論文

多環芳香烴化物暴露對煉焦勞工氧化傷害評估研究

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摘要

煉焦爐勞工長期暴露煉焦爐排放物，其中對健康影響最為嚴重者為多環芳香烴化物(PAHs)，PAH除了會導致肺癌等呼吸道癌症之外，亦有可能導致泌尿系統癌症、皮膚癌與神經系統損失等疾病，本研究針對台灣某鋼鐵公司煉焦作業勞工進行橫斷面流行病學研究，由問卷調查區分為爐頂煉焦勞工（高暴露組，N=110）、爐側煉焦勞工（低暴露組，N=182）。暴露偵測包括16種PAHs，及以尿液中的1-羥基焦腦油(1-OHP)作為PAH的內在劑量暴露指標，並以尿液8-羥基-2-去氧鳥嘌呤核甘(8-OHdG)作為DNA氧化傷害指標。資料分析以線性混合效應迴歸模式評估員工之尿液中8-OHdG與1-OHP的相關性。研究結果顯示，爐頂煉焦勞工個人採樣空氣中之PAHs濃度、尿液中8-OHdG、1-OHP濃度皆顯著高於爐側煉焦勞工。以線性混合效應迴歸模式分析顯示：在校正其他干擾因子後，尿液中1-OHP、爐頂煉焦工作為尿液中8-OHdG的二個顯著影響因子，尿液中1-OHP、爐頂煉焦工作為PAHs暴露造成DNA氧化傷害的良好預測因子；本研究結果並指出煉焦勞工的DNA氧化傷害與暴露PAHs有顯著相關。

關鍵字：多環芳香烴化物、煉焦勞工、尿液中1-羥基焦腦油、尿液中8-羥基-2-去氧鳥嘌呤核甘

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前言

焦炭為鋼鐵冶煉所不可缺少的原料之一，焦碳主要來自煤，在鋼鐵廠中它是當做鐵礦精製成為鐵的主要還原劑。當煤被運至煉焦廠(Coke oven plant)時，首先從煉焦爐爐頂加入，加料完成後，推焦側爐門之上端平煤口被打開，之後以推焦車之平煤桿將爐室內煤堆堆平，當爐頂打開添加煤時及焦碳被收集和轉運的過程中，會造成瞬時性污染物排放；而爐門洩漏和爐頂蓋及氣體輸送線的洩漏，會造成連續性污染物排放[1-3]，而煉焦爐排放物含有高濃度的多環芳香烴化物(Polycyclic Aromatic Hydrocarbons,PAH)，其來源主要由於有機物燃燒不完全而產生，煉焦爐勞工長期暴露所暴露的煉焦爐排放物中，對健康影響最為嚴重者為PAH，PAH除了會導致肺癌等呼吸道癌症之外，亦有可能導致泌尿系統癌症、皮膚癌與神經系統損失等疾病；此由於PAH進入人體時，某些物種可藉由代謝而形成致癌性與致突變性物質[4]。在從動物實驗中發現PAH中具致癌性者，以含4~7環的PAH為主，其中包括Pyrene, Benzo[a]anthracene, Chrysene, Benzo[a] fluoroanthene, Benzo[e]pyrene, Benzo[a]pyrene, Benzo[k] fluoroanthene, Indeno[1,2,3-cd]pyrene, Dibenz[a,h]anthracene, Benzo[ghi]perylene等物種，致癌性強度又以Benzo[a]pyrene最具代表性[5]，因此科學界常以Benzo[a]pyrene濃度作為都市空氣污染PAH之致癌指標。

對於勞工暴露PAHs的內在劑量指標，可藉由測定尿液中的代謝物加以評估，而芘(pyrene)在PAHs中含量高，常被用來作為職業與環境中PAHs的指標物，Pyrene 由人體肺部或皮膚所吸收，然後代謝為1-羥基焦腦油(1-hydroxypyrene, 1-OHP)，最終以尿液1-OHP的型態排出體外，因此尿液中1-OHP被認為是PAHs的一項生物暴露指標[6]，可反映消防人員、鐵鑄造勞工、煉焦勞工與餐館業勞工近期的職業PAHs暴露。

