ankara and western provinces, while 11.1% ($n=30$) worked in eastern provinces.

The majority of anesthesiologists were working in university hospitals. When responses to the question of whether they had ever heard the name of DEHP are assessed, 70.4% had not heard the name DEHP or had no idea about it ($p=0.0001$). When rates of hearing about DEHP according to academic career

were compared, the majority of research assistants and specialists had not heard the name of DEHP, while the majority of lecturers had heard of DEHP ($p=0.0001$) (Table 1).

Table 1. Awareness rate of the name DEHP according to academic career

	Research Assistant	Specialist Doctor	Teaching Assistant	Lecturer	Total
Heard of DEHP	17.3% (n=18)	26.8% (n=26)	43.6% (n=17)	63.3%*(n=19)	29.6% (n=80)
Not heard of DEHP	61.5% (n=64)	61.9% (n=60)	43.6% (n=17)	23.3% (n=7)	54.8% (n=148)
No idea about DEHP	21.2% (n=22)	11.3% (n=11)	12.8% (n=5)	13.3% (n=4)	15.6% (n=42)
Total	100% (n=104)	100% (n=97)	100% (n=39)	100% (n=30)	100% (n=207)

* $p=0.0001$

According to professional experience duration, 120 of those answering the survey had worked for >10 years, while 150 had worked for <10 years. As the working duration increased, the rate hearing about DEHP was identified to increase ($p=0.0001$).

The rate of those answering the survey who did not know where DEHP was used or had no idea about it was 68.5%. It was determined that participants with longer working duration knew where DEHP was used at higher rates ($p=0.0001$) (Table 2).

Table 2. Rates of knowing where DEHP is used according to employment duration

	>10 years working duration	<10 years working duration	Total
Know where to use DEHP	36.8%* (n=42)	17.5% (n=24)	26.3% (n=66)
Don't know where to use DEHP	37.7% (n=43)	36.5% (n=50)	37.1% (n=93)
No idea where to use DEHP	25.4% (n=29)	46.0% (n=63)	36.7% (n=92)
Total	100% (n=114)	100% (n=137)	100% (n=251)

* $p=0.0001$

The rate of knowing where DEHP was used was increased as academic career progressed according to academic career was lowest for research assistants, the rate of knowing where DEHP was used (p=0.0001) (Table 3).

Table 3. Rates of knowing where DEHP is used according to professional career

	Research Assistant	Specialist Doctor	Teaching Assistant	Lecturer	Total
Know	15.1% (n=14)	23.6% (n=21)	35.9% (n=14)	56.7%* (n=17)	26.3% (n=66)
Don't know	36.6% (n=34)	39.3% (n=35)	35.9% (n=14)	33.3% (n=10)	37.1% (n=93)
No idea	48.4% (n=45)	37.1% (n=33)	28.2% (n=11)	10.0% (n=3)	36.7% (n=92)
Total	100% (n=93)	100% (n=89)	100% (n=39)	100% (n=30)	100% (n=251)

*p=0.0001

In answer to the question “do you use material(s) containing DEHP?”, 18.5% of participants responded yes (n=50), while 8.1% responded no (n=22) and

64.4% stated they had no idea (n=174). The responses to questions asked about awareness of DEHP content in products used are given in Table 4.

Table 4. Awareness of products used containing DEHP

Product	Yes - contains DEHP	No- does not contain DEHP	No idea	Did not answer	Awareness of brand	Most commonly used brand
Examination gloves	6.7% (n=18)	5.9% (n=16)	74.8% (n=202)	12.6% (n=34)	35.2% (n=95)	Beybi-28.5% (n=77)
Intravenous/ arterial cannula	6.3% (n=17)	4.4% (n=12)	78.5% (n=212)	10.7% (n=29)	37.4% (n=101)	Braun-17.8% (n=48)
Aspiration and nasogastric probe	6.3% (n=17)	4.8% (n=13)	77.4% (n=209)	11.5% (n=31)	27.8% (n=75)	Bıçakçılar- 26.3% (n=71)
Peripheral and central venous catheter	4.8% (n=13)	5.2% (n=14)	78.5% (n=212)	11.5% (n=31)	37.8% (n=102)	Braun-18.5% (n=50)
Epidural set	5.2% (n=14)	4.4% (n=12)	79.6% (n=215)	10.7% (n=29)	45.6% (n=123)	Braun-29.3% (n=79)

