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PAPER

Increased metal concentrations in exhaled breath condensate of industrial welders†

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It was the aim of this study to evaluate the effect of different devices on the metal concentration in exhaled breath condensate (EBC) and to prove whether working conditions in different welding companies result in diverse composition of metallic elements. The influence of two collection devices (ECoScreen, ECoScreen2) on detection of metallic elements in EBC was evaluated in 24 control subjects. Properties of ECoScreen and a frequent use can alter EBC metal content due to contamination from metallic components. ECoScreen2 turned out to be favourable for metal assessment. Concentrations of iron, nickel and chromium in EBC sampled with ECoScreen2 were compared between non-exposed controls and industrial welders. Metal concentrations in EBC were higher in 36 welders recruited from three companies. Exposure to welding fumes could be demonstrated predominantly for increased iron concentrations. Concentrations of iron and nickel differed by working conditions, but chromium could not be detected in EBC.

Introduction

The respiratory system represents the route of entry for many environmental and occupational pollutants. During the last decades the concept of inflammation as a hallmark in the pathophysiologic cascade leading to respiratory diseases has gained much attention. Therefore, characterization of the underlying mechanisms and evaluation of local biomarkers involved in inflammation and oxidative stress could help to verify respiratory diseases at a subclinical stage.[1] Sampling of exhaled breath condensate (EBC) is a non-invasive way to get information on inflammation without affecting airway function.[2] A wide variety of locally produced or released substances reflecting inflammation and oxidative stress have already been detected in EBC. With respect to respiratory physiology particulate size substances like metals reaching the lung by inhaled air could also be detected in EBC.[3]

Inhaled metallic elements are implicated in alteration of cellular homeostasis, cellular damage, tissue remodelling and the development of inflammatory lung diseases. They represent a risk factor for asthma, chronic obstructive pulmonary disease (COPD) or may lead to pulmonary fibrosis or even lung cancer.[4] High level exposure to metals is often a consequence of special working conditions and it was shown that occupationally inhaled metals are detectable in EBC (chromium,[5,6] cobalt, tungsten[7,8]). Welding is widely applied in industry and indispensable in modern society. Different metal fumes and gases are generated according to the material and method used for the welding process. Stainless steel (SS) welding fumes contain significant

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Environmental impact

Collection of exhaled breath condensate (EBC) is completely non-invasive and provides a matrix for the evaluation of airways diseases. Besides the analyses of markers reflecting effects, *e.g.* inflammation, EBC may contribute to monitor environmental exposures. Amongst others, the composition of the condensate depends on physical characteristics of the condensing device. Concerning the assessment of metallic elements in EBC, we identified contaminations from metallic components of a device (ECoScreen). Using a condensing device with special surface properties (ECoScreen2), we measured increased metal concentrations in EBC of industrial welders. Our findings reinforce the idea that metal content of EBC might reflect different exposure conditions at a target level.

levels of nickel and chromium added for resistance against corrosion, whereas mild steel (MS) predominantly causes iron fumes. These metals have a specific relevance in the assessment of work-related health hazards.[9] Different metals involved in welding processes, namely chromium and nickel, are classified as class 1 carcinogens according to the International Agency for Research on Cancer (IARC).[10]

EBC may not only be a suitable matrix for assessing markers of inflammation and oxidative stress. As EBC reflects the epithelial lining fluid, metal analysis in EBC may be a suitable way to assess pneumotoxic substances such as metals at the target level providing a measure of exposure.[11] Recent studies highlighted that physical characteristics of the condensing device influence the efficiency of collection and detection of biomarkers in EBC.[12] Moreover, there is evidence that the device itself can cause errors in the measurement of markers.

The first aim of our study was to evaluate different collecting devices and to validate the detection of metals in EBC. ECoScreen is a commercially available device and widely used for EBC sampling.[13] However, it may have limitations in metal analysis as exhaled breath is condensed on a Teflon-coated metal surface which is repeatedly used. Therefore, we addressed the feature of wearing down comparing EBC collected by a new and an old device. In addition, EBC was also recovered by ECoScreen2 and analyzed for metal content. ECoScreen2 is also temperature-controlled but uses polyethylene bags as disposable condensing modules and its validity for measurement of biomarkers has recently been demonstrated.[14]

Secondly, we investigated whether EBC metal composition might reflect special working conditions in different welding companies. EBC might be of particular interest in preventive medicine since inflammatory processes triggered by environmental and occupational pollutants usually precede changes in lung function. Previous studies on EBC have shown a trend for pH increase in healthy workers exposed to welding fumes[15] and an occult airway inflammation being a function of the exposure profile.[16] To the best of our knowledge, there are no data so far concerning patterns of metal concentrations in EBC of industrial welders.