細胞基因物質的危害為引發癌症的一個先期過程，8-hydroxy-2-deoxyguanosine(8-OHdG)是生物體內最豐富的氧化DNA型態，可檢測出環境中的污染物誘導生物體突變的效應[7]。測定尿液中的8-OHdG可反應出多種致癌物的影響效應，包括PAH的影響效應；8-OHdG經由化學品損壞DNA與體內核酸的修復機制，在沒有經過進一步代謝作用的情況下，經由尿液排出體外。尿液中8-OHdG的分泌反應目前氧化的DNA之損害與修補。以8-OHdG可確切評估老化、致癌情形與衍生疾病，已有充分的研究[8]。消防隊員在暴露高量的致癌物，例如：PAH，會導致尿液中8-OHdG的濃度升高[9]。

由於暴露PAHs會對人體健康造成危害，因此評估PAHs的暴露與健康效應有其必要性，本研究測定煉焦廠勞工作業環境空氣中PAHs濃度，以尿液中1-OHP做為暴露PAHs的內在劑量指標，並以尿液中8-OHdG為DNA氧化傷害指標，藉以評估暴露PAHs對煉焦作業勞工的健康效應。

研究方法

1. 研究對象

選取無心血管疾病（無心血管疾病的定義為無胸腔心臟血管部位與心臟部位疾病）、腦血管疾病、高血脂、糖尿病、腎臟病的某煉焦工廠292名男性煉焦勞工做為研究對象，並依據過去對煉焦廠勞工所測定的空氣中PAHs濃度[10]，區分爐頂煉焦勞工（包括加料車操作員、加料助手、管路員與爐頂操作員）為PAHs

暴露的高暴露組，而爐側煉焦勞工（包括推焦車操作員、導焦車操作員、淬火車操作員與燃調員和領班）為低暴露組。本研究經國防醫學院三軍總醫院人體試驗審議委員會審核通過，所有參與之研究對象，皆有繳交受試者同意書。

2. 健康問卷調查

以面對面問卷方式，蒐集研究對象(包括高暴露組與低暴露組)的基本資料（包括:年齡、身高、體重等）、工作狀況（包括：工作年資）、生活型態（包括吸菸習慣、喝酒習慣、及服用綜合維他命習慣），與疾病狀態。

3. 作業環境中空氣中多環芳香烴化物之粒狀物個人採樣測定[10]

以玻璃纖維濾紙為採樣介質，主動式採樣泵採集作業環境空氣中粒狀物之多環芳烴化物，採樣流速為2.0L/min，採集時間8小時，之後將採集的玻璃纖維濾紙加入2ml n-Hexane以超音波萃取20min，再加入4ml 5%NaOH處理，以3,000rpm離心10min，取1.5ml上清液，以二甲基硫酸鹽(dimethyl sulfate)進行溶劑置換，之後用氮氣濃縮，使用氣相層析質譜儀(GC/MS)分析16種多環芳烴化物，包括naphthalene, acenaphthylene, acenaphthene, fluorene, phenanthrene, anthracene, pyrene, fluoranthene, benzo(a)anthracene, chrysene, benzo(b)fluoranthene, benzo(k)fluoranthene, BaP, indeno(1,2,3-cd)pyrene, dibenzo(a,h)anthracene, benzo(ghi)perylene，分析方法偵測極限範圍為6.1 ng(dibenzo(a,h)anthracene)- 9.0 ng (phenanthrene)。

4. 尿液中1-羥基焦腦油 (1-OHP) 測定分析 [11, 12]