Dropadjustment set/pain infusion set/venous extension line	6.7% (n=18)	3.0% (n=8)	79.6% (n=21)	10.7% (n=29)	21.1% (n=57)	Bıçakçılar-17.8% (n=48)
Injector	5.9% (n=16)	3.3% (n=9)	80% (n=216)	10.7% (n=29)	39.2% (n=106)	Hayat-12.2% (n=3)
Endotracheal tube (double lumen/single lumen)	6.3% (n=17)	4.8% (n=13)	77.4% (n=209)	11.5% (n=31)	32.2% (n=87)	Bıçakçılar-21.9% (n=59)
Laryngeal mask	5.9% (n=16)	4.4% (n=12)	78.5% (n=212)	11.1% (n=30)	27% (n=73)	Promed-8.9% (n=24)
Ventilator cycle/respiration mask	6.7% (n=18)	3.0% (n=8)	79.3% (n=214)	11.1% (n=30)	16.3% (n=44)	Covidien-3.7% (n=10)
Blood and serum set, blood bag, triple tap	6.3% (n=17)	4.8% (n=13)	77.8% (n=210)	11.1% (n=30)	19% (n=51)	Bıçakçılar-6.7% (n=18)
Dialysis material/ ECMO set/ hot chemotherapy device sets	5.6% (n=15)	1.1% (n=3)	81.9% (n=221)	11.5% (n=31)	1.8% (n=5)	Maquet-1.1% (n=3)

It is known that different amounts of DEHP are used in products from different plastic producers. In answer to the question of whether there were differences between DEHP content between plastic producing companies, 25.9% (n=70) answered yes, 2.6% (n=7) answered no, and 68.5% (n=185) answered they had no idea. It is thought that the majority of purchasing commissions in private and public hospitals have no information about DEHP content and toxicity in products.

When asked whether DEHP content is checked during selection or purchasing of medical material at your hospital, 6.3% (n=17) said yes, 21.5% (n=58) said no and 68.9% (n=186) said they had no idea. It is known that patients receiving

anesthesia and monitored in intensive care are exposed to DEHP. When asked whether patients receiving anesthesia or in intensive care are exposed to DEHP, 33% (n=89) said yes, 1.5% (n=4) said no and 63% (n=170) had no idea.

DEHP is transmitted via perioral, IV, inhalation and dermal routes. We asked what are the routes of exposure to DEHP during anesthesia administration and the responses to the question with multiple answers allowed were 25.2% (n=68) perioral route, 28.9% (n=78) inhalation route, 33.3% (n=90) intravenous route, 33% (n=68) dermal route and 49.3% (n=133) had no idea.

Exposure to DEHP may cause harmful effects to the fetus, abnormalities in pubertal

development, undescended testis and hypospadias development, increased anogenital openings, endometriosis, liver adenoma and HCC development, and changes to the thyroid structure and activity. When asked what exposure to DEHP may cause, the participants responses were 23.7% (n=64) harmful effects to the fetus, 22.2% (n=60) abnormalities of pubertal development, 18.9% (n=51) undescended testis and hypospadias development, 14.1% (n=38) increased anogenital openings, 13% (n=35) endometriosis, 24.1% (n=65) liver adenoma and HCC development, 14.8% (n=40) changes to thyroid structure and activity, and 56.7% (n=153) had no idea.

Everyone in the anesthesia is exposed to DEHP. However, the group with the highest DEHP exposure are were the preterm. When asked which patient groups were most exposed to DEHP, the answers were 32.2% (n=87) pregnant cases, 37.4% (n=101) premature cases, 37.4% (n=101) children, 19.6% (n=53) adults and 50.7% (n=137) had no idea.

The release of DEHP from PVC is influenced by pH, temperature, fluid content within the material, and exposure duration. Participants' responses to the question about what affects release rates of DEHP from material used were 20% (n=54) pH, 30.7% (n=83) temperature, 18.1% (n=49) fluid content, 37% (n=100) exposure duration and 51.1% (n=138) had no idea.

DEHP exposure may cause pulmonary damage, bronchopulmonary dysplasia, and increased bronchial sensitivity.