Experimental

Study population

Sixteen non-smoking and eight smoking healthy volunteers without lung diseases and without occupational exposure participated in the study for the evaluation of the different devices. All reference subjects were without medication, had no history of chronic respiratory disorders and reported no symptoms of an upper respiratory infection within the previous six weeks. These healthy volunteers were compared with the welders.

A total of 36 workers from three different companies were enrolled; 12 welders were recruited from each company, respectively. All participants were without respiratory symptoms and underwent regular medical health surveillance. They were processing different quantities of SS and/or MS under different working conditions expected to result in different levels of metal exposure. According to this, welders of company B were solely exposed to MS, whereas welders of companies A and C were exposed to MS or SS. All participants underwent evaluation of spirometry within 1 day of the measurement of EBC using a MasterLab pro (Software version 4.67a, Cardinal Health, Hoechberg, Germany). According to the American Thoracic Society (ATS) criteria, forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV_1) were obtained from three acceptable maneuvers.[17] Normal lung function was defined as $FEV_1 \geq 80\%$ predicted and FEV_1/FVC ratio $\geq 70\%$. The study was approved by the local Ethics Committee and all participants gave written informed consent. Demographic and clinical characteristics of the study populations are depicted in Table 1.

Collection of EBC

EBC in each subject was collected *ante meridiem* as previously described.[18] Briefly, EBC was collected during tidal breathing while sitting comfortably; the subjects used a nose-clip, breathed through a mouthpiece and they were instructed to swallow excess of saliva after coming off the mouthpiece. Two different types of condensers, ECoScreen (Cardinal Health, Hoechberg, Germany) and ECoScreen2 (FILT, Berlin, Germany), were used for assessment of metals in EBC. ECoScreen condenses the exhaled breath on a Teflon coated surface which is repeatedly used and therefore washed with ultra-pure water and wiped clean before each test. The ECoScreen2 device directly condensed and collected the EBC in disposable bags on a special polyethylene surface. EBC collections were performed at the same day with a 30 min interval between each sample collection. Total ventilation was measured by an inserted pneumotachograph (Eco-Vent, Cardinal Health, Hoechberg, Germany) when using ECoScreen or by an integrated pneumotachograph in the case of ECoScreen2. For each time point, EBC was collected for exactly 10 min and during the collection period a temperature of −20 °C was maintained by both condenser types. Good reproducibility of minute ventilation, volume of condensate and various biomarkers was demonstrated recently.[14]

Table 1 Characteristics of the study subjects[a]

Category	Reference group	Welders (total)	Company A	Company B	Company C
N (female/male)	14/10	0/36	0/12	0/12	0/12
Smoking (no/yes)	16/8	23/13	7/5	9/3	7/5
Age (years)	48.0 (18–60)	46.0 (23–59)	47.4 (23–59)	42.8 (35–55)	44.1 (27–56)
FVC % predicted	108.8 (91.1–137.2)	110.1 (85.5–145.9)	106.1 (85.5–115.7)	115.9 (98.3–131.3)	117.0 (96.7–145.9)
FEV_1 % predicted	100.3 (80.1–132.8)	105.0 (78.5–130.2)	100.5 (78.5–113.2)	113.2 (90.3–126.3)	105.8 (89.8–130.2)
FEV_1/FVC (%)	80.7 (70.1–94.2)	77.3 (63.7–87.6)	78.5 (69.1–86.1)	79.1 (74.0–87.6)	74.3 (63.7–80.6)

[a] Data are expressed as median (range). FVC = forced vital capacity; FEV_1 = forced expiratory volume in 1 s.

The effect of long term mechanical wear was evaluated in the healthy non-exposed volunteers (n = 24). Therefore, a new ECoScreen device and a 20 month old frequently and repeatedly used one (old ECoScreen) were applied and compared to ECoScreen2 in a randomised sequential order. The order of EBC collection was randomized and performed according to general methodological recommendations on the collection and analysis of EBC.[19] EBC in welders was collected after shift using ECoScreen2.