取尿液上清液10mL置於三角燒瓶中，加入10mL醋酸鹽緩衝溶液並調整pH值至5.0，再加入20 μl β-glucuronidase/sulfatase酵素進行水解，於37℃之水浴振盪槽中培養24小時。濃縮淨化步驟先以5mL之甲醇通過固相萃取管達到淨化目的後，以10mL去離子水沖洗予以活化。將培養完成的尿液以固相萃取管進行萃取，利用真空裝置輔助控制過濾流速在3mL/min以內，當尿液樣本完全過濾後再以10mL去離子水沖洗固相萃取管並將濾液捨棄。以6mL異丙醇進行沖提將濾液收集於試管中，將此試管置於吹氮濃縮裝置，在50℃乾浴下以氮氣將溶液吹乾，再加入2mL異丙醇將殘留物溶出並放置於超音波振盪器中予以振盪4分鐘。最後以塑膠針筒配合圓盤過濾頭將濃縮液進行過濾並將濾液收集於1.8mL玻璃小瓶中，以Waters 2695 HPLC與Water474螢光檢測器於激發波長(Excitation wavelength)：281nm、放射波長(Emission wavelength)：388nm進行分析。分析方法的偵測極限將1.0 μg/L的1-OHP標準溶液，依照實驗中所使用的最佳操作條件重複測定七次，計算所得標準偏差乘上3倍，即得分析方法偵測極限。1-OHP的分析方法偵測極限為 0.1 μg/L，重複分析所測得的變異係數低於10%。

5. 尿液中8-OHdG [11]

將尿液樣品以去離子水稀釋五倍後，以HPLC/MS/MS儀器分析尿液中8-OHdG測定分析。將試劑空白（純水）依照實驗中所使用的

最佳操作條件重複測定七次，計算所得標準偏差乘上3倍，即得分析方法偵測極限。8-OHdG的偵測極限為5.7ng/L，重複分析所測得的變異係數低於5%。

6. 尿液中肌酸酐(creatinine)

尿液中肌酸酐以Jaffe反應法[11]測定，尿液中1-OHP與8-OHdG皆分別以肌酸酐作校正。

7. 採樣時間

多環芳香族碳氫化合物之粒狀物個人採樣測定於週末進行採樣測定，尿液中1-OHP與8-OHdG於週末下工後進行採樣測定。

8. 統計分析

健康問卷資料、作業環境測定結果、生物檢體測定結果經整理、確認無誤後，編碼與電腦鍵入建檔，及進行描述性統計分析、卡方分析、學生式t檢定、無母數分析（Mann-Whitney U test 檢定）、線性混合效應迴歸模式(Linear mixed-effects regression analysis)，以Spearman相關分析評估1-OHP與16種PAHs之相關性，以及評估8-OHdG與16種PAHs之相關性，統計套裝軟體則使用S-PLUS 2000(MathSoft Inc., Cambridge, MA, USA)，並設定顯著水準 α=0.05。

結果

煉焦勞工之基本資料如表1所示，共完成292名男性煉焦勞工之問卷調查，煉頂煉焦勞工之平均年齡為44.6±8.9歲，與爐側煉焦勞工之平均年齡44.9±9.5歲無顯著差異；爐頂煉焦勞工的平均BMI為24.4±3.7kg/m^2，與爐側煉焦勞工的BMI(24.9±9.8kg/m^2) 無顯著差異；煉頂煉焦勞工的平均工作年資為為13.1±7.1年，顯著低於爐側煉焦勞工的17.6±12.4年；而煉頂煉焦勞工有吸菸習慣者的比率為60.0%，顯著高於爐側煉焦勞工有吸菸習慣者的比率(44.5%)(p=0.007)；煉焦勞工有飲酒習慣者佔17.3%，與爐側煉焦勞工無顯著差異；煉頂煉焦勞工有服用維生素習慣者的比率為27.2%，與爐側煉焦勞工之有服用維生素習慣者的比率無顯著差異。