When participants were asked what DEHP release causes in the lungs, 22.6% (n=61) said pulmonary damage, 18.1% (n=49) said bronchopulmonary dysplasia and, 24.1% (n=65) stated increased bronchial sensitivity. There were 56.7% (n=153) who said they had no idea.

The use of material containing DEHP may cause platelet aggregation and complement activation

in the cardiovascular system. In response to the question "What complications may be expected due to the use of tools containing DEHP in surgeries related to the cardiovascular system?", 15.9% of participants (n=43) said platelet aggregation, 17.8% (n=48) said complement activation and 69.9% (n=188) said they had no idea.

The Ministry of Health has two announcements about DEHP (2005, 2011). When participants were asked whether the Ministry of Health had made any announcements about DEHP, 11.1% (n=30) said yes, 8.1% (n=22) said no, and 75.2% (n=203) had no idea.

The Food and Drug Administration (FDA) has made warnings about DEHP in different years (2001, 2008, 2010). When participants were asked whether the Food and Drug Administration (FDA) had made any announcements about DEHP, 24.4% (n=66) said yes, 1.9% (n=5) said no, and 69.9% (n=188) had no idea.

DISCUSSION

In our survey study aiming to assess the knowledge and experience about harmful effects of (DEHP), of Anesthesia and Reanimation physicians in our country, 70% of the 270 anesthesiologists who responded to the survey had not heard the name of DEHP. We determined that 75% did not know where DEHP was used. When we asked whic medical materials and devices were contain DEHP, 90-95% did not know whether the medical materials they used contained DEHP or not. Another interesting finding in the research is that 70-99% of anesthesiologists did not know the brand of the material they used.

When asked about differences in DEHP content between plastic producers, 75% of anesthesiologists did not know and 93.7% had no idea about the selection and purchasing of material. More than 50% of anesthesiologists had no idea about the topics of how DEHP was transmitted to humans, what affected release, which patient groups it was more

dangerous for and the effects on the human body. It was determined that more than 70% of anesthesiologists had no information about national and international warnings about DEHP. In addition to all of this, as the academic career and professional experience increased, the proportion who had heard of DEHP increased, which is an expected and predicted result.

During a literature search, we did not find any studies that questioned any knowledge on topics related to “anesthesiologist, DEHP, material and devices containing DEHP, DEHP effects on human health, and efforts of national and international organizations about DEHP”. As a result, we sent all anesthesiologists in Türkiye a survey “questioning knowledge about DEHP and aiming to increase awareness of DEHP” via electronic mail.

According to our survey data, 70% of anesthesiologists had never heard the name of DEHP and had insufficient knowledge about the material they used, which exceeded our expectations. Material and devices containing DEHP are used by physicians in various branches in all fields of the health sector.

DEHP exposure is mostly experienced in intensive care units (18-19) and in surgeries (20). Apart from these, the DEHP exposure in areas like dialysis units (18-19), nutritional units (15, 19,21), blood banks (15,19,22,23),and oncology departments (15,21,24) is high..

Unsurprisingly, given the ubiquity of phthalates and bisphenols, biomonitoring studies reported detectable levels of DEHP and BPA in 75-90% of the general population in the study by Ramadan et al. (25). One study clearly demonstrated that ECMO patients receive a significantly higher internal exposure to DEHP, the most prominent plasticizer in medical devices to date (26).

Gaynor et al found large postoperative increases in urinary BPA (42%) and DEHP metabolite (1,500-2,100%) levels in pediatric patients undergoing cardiac surgery (27).

Many alternative plasticizers are now available and increasingly used in medical devices (28).

One of these plasticizers developed specifically for use in medical devices is tri-2-ethylhexyl trimellitate (TOTM or TEHTM). The different structure of TEHTM is hypothesized to lead to a higher degree of stability associated with a lower migration rate in blood or other fluids compared to DEHP, which has been shown in previous studies (29).

In our literature search, we did not find any study researching the knowledge of physicians and other health personnel working in these fields about DEHP. However, we did encounter a small number of animal and human research studies about DEHP exposure (3-30). As a result, we think the knowledge, experience and sensitivity of health personnel about DEHP are insufficient. Our survey results confirm this data.

The Republic of Türkiye Ministry of Health Turkish Medicines and Medical Devices Agency (TMMDA) states it has a duty to “serve human health by developing and applying regulatory, supervisory and directive policies about medicine, medical devices and cosmetic products” according to their main website (31). The target of this organization is defined as “being a pioneering and reference organization in the international field, based on health-oriented science and targeting perfection”.