Sample processing and metal determination

After EBC collection, samples were aliquoted and immediately stored at −70 °C. Within 2 months the aliquoted samples were thawed and analysed for the metals chromium, iron, and nickel, respectively. All EBC samples were analysed in a blinded way for the new ECoScreen, old ECoScreen and ECoScreen2 device. The samples were analysed in duplicate or triplicate and run together to exclude interassay variation.

Measurements of metals in EBC were determined by means of atomic absorption spectrometry using the graphite furnace technique (GF-AAS; ZEEnit 700 from Analytic Jena, Germany). No previous sample preparation was performed. For the purpose of analysis, dilute nitric acid was added to the EBC sample. Atomization temperatures were 2450 °C for chromium, 2150 °C for iron and 2500 °C for nickel, and the atomic absorption wavelengths were 357.9, 248.3 and 232.0 nm, respectively. Interference caused by matrix effects was minimized by the use of the Zeeman effect background compensation. Calibration was carried out using the standard calibration procedure. The limit of detection (LOD), calculated as three times the standard deviation of the reagent blank value, was 0.25 μg L^{-1} for chromium and 1.0 μg L^{-1} for iron and nickel, respectively. Chromium was determined as total chromium (Cr—VI and reduced Cr—III). Quality control material was prepared in the laboratory. For this purpose water was spiked with chromium (0.3 μg L^{-1}), iron (2.5 μg L^{-1}) or nickel (2.5 μg L^{-1}). Aliquots of these materials were stored at −19 °C and used for quality control for every day analysis. The mean expected values and the tolerance ranges (±3fold standard deviation) of these quality control materials were obtained in a pre-analytical period. The between series imprecision (n = 12) was 10.3% for chromium, 4.0% for iron, and 3.8% for nickel, and the mean recovery (n = 12) was 101%, 98% and 99%, respectively.

In vivo study for blank contamination

Ultrapure water (10 mL, Merck, Darmstadt, Germany) was exposed to the various sampling devices (new ECoScreen, old ECoScreen, and ECoScreen2) for 1 and 10 min, respectively. These control experiments were performed three times and subsequently samples of the blank solutions were analysed in a blinded way for chromium, iron, and nickel.

Statistical analysis

Value distribution was assessed using the D'Agostino & Pearson omnibus normality test. Comparisons of paired data were performed with paired t-test or Wilcoxon test and of unpaired data with unpaired t-test and Welch's correction, where appropriate. Values below the LOD were set to 2/3 of LOD. The data were analysed by using GraphPad Prism version 5.01 for Windows (GraphPad Software, San Diego, California, USA, www.graphpad.com). A two-sided significance level of 0.05 was chosen for all tests. Metal concentrations were expressed as medians with interquartile ranges.

Results

Measurable metal concentrations in control subjects

All 24 subjects from the reference group produced sufficient total EBC sample volumes. Triplets of aliquots derived from the old ECoScreen, the new ECoScreen and ECoScreen2 were available for the pairwise assessment of the influence of device properties on the metal concentrations in EBC. The following EBC volumes could be collected within 10 min of tidal breathing: new ECoScreen (median 1.20 mL; interquartile range 1.00–1.50 mL), old ECoScreen (1.40; 1.30–1.60 mL), and ECoScreen2 (1.45; 1.11–1.95 mL). Although the volume differed significantly when comparing the old and new ECoScreen devices (p = 0.0046), there was still a strong correlation apparent between the sample volumes collected with both devices ($r = 0.84$, $p < 0.0001$). After 10 min of tidal breathing, a lower EBC volume was collected from smokers compared to non-smokers (median 1.25 mL; interquartile range 1.05–1.44 mL *vs.* 1.48; 1.16–1.70 mL); although this did not reach a statistical significance ($p = 0.062$). Voluntary ventilations in 10 min assessed by an integrated tachograph (ECoScreen2) or by EcoVent (ECoScreen) were not significantly different ($p > 0.05$, data not shown).

In most of the EBC samples, chromium was below the LOD. With the old ECoScreen condenser, 5 of 24 samples demonstrated chromium concentrations above the LOD of the assay; with the new ECoScreen and with the ECoScreen2 device 2 of 24, respectively. However, nickel and iron could be determined above LOD in most EBC samples. Again, the collection procedure was a significant determinant for measurable concentrations of both metals. Concerning nickel, the proportions were 23/24 (old ECoScreen), 20/24 (new ECoScreen), and 16/24 (ECoScreen2), respectively. Finally, in the case of iron the proportions were 17/24 (old ECoScreen), 15/24 (new ECoScreen), and 14/24 (ECoScreen2), respectively.