尿液中8-OHdG濃度，用於評估DNA氧化傷害指標，而尿液中1-OHP為勞工暴露PAHs的良好內在劑量指標[11]，煉焦勞工的尿液中8-OHdG與1-OHP濃度如表1所示，煉頂煉焦勞工的尿液中8-OHdG的幾何平均濃度，顯著高於爐側煉焦勞工；而煉頂煉焦勞工的尿液中1-OHP的幾何平均濃度，亦顯著高於爐側煉焦勞工。

煉焦勞工之多PAHs的個人採樣濃度比較分析如表2所示，煉頂煉焦勞工作業環境空氣中acenaphthene, phenanthrene, anthracene, pyrene, fluoranthene, benzo(a)anthracene, chrysene, benzo(b)fluoranthene, benzo(k)fluoranthene, BaP, indeno(1,2,3-cd)pyrene, dibenzo(a,h)anthracene, benzo(ghi)perylene之個人採樣的中位數濃度皆顯著高於爐側煉焦勞工；而煉頂煉焦勞工作業環境空氣中naphthalene, acenaphthylene, fluorene 之個人採樣的中位數濃度則與爐側煉焦勞工無顯著差異。

煉焦勞工尿液中1-OHP及8-OHdG與固相PAHs之相關性分析如表3所示，1-OHP濃度與acenaphthylene, acenaphthene , phenanthrene, pyrene, benzo(a)anthracene, benzo(b)fluoranthene, BaP, dibenzo(a,h)anthracene, benzo(ghi)perylene及總固相PAHs濃度呈顯著正相關。而8-OHdG濃度則與 fluoranthene, anthracene, pyrene,

benzo(b)fluoranthene, BaP, indeno(1,2,3-cd) pyrene及總固相PAHs濃度呈顯著正相關。1-OHP及8-OHdG則皆與pyrene, benzo(b) fluoranthene, BaP及總固相PAHs濃度呈顯著正相關，顯示benzo(b)fluoranthene, BaP, indeno(1,2,3-cd)pyrene有顯著增加氧化傷害的趨勢。

尿液中8-OHdG與1-OHP濃度之線性混合效應迴歸模式分析如表4所示，工作區域為與尿液中1-OHP濃度的顯著相關因子，爐頂煉焦工作與尿液中1-OHP濃度呈顯著正相關；工作區域與尿液中8-OHdG濃度呈顯著正相關；爐頂煉焦工作與尿液中8-OHdG濃度呈顯著正相關；煉焦勞工尿液中8-OHdG濃度與尿液中1-OHP濃度呈顯著正相關。在校正了尿液中1-OHP濃度之後，工作區域仍為尿液中8-OHdG濃度的顯著相關因子。

表1　煉焦勞工基本資料

基本資料，平均值　標準差[#]	爐側煉焦勞工(n=182)	爐頂煉焦勞工(n=110)	*p* value
年齡（歲）	44.9±9.5	44.6±8.3	0.788
BMI(kg/m^2)	24.9±9.8	24.4±3.7	0.500
工作年資（年）	17.6±12.4	13.1±7.1	0.001*
生活型態，n(%)[†]			
吸菸	81 (44.5%)	66 (60.0%)	0.007*
飲酒	39 (21.4%)	19 (17.3%)	0.368
服用維他命	69 (37.9%)	30 (27.2%)	0.058
尿中1-羥基焦腦油，幾何平均（幾何標準差），g/g creatinine	9.4 (3.5)	66.7 (3.5)	<0.001*
8尿中-羥基-2-去氧鳥嘌呤核甘，幾何平均（幾何標準差），g/g creatinine	5.6 (3.1)	16.5 (2.4)	<0.001*