The 5th item of the duty statement declare that their duty is “to observe and supervise medicines, medical devices and products entering the market, if necessary to collect, destroy or have them destroyed, to determine reliable reporting methods for products in the market, to make the necessary declarations, to perform laboratory analyses or have them performed” (32). As understood from these statements, the licensing, regulation and control of material or medicines are under the auspices of the Ministry of Health.

The purchasing commissions of state and university hospitals work in conjunction with the

chief physician's office. Doctors, nurses and technical personnel serve on these commissions. The basic duty of these commissions under current circumstances is to obtain the cheapest and best quality material on time and to make it available for use.

No matter their branch, the duty of health personnel may be summarized by the statement 'Primum non nocere' attributed to Hippocrates; in other words, 'Do no harm'.

In this situation, the duty of health personnel includes having sufficient knowledge about treatment methods that do not harm the patient or themselves and in the selection of medicines, material and devices used. The prevention of production of toxic products containing DEHP may be obstructed by not licensing them at Ministry of Health level.

Toxic products passing this stage may be prevented from entering hospitals at the purchasing stage. The first route to achieve this for is national units like the Ministry of Health that provide import permissions, licenses for use and health certificates on the topics of medicine-material-devices, to become more aware of this topic.

The second route is to inform physicians serving on purchasing and medical material device technical specifications commissions at chief physician level. The third route is to inform and sensitize all health personnel and patients through professional organizations, patient safety organizations, etc.

Despite the Ministry of Health releasing 2 announcements related to DEHP in 2005 and 2011 (17-33), it is interesting that only 11% of anesthesiologists participating in our study had any information related to DEHP. A slightly higher amount (24.4%) of anesthesiologists were aware of repeated announcements by international organizations like the FDA(15). Considering that the physicians most informed about DEHP were experienced academics in universities, it is understood that physicians employed in state

hospitals serving large public masses will not have sufficient information about this topic. The Ministry of Health announcement in the Official Gazette published on 7th June 2011 described phthalates in the 7th item of the Medical Device Regulation and included the statement "the label of the product must state that it contains phthalate".

The FDA recommends that instead of PVC containing DEHP, material not containing DEHP (containing alternative chemicals, e.g., trioctyl trimellitate, and diethyl hexyl adipate) should be used for special patient groups (premature cases, especially male newborns, pregnant, and breastfeeding mothers, etc.) (15-34).

In line with this research, defining PVC/DEHP containing material initially, it is recommended that alternatives should be used for these risk groups. It is reported that to reduce individuals' DEHP exposure to a minimum, PVC free material should be chosen (35). It is clear that these precautions will only be taken through the efforts of informed, sensitive physicians.

The "European Chemical Agency Socio-Economic Analysis Committee" in 2015 recommended limiting the use of the majority of chemicals included in the EU's "Registration, Evaluation, Authorisation and Restriction of Chemicals" (REACH) law.

The target was to ban 4 phthalates called butyl benzyl phthalate (BBzP), di (2-ethylhexyl) phthalate (DEHP), dibutyl phthalate (DBP), and di isobutyl phthalate (DIBP), especially. Plasticizers commonly used in a majority of products were banned above levels of 0.1% by weight (36).

The passing of laws and bans clearly did not solve the problem. It is necessary for international organizations like the FDA, national authorities like the Ministry of Health, environmental and professional organizations, and physicians themselves to expend effort on this topic. The duty of industrial organizations should be to produce

products that do not harm human and animal health and do not pollute the environment.

There are some limitations to our study. The low number of participants in our study may not sufficiently reflect the opinions and information of all anesthesiologists employed in Türkiye.

CONCLUSION

In conclusion, according to our study data, the majority of anesthesiologists working in Turkey were identified to have insufficient knowledge about DEHP. Linked to this lack of knowledge, physicians and patients are exposed to the toxic effects of chemicals.

To prevent this unwanted exposure, recommendations of international organizations should be followed more closely to increase the safety for patients and health personnel; national units like the Ministry of Health should provide training in line with international recommendations, and more closely regulate announcements; hospitals should become more sensitive and material and products considered harmful should be prevented from entering the hospital by trained purchasing commissions;

Manufacturing firms should avoid toxic products and be supported to develop non-toxic products. There is a need for multidisciplinary studies involving industrial organizations and health organizations to prevent the release and use of these toxic products.