Metal concentrations according to sampling devices

Significant differences could be revealed when metals were analysed in samples from the same volunteers obtained either with the old ECoScreen, the new ECoScreen or the ECoScreen2.

Collecting EBC by the two ECoScreen devices yielded significantly higher nickel concentrations than by using ECoScreen2 (old ECoScreen: 3.68 (1.95–5.38) μg L^{-1} *vs.* 1.20 (0.67–2.07) μg L^{-1}, $p < 0.0001$; new ECoScreen: 2.16 (1.40–4.14) μg L^{-1} *vs.* 1.20 (0.67–2.07) μg L^{-1}, $p = 0.005$). A significant difference was also determined concerning the feature of frequent use (old ECoScreen: 3.68 (1.95–5.38) μg L^{-1} *vs.* new ECoScreen: 2.16 (1.40–4.14) μg L^{-1}; $p = 0.027$) (Fig. 1A).

Concerning iron, there was also a significant influence of the collection device. Samples derived from the old ECoScreen showed the highest concentrations (old ECoScreen: 4.09 (0.67–7.82) μg L^{-1} *vs.* new ECoScreen: 1.27 (0.67–3.36) μg L^{-1},

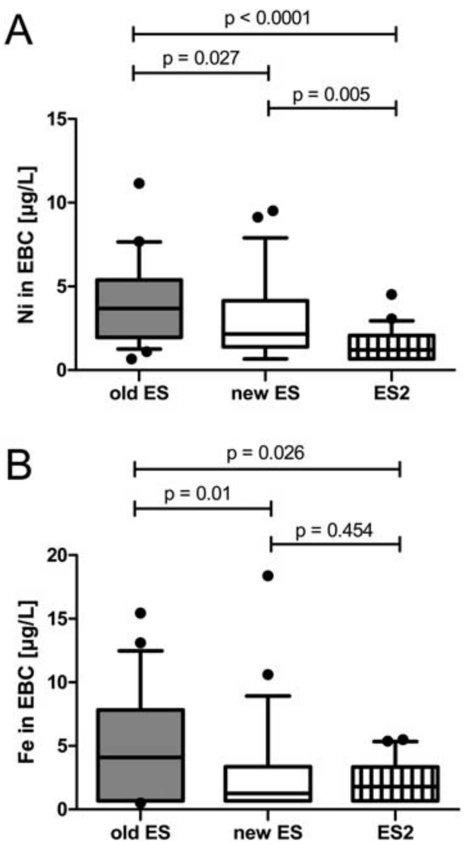

Fig. 1 Ni (A) and Fe (B) concentrations in EBC of reference subjects ($n = 24$) sampled with a frequently used (old ES) or new ECoScreen (new ES), and ECoScreen2 (ES2).

$p = 0.010$ and *vs.* ECoScreen2: 1.79 (0.67–3.34) µg L^{-1}, $p = 0.026$, respectively). However, there was no significant difference in the iron concentration detected in EBC derived from the new ECoScreen or ECoScreen2 device (new ECoScreen: 1.27 (0.67–3.36) µg L^{-1} *vs.* ECoScreen2: 1.79 (0.67–3.34) µg L^{-1}, $p = 0.454$) (Fig. 1B).

Evaluation of blank solutions after exposure to ECoScreen2 for up to 10 min did not reveal any measurable metal concentrations. In contrast, the concentrations of the selected metals were significantly altered post-incubation in the aged ECoScreen device. The concentrations of chromium, iron, and nickel showed good reproducibility in the three experiments. In the case of iron, a significant contamination due to ECoScreen could be demonstrated even in the new condenser in 2 out of 3 experiments (Fig. S1†).