[#]平均值 ± 標準差，以學生式t檢定分析爐側煉焦勞工與爐頂煉焦勞工之差異。

[†]人數（百分率），以卡方分析爐側煉焦勞工與爐頂煉焦勞工之差異。

* $p<0.05$

表2　爐頂煉焦工人與爐側煉焦工人之作業環境空氣中PAH暴露濃度比較

PAH (ng/m^3)	爐側煉焦工人(n=28)		爐頂煉焦工人(n=28)		*p* value[#]
	中位數	幾何平均（幾何標準差）	中位數	幾何平均（幾何標準差）	
Naphthalene	594.8	401.9 (2.5)	725.7	505.3 (3.0)	0.479
Acenaphthylene	158.0	144.0 (1.7)	227.7	209.0 (2.0)	0.065
Acenaphthene	52.9	53.9 (1.3)	71.0	64.5 (1.3)	0.038
Fluorene	225.3	232.9 (1.9)	222.9	300.5 (1.9)	0.212
Phenanthrene	15.7	23.9 (4.8)	112.7	148.1 (8.2)	0.003*
Anthracene	211.6	139.5 (4.8)	410.6	406.1 (1.9)	0.001*
Fluoranthene	94.2	97.8 (2.8)	323.7	308.5 (2.0)	<0.001*
Pyrene	227.0	178.9 (2.7)	1,220.0	543.4 (2.1)	<0.001*
Benzo(a)anthracene	2,103.2	1,568.6 (2.0)	3,019.6	2,707.6 (1.5)	0.005*
Chrysene	241.8	159.5 (2.6)	446.0	419.6 (1.4)	<0.001*
Benzo(b)fluoranthene	56.9	56.8 (5.0)	313.0	260.4 (1.2)	0.002*
Benzo(k)fluoranthene	139.1	130.7 (1.7)	260.6	213.0 (2.1)	0.021*
Benzo(a)pyrene	247.2	222.2 (2.2)	577.3	487.4 (1.7)	0.001*
Indeno(1,2,3-cd)pyrene	42.8	27.5 (7.2)	311.3	194.2 (3.4)	0.001*
Dibenzo(a,h)anthracene	72.7	24.9 (6.7)	216.2	196.0 (1.3)	<0.001*
Benzo(ghi)perylene	3.3	8.6 (4.6)	119.5	47.9 (5.4)	0.002*
Total PAHs	4,942.8	4,210.4 (1.6)	9,210.9	8,621.5 (1.5)	<0.001*

[#]Mann-Whitney U tests.

* $p<0.05$

表3　煉焦勞工尿液中1-羥基焦腦油(1-OHP)及 8-羥基-2-去氧鳥嘌呤核甘(8-OHdG)與PAHs之相關性分析(n=56)

	1-OHP		8-OHdG	
PAHs	r	*p* value[#]	r	*p* value[#]
Naphthalene	0.098	0.546	0.004	0.981
Acenaphthylene	0.541	<0.001[*]	0.276	0.085
Acenaphthene	0.312	0.048	0.292	0.067
Fluorene	0.012	0.942	0.253	0.073
Phenanthrene	0.592	<0.001[*]	0.025	0.880
Anthracene	0.189	0.244	0.787	<0.001[*]
Fluoranthene	0.306	0.055	0.394	0.012[*]
Pyrene	0.330	0.038[*]	0.290	0.042[*]
Benzo(a)anthracene	0.354	0.025[*]	0.252	0.117
Chrysene	0.126	0.438	0.295	0.065
Benzo(b)fluoranthene	0.314	0.048[*]	0.340	0.032[*]
Benzo(k)fluoranthene	0.063	0.701	0.150	0.355
Benzo(a)pyrene	0.414	0.008[*]	0.357	0.024[*]
Indeno(1,2,3-cd)pyrene	0.160	0.323	0.330	0.038[*]
Dibenzo(a,h)anthracene	0.320	0.044[*]	0.252	0.116
Benzo(ghi)perylene	0.343	0.030[*]	0.040	0.805
Total PAHs	0.452	0.003[*]	0.374	0.017[*]

[*] $p<0.05$

[#] *p* value calculated using Spearman correlation analysis.