REFERENCES

1. ATSDR. Agency for Toxic Substances and Disease Registry (2002) Toxicological profile for di(2-ethylhexyl) phthalate. URL: www.atsdr.cdc.gov/toxprofiles/tp9.pdf
2. Hall AG. Nurses: Taking precautionary action on a pediatric environmental exposure: DEHP. *Pediatric Nursing* 2006;32:91-3.
3. Latini G. Monitoring phthalate exposure in humans. *Clin Chim Acta* 2005;361:20-9
4. Tickner JA, Schettler T, Guidotti T, McCally M, Rossi M. Health risks posed by use of Di-2-Ethylhexyl Phthalate (DEHP) in PVC Medical Devices: A critical review. *Am J Ind Med* 2001;39:100-11.
5. Heudorf U, Mersch-Sundermann V, Angerer J. Phthalates: Toxicology and exposure. *Int J Hyg Environ Health* 2007;210: 623-34.
6. Bradbury J. UK panics over phthalates in baby milk formulae. *Lancet* 1996;347:1541
7. Wensing M, Uhde E, Salthammer T. Plastics additives in the indoor environment-Flame retardants and plasticizers. *Sci Total Environ* 2005;339:19-40.
8. Schettler T. Human exposure to phthalates via consumer products. *Int J Androl* 2006;29: 134-9
9. Koch HM, Rossbach B, Drexler H, Angerer J. Internal exposure of the general population to DEHP and other phthalates—determination of secondary and primary phthalate monoester metabolites in urine. *Environ Res* 2003;93:177-85.
10. Lottrup G, Andersson AM, Leffers H, Mortensen GK, Toppari J, Skakkebaek NE, Main KM. Possible impact of phthalates on infant reproductive health. *Int J Androl* 2006;29:172-80.
11. Silva MJ, Reidy JA, Herbert AR, Preau JL, Needham LL, Calafat AM. Detection of phthalate metabolites in human amniotic fluid. *Bull Environ Contam Toxicol* 2004;72:1226-31.
12. Latini G, Del Vecchio A, Massaro M, Verrotti A, DE Felice C. In utero exposure to phthalates and fetal development. *Curr Med Chem* 2006;13:2527-34.
13. Green R, Hauser R, Calafat AM, Weuve J, Schettler T, Ringer S, et al. Huttner K, Hu H. Use of di(2-ethylhexyl) phthalate-containing medical products and urinary levels of mono(2-ethylhexyl) phthalate in neonatal intensive care unit infants. *Environ Health Perspect* 2005; 113:1222-5.
14. Erkekoğlu P, Giray B, Durmaz E, Özmert E, Kızılgün M, Derman O, et al. Fitalat teması ile plazma amilaz ve lipaz düzeyleri arasındaki ilişkinin pubertal jinekomasti hastalarında değerlendirilmesi. *Türk Ped Arş* 2010;45:366-70.
15. Food and Drug Administration (FDA) Safety Assessment: Safety Assessment of Di(2-ethylhexyl) phthalate (DEHP) Released from PVC Medical Devices. Center for Devices and Radiological Health. URL: <https://www.fda.gov/downloads/MedicalDevices/.../UCM080457.pdf>
16. Draft position statement on DEHP in medical devices for stakeholder consultation. Canadian Government Agency Expert Panel Position. Health Canada (2003) URL: <https://www.canada.ca/en/health->