Metal concentrations in welders compared to non-exposed subjects

EBC was collected by ECoScreen2 in 36 welders recruited from three companies and concentrations of iron, nickel and chromium were assessed and compared to levels derived from the reference subjects group applying ECoScreen2. In all of the 36 welders' samples, iron concentrations could be quantified. All but one welder produced a sufficient sample volume for assessment of the other two metal concentrations. In most of these samples (31/35) the concentrations of chromium were below the LOD of the assay, whereas nickel could be determined in most EBC samples (33/35). There was a significant increase of both nickel and iron concentrations in EBC from welders compared to

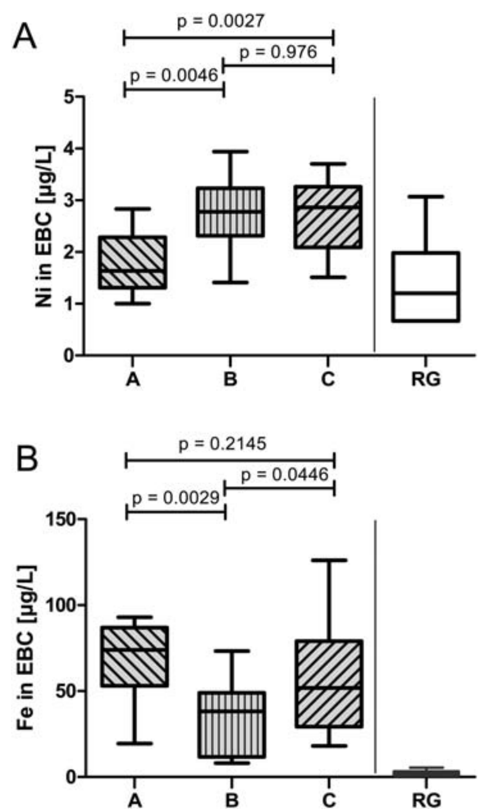

Fig. 2 Ni (A) and Fe (B) concentrations in EBC sampled with ECoScreen2 in the reference group ($n = 24$; RG) and in 36 welders from three companies. Company A ($n = 12$; MS/SS), company B ($n = 12$; MS), and company C ($n = 12$, MS/SS).

Table 2 Metal concentrations of nickel and iron in EBC (ECoScreen2) by smoking and exposure[a]

	Reference group		Welders	
Metal (EBC)	Non-smokers	Smokers	Non-smokers	Smokers
Ni/µg L^{-1}	($n = 16$) 1.65 (0.76–2.05) $p = 0.330$	($n = 8$) 0.86 (0.67–1.99)	($n = 23$) 2.47 (1.58–2.93) $p = 0.486$	($n = 12$) 2.63 (1.75–3.17)
Fe/µg L^{-1}	($n = 16$) 1.79 (0.67–4.51) $p = 0.887$	($n = 8$) 1.30 (0.67–4.74)	($n = 23$) 49.84 (25.86–84.81) $p = 0.719$	($n = 13$) 50.19 (32.24–65.10)

[a] Data are expressed as median (interquartile range).

control subjects when EBC was collected with the ECoScreen2 device (nickel: 2.47 (1.65–2.99) μg L^{-1} *vs.* 1.20 (0.67–2.07) μg L^{-1}, $p = 0.0003$ and iron: 50.02 (26.46–79.01) μg L^{-1} *vs.* 1.79 (0.67–3.34) μg L^{-1}, $p < 0.0001$, respectively). Exposure to cigarette smoke did not lead to altered metal concentrations in EBC. Results stratified according to the smoking habit are depicted in Table 2.

Metal concentrations in welders according to working conditions in different companies

Referring to nickel, concentrations determined in EBC were significantly lower in company A (1.64 (1.31–2.28) μg L^{-1}) compared to values obtained in welders of company B (2.78 (2.31–3.23) μg L^{-1}, $p = 0.0027$) or company C (2.86 (2.09–3.26) μg L^{-1}, $p = 0.0046$), respectively. There was no difference in nickel concentrations between companies B and C ($p = 0.976$) (Fig. 2A).

Referring to iron, concentrations determined in EBC were significantly lower in company B (38.13 (11.63–48.96) μg L^{-1}) compared to values obtained in welders of company A (73.91 (53.06–86.92) μg L^{-1}, $p = 0.0029$) or company C (51.76 (29.29–79.01) μg L^{-1}, $p = 0.0446$), respectively. There was no significant difference between companies A and C ($p = 0.2145$) (Fig. 2B).

Taken together, there was only a minority of welders with elevated levels (>LOD) of chromium. Welders of the three companies could be discriminated by the metal concentrations of nickel and iron in EBC. Metal concentrations in EBC of both nickel and iron were quite high in company C, whereas nickel in company A and iron concentrations in company B were comparable low but still higher than in the reference group, respectively.