表4　尿液中8-羥基-2-去氧鳥嘌呤核甘(8-OHdG)與1-羥基焦腦油(1-OHP)濃度之線性混合效應迴歸模式(=292)

預測因子	Log_{10} 1-OHP (μg/g creatinine)	Log_{10} 8-OHdG (μg/g creatinine)
	迴歸係數（95% 信賴區間）	迴歸係數（95% 信賴區間）
工作區域（爐頂vs.爐側）	0.736 (0.603 to 0.869)[*]	0.238 (0.109 to 0.367)[*]
吸菸（是 vs. 否）	0.058 (-0.066 to 0.182)	0.066 (-0.035 to 0.167)
飲酒（是 vs. 否）	0.020 (-0.138 to 0.178)	0.052 (-0.077 to 0.180)
服用維他命（是 vs. 否）	-0.056 (-0.183 to 0.072)	-0.014 (-0.118 to 0.089)
工作年資（年）	0.003 (-0.002 to 0.009)	0.001 (-0.004 to 0.005)
年齡（歲）	-0.003 (-0.010 to 0.004)	0.001 (-0.005 to 0.006)
BMI(kg/m^2)	-0.001 (-0.009 to 0.006)	-0.003 (-0.009 to 0.003)
Log_{10} 1-OHP(μg/g reatinine)	—	0.264 (0.168 to 0.360)[*]

[*] $p<0.001$

討論

研究結果顯示煉焦作業環境空氣中BaP、總PAHs濃度、及尿液中1-OHP與pyrene濃度呈顯著正相關，並由 Student's t 檢定與線性混合效應迴歸模式煉焦勞工在不同的PAHs濃度暴露情況下，其尿液中1-OHP濃度有顯著差異；此發現顯示尿液中1-OHP是一個煉焦勞工PAHs暴露的適當內在劑量生物指標。值得注意地，吸菸、飲酒、服用維他命、工作年資、年齡、BMI皆不是尿液中1-OHP的顯著相關因子(p>0.05)；此結果與之前的一篇文獻，針對男性餐飲業勞工尿液中1-OHP的研究有一致的結果[12]。

一支香菸約含有50-200 ng 的pyrene[13]，然而數個對吸菸與尿液中1-OHP的相關性研究，顯示初不一致的結果；本研究與吳氏等的研究顯示吸菸並沒有顯著影響尿液中1-OHP的濃度[14]，而本研究煉焦作業之PAHs暴露為尿液中1-OHP的顯著影響因子，顯示煉焦作業勞工之職業性PAHs暴露影響高於吸菸的PAHs暴露。但相反地，Kang等人的研究指出，在一個鋼鐵工廠，有吸菸的勞工其尿液中1-OHP的濃度顯著高於沒有吸菸者[13]，因此需有更多的研究來釐清吸菸、職業性PAHs暴露對尿液中1-OHP的濃度影響。

尿液中 8-OHdG來自於三種來源：1. DNA氧化的修復產物；2. 核苷酸移除氧化的dG；3. 細胞的翻覆(cell turnover)，如此顯示尿液中8-OHdG代表全身DNA氧化傷害的平均狀態。本研究顯示煉焦勞工尿液中 8-OHdG的濃度與其作業環境空氣個人採樣之BaP及benzo(b)fluoranthene濃度成正比，而BaP及benzo(b)fluoranthene為PAHs的主要致癌物，且BaP及benzo(b)fluoranthene會提高DNA氧化傷害，此發現與先前/的動物實驗研究指出PAHs(BaP及benzo(b)fluoranthene)會擴增DNA氧化傷害的途徑，有一致的結果[15]

尿液中1-OHP、爐頂煉焦工作為尿液中8-OHdG的二個顯著相關因子，尿液中1-OHP、爐頂煉焦工作為PAHs暴露造成DNA氧化傷害的良好預測因子，而尿液中1-OHP與8-OHdG成顯著正相關，此結果與另一個探討PAHs對煉焦勞工之DNA氧化傷害與劑量效應反應的研究，有一致性的結果[16]。在線性混合效應迴歸模式，以爐頂煉