- canada/corporate/about-health-canada/accountability-performance-financial-reporting/evaluation-reports/evaluation-medical-devices-program-1999-2000-2011-2012.html
17. URL:<http://www.resmigazete.gov.tr/main.aspx?home=http://www.resmigazete.gov.tr/eskiler/2011/06/20110607.htm&main=http://www.resmigazete.gov.tr/eskiler/2011/06/20110607.htm>
 18. U.S. Department of Health and Human Services. Toxicological profile for di(2ethylhexyl) Phthalate. September 2002.
 19. Hauser R, Calafat AM. Phthalates and human health. *Occup Environ Med* 2005;62:806-18.
 20. Latini G, Avery GB. Materials degradation in endotracheal tubes: a potential contributor to bronchopulmonary dysplasia. *Acta Paediatr* 1999;88:1174-5.
 21. Von Rettberg H, Hannman T, Subotic U, Brade J, Schettler T, Ringer S, et al. Use of Di(2Ethylhexyl) Phthalate containing infusion systems increases the risk for cholestasis. *Pediatrics* 2009;124:710-16.
 22. Sjöberg PO, Bondesson UG, Sedin EG, Gustafsson JP. Dispositions of di- and mono-(2-ethylhexyl) phthalate in newborn infants subjected to exchange transfusions. *Eur J Clin Invest* 1985;15:430-6.
 23. Kavlok R, Boekelheide K, Chapin R, Cunningham M, Faustman E, Foster P, et al. NTP Center for the Evaluation of Risks to Human Reproduction: phthalates expert panel report on the reproductive and developmental toxicity of di(2-ethylhexyl) phthalate. *Reprod Toxicol* 2002;16:529-653.
 24. Mazzo DJ, Nguyen-Huu JJ, Pagniez S, Denis P. Compatibility of docetaxel and paclitaxel in intravenous solutions with polyvinyl chloride infusion materials. *Am J Health-Syst Pharm* 1997;54:566-9.
 25. Ramadan M, Cooper B, & Posnack NG. Bisphenols and phthalates: plastic chemical exposures can contribute to adverse cardiovascular health outcomes. *Birth Defects Res.* 2020;112:1362–1385.
 26. Kaestner F, Seiler F, Rapp D, Eckert, E, Muller J, Metz C, et al. Exposure of patients to di(2-ethylhexyl) phthalate (DEHP) and its metabolite MEHP during extracorporeal membrane oxygenation (ECMO) therapy. *PlosOne* 2020;15(1):e0224931. doi: 10.1371/journal.pone.0224931.
 27. Gaynor JW, Ittenbach RF, Calafat AM, Burnham NB, Bradman A, Bellinger DC, et al. Perioperative exposure to suspect neurotoxicants from medical devices in newborns with congenital heart defects. *Ann. Thorac. Surg* 2018;107:567–572.
 28. Malarvannan G, Onghena M, Verstraete S, van Puffelen E, Jacobs A, Vanhorebeek I, et al. Phthalate and alternative plasticizers in indwelling medical devices in pediatric intensive care units. *J. Hazard. Mater* 2019;363:64–72.
 29. Münch F, Höllerer C, Klapproth A, Ecker, E, Rüffer A, et al. Effect of phospholipid coating on the migration of plasticizers from PVC tubes. *Chemosphere* 2018;202:742–9.
 30. Tasdogan A, Erkin Y, Gonullu E, Duru LS. Effects of line type blood-liquid warmer on two different infusion sets. *J Pak Med Assoc* 2015;65:362-5.
 31. URL: <http://www.titck.gov.tr/Kurumsal>
 32. URL: <http://www.titck.gov.tr/Kurumsal/GorevAlanlari>
 33. URL:<http://www.resmigazete.gov.tr/main.aspx?home=http://www.resmigazete.gov.tr/eskiler/2005/10/20051020.htm&main=http://www.resmigazete.gov.tr/eskiler/2005/10/20051020.htm>
 34. Chiellini F, Ferri M, Morelli A, Diapola L, Giuseppe L. Perspectives on alternatives to phthalate plasticized poly(vinyl chloride) in medical devices applications. *Progress in Polymer Science* 2013;38:1067–88.
 35. Latini G, Felice CD, Verrotti A. Plasticizers, infant nutrition and reproductive health. *Reprod Toxicol* 2004;19:27-33.
 36. URL:<http://www.kimyahaberleri.com/avrupa-birligi-dort-ftalatli-kimyasali-daha-kisitlamaya-hazirlaniyor/>

Appendix1: The survey used in this study

A1. Your age:

A2. Your gender:

☐ Female

☐ Male

A3. Your academic career:

☐ Research assistant

☐ Specialist

☐ Teaching assistant

☐ Lecturer

A4. Number of years working in the field of
anesthesia (years):

A5. Province of employment:

A6. Organization of employment:

☐ State Hospital

☐ University Hospital

☐ Education and Research Hospital

☐ Private Hospital

☐ Other ()

B1. Have you ever heard the name DEHP?

☐ Yes

☐ No

☐ No idea

**If your answer is “No” or “No idea”, just write
the brand names of material you use in answer to
B3.1 to B3.12 and then complete the survey.**

B2. Do you know where DEHP is used?