Discussion

Occupational exposure to metals occurs mainly by inhalation. Welding is a major source of fumes containing several metals like chromium, nickel or iron. Metals are essential co-factors in enzymes and proteins, but can also promote oxidative injury, exhibit toxic features and are involved in triggering inflammatory processes. There is evidence that EBC may not only be a matrix for assessing inflammatory processes in the airways but could also reflect exposure to inhaled agents at the target level.[11]

It was reported that the collecting device itself may account for modulation of the level of compound under investigation. There are only limited data reporting concentrations of metallic elements in EBC and comparative studies concerning methodical impacts on metal analysis in EBC are lacking. As EBC mainly consists of water that is practically free of interfering substances, it is an ideal matrix for determinations of metals relying on techniques such as the applied graphite furnace atomic absorption spectrometry (GF-AAS).

The results of our study indicate that the commercially available collecting system ECoScreen might have limitations when analysing metals (*e.g.* Ni and Fe) in EBC, especially when the device is aged and frequently used. In this context, it is to stress that the exhaled breath condenses in that device on the surface of a re-useable double lumen lamellar metal module with a modified inner Teflon coating. The significant higher metal level in the old device indicated the probability that the Teflon coating becomes inefficient and the underlying metal is a source of EBC contamination. We could demonstrate significant concentrations of metals in blank solutions after exposure to the Teflon-coated metal module of the ECoScreen device. This effect was time dependent and most apparent in the case of an aged and frequently used device and indicates contamination. Overall, even in a new ECoScreen device, contamination with metals should be considered. In contrast, the concentration of metals was below the LOD in the case of ECoScreen2 and this device was applied for further studies on metals in exhaled breath condensate. ECoScreen2 is a single-use disposable condensing and collection system composed of a special polyethylene surface demonstrated to be suitable in terms of mediator assessment.[14]

Despite the fact that the LOD of the chromium assay was lower in comparison with the iron and nickel ones (0.25 *vs.* 1.0 μg L^{-1}), the concentrations of Cr were below this method's LOD of 0.25 μg L^{-1} in most of the samples collected. In healthy adults serving as control group for chrome-plating workers, a mean total Cr in EBC of 0.28 μg L^{-1} was measured with GF-AAS (LOD: 0.05 μg L^{-1}).[5] Concerning Ni, our results are consistent with reports on healthy controls presenting a concentration of approx. 0.77 μg L^{-1}; smokers had lower levels.[20]

Our results are also in line with recent investigations reporting median Fe concentrations of 1.2 μg L^{-1} in EBC from healthy non-smokers using TURBO-DECCS (ItalChill, Parma, Italy).[21] However, the same group also reported median concentrations close to 10 μg L^{-1} in samples of a group with comparable age when applying the same device.[20] Interestingly, lower levels of EBC-iron were reported in children with asthma which may be related to modification of iron homeostasis.[22] EBC concentrations of the pneumotoxic metallic elements Cr and Ni were recently shown to be higher in patients with interstitial lung diseases (ILD) of unknown aetiology compared to non-smoking healthy controls.[21] Like in our study, Cr was below the LOD in most of the controls.

There are only limited data on EBC metal levels in the context of occupational exposure. It was shown that cobalt and tungsten are detectable in EBC of accordingly exposed workers.[7,8] Other field studies focused on EBC-chromium and investigated total[5] as well as hexavalent chromium in chrome-plating workers.[6] Exposed workers had higher concentrations of chromium in EBC than controls. Moreover, the fractional contribution of hexavalent Cr to total Cr in EBC decreased with the time from the last exposure.

The main objective of this study was to evaluate the metal composition of EBC in welders in an occupational field setting. The chemical properties of welding fumes vary due to differences in the materials used and methods employed and can be quite complex. Potentially harmful agents include metallic elements. Stainless steel (SS) welding fumes contain significant levels of nickel (approx. 10%) and chromium (approx. 20%), whereas mild steel (MS) welding fumes are known to contain mostly iron (>80%). Often, welding materials are alloy mixtures of metals characterized by different steels. For our preliminary study, we chose three companies where different steels were predominantly processed expected to differ significantly in the metal composition of the corresponding welding fumes. In this way, employees of company B processed mostly MS, while welders of companies A and C had no preference of steels and were expected to be exposed to fumes of SS and MS.