☐ Yes

☐ No

☐ No idea

B3. Do you use material(s) containing DEHP?

☐ Yes

☐ No

☐ No idea

B3.1. Do the “examination gloves” you use contain
DEHP?

☐ Yes

☐ No

☐ No idea

*** Brand name:

I don't know : ☐

B3.2. Does the “brannula” you use contain DEHP?

☐ Yes

☐ No

☐ No idea

*** Brand name:

I don’t know : ☐

B3.3. Does the “nasogastric probe” you use contain DEHP?

☐ Yes

☐ No

☐ No idea

*** Brand name:

I don’t know : ☐

B3.4. Does the “central venous catheter” you use contain DEHP?

☐ Yes

☐ No

☐ No idea

*** Brand name:

I don’t know : ☐

B3.5. Does the “epidural set” you use contain DEHP?

☐ Yes

☐ No

☐ No idea

*** Brand name:

I don’t know : ☐

B3.6. Does the “dosiflow” you use contain DEHP?

☐ Yes

☐ No

☐ No idea

*** Brand name:

I don’t know : ☐

B3.7. Does the “injector” you use contain DEHP?

☐ Yes

☐ No

☐ No idea

*** Brand name:

I don’t know : ☐

B3.8. Does the “endotracheal tube” you use contain DEHP?

☐ Yes

☐ No

☐ No idea

*** Brand name:

I don’t know : ☐

B3.9. Does the “laryngeal mask” you use contain DEHP?

☐ Yes

☐ No

☐ No idea

*** Brand name:

I don't know : ☐ Evet

B3.10. Does the “ventilator cycle” you use contain DEHP?

☐ Yes

☐ No

☐ No idea

*** Brand name:

I don't know : ☐

B3.11. Does the “blood and serum set” you use contain DEHP?

☐ Yes

☐ No

☐ No idea

*** Brand name:

I don't know : ☐

B3.12. Do the “dialysis material” or “ECMO set” you use contain DEHP?

☐ Yes

☐ No

☐ No idea

*** Brand name:

I don't know : ☐

B4. Do you think there are differences between companies producing plastic material in terms of DEHP?

☐ Yes

☐ No

☐ No idea

B5. Does your hospital check whether material contains DEHP or not while choosing or buying medical material?

☐ Yes

☐ No

☐ No idea

B6. Do you think patients receiving anesthesia or in intensive care are exposed to DEHP?

☐ Yes

☐ No

☐ No idea

C1. What are the exposure routes for DEHP in anesthesia administration? (You may mark more than one)

- ☐ Peroral
- ☐ Inhalation
- ☐ Intravenous
- ☐ Dermal
- ☐ No idea

C2. Which of the following do you think DEHP exposure can cause? (You may mark more than one)

- ☐ Harmful effects on the fetus
- ☐ Abnormalities in pubertal development
- ☐ Undescended testis, hypospadias development
- ☐ Increased anogenital openings
- ☐ Endometriosis
- ☐ Liver adenoma and hepatocellular cancer development
- ☐ Thyroid structure and activity changes
- ☐ No idea

D1. Which patient(s) are at risk of DEHP exposure in anesthesia administration? (You may mark more than one)

- ☐ Pregnant cases
- ☐ Premature case
- ☐ Children
- ☐ Adults
- ☐ No idea

D2. What do you think affects the DEHP release rate from material used? (you may mark more than one)

- ☐ pH
- ☐ Temperature
- ☐ Fluid content
- ☐ Exposure duration
- ☐ No idea

D3. What do you think DEHP release may cause in the lungs? (you may mark more than one)

- ☐ Pulmonary injury
- ☐ Bronchopulmonary dysplasia
- ☐ Increased bronchial sensitivity
- ☐ No idea

D4. What complications may be expected due to the use of tools containing DEHP in surgeries related to the cardiovascular system? (You may mark more than one)

- ☐ Platelet aggregation
- ☐ Complement activation
- ☐ No idea

D5. Do you think the Ministry of Health has made any announcements about DEHP?

- ☐ Yes
- ☐ No
- ☐ No idea

D6. Do you think the *Food and Drug Administration* (FDA) has made any announcements about DEHP?

- ☐ Yes
- ☐ No
- ☐ No idea