Alveolar macrophages and epithelial cells are known to be efficient in removing metals from the lower airways; however, one fifth of the iron amount is to be expected to remain in the epithelial lining fluid.[23] As EBC reflects the epithelial lining fluid, metal analysis in EBC may be suitable to assess the metal dose at target level. Compared to bronchoalveolar lavage (BAL), sampling of EBC is non-invasive. Moreover, performing BAL in different lobes demonstrated metals to be located not homogenously but revealed an increased iron deposition with predominance within the upper lobes of smokers.[24] As BAL solely reflects the selected region of the lung, EBC reflects the total epithelial lining fluid of all ventilated airways.[25] Thus, EBC samples are expected to have several advantages in the measurement of metals in the lung.

In our study the metal composition in EBC (sampled with ECoScreen2) of welders was analyzed for the metals Fe, Cr and Ni. We measured significantly higher concentrations of iron and nickel with ECoScreen2 in welders than in non-exposed volunteers in the initial validation study. In particular iron levels in EBC of welders were in the order of a magnitude higher than values of the reference group and reported values in the literature.[21] In contrast, Cr could be measured in only a minority of samples and values were not higher than those of the reference group. In addition, our findings demonstrate that the pattern of metals in EBC reflected respective occupational exposure conditions. This is in line to recent investigations reporting that the particle burden and inflammatory cells analyzed in induced sputum depended on the type and duration of welding.[16]

It is known that metals can accumulate in tissues and metal loads of Cr, Ni and Fe increase during lifetime, especially in the lung.[26] A significant effect of age on EBC iron levels was reported.[20] Thus, it is of relevance that the mean age of the welders in the three companies did not differ significantly and therefore the observed differences in metal concentrations could not be simply attributed to the age. An important environmental source of metals is tobacco smoke. Its content depends among others on the farming conditions of tobacco plants and the metal contaminations from the soil leading to differences in the metal load according to the cigarette brands.[27] Interestingly, reduced levels of iron were reported in EBC of smokers.[20] In our validation study no impact of smoking on EBC metal content could be detected. However, larger studies are required to determine the confounding of current as well as previous smoking habits.

Metallic elements are known to be involved in the generation and detoxification of reactive oxygen species as well as in scavenging of free radicals. A good correlation between chromium levels and biomarkers of oxidative stress (H_2O_2, MDA) could be observed in EBC of otherwise asymptomatic chrome-plating workers.[5] The effect of welding on biological effect markers in exhaled breath condensate was recently addressed. Measurements of pH and hydrogen peroxide in EBC demonstrated the presence of airway inflammation in asymptomatic welders which was modulated by the different metal fumes and gases generated according to material and method used for the welding process reflecting a special exposure profile.[16] The scope of our study was to assess the internal exposure of welders and compare them with non-exposed controls. It was not designed to investigate biological effect markers. However, pH was also measured and we like to refer to these results (Fig. S2†) as corresponding changes in EBC pH with metal patterns of differently exposed welders add further validity to our findings. Recently, welding-associated health effects could be detected in pre- and post-shift measurements.[28] The results suggested that protection measures were of particular importance and nitrate in EBC seemed to be sensitive to welding fume exposure, while hydrogen peroxide in EBC might be associated with smoking rather than with welding fumes.

Conclusion

Our study demonstrates that the concentrations of metallic elements in the EBC of welders reflect different patterns according to the exposure conditions. EBC might be of particular interest in preventive occupational medicine as a matrix for biomarkers of exposure since inflammatory processes triggered by environmental and occupational pollutants may long precede airway remodelling and consecutive changes in lung function. Aside from the processed types of steel and the method used for the welding process, other variables like efficiency of ventilation or use of personal protection have to be taken into account for defining personal exposure conditions. Currently, investigations including metal determinations in EBC are under way in order to assess health effects of metal exposure in a large group of welders. Recently, we demonstrated ECoScreen2 to be particularly suitable for the detection of biomarkers involved in the pulmonary inflammatory response. Therefore, sampling of EBC in occupational research may provide a target matrix for the simultaneous monitoring of metal levels (exposure) and biomarkers reflecting the inflammatory response (effect) in the respiratory tract.

Disclosures

There are no conflicts of interest or sponsorships.

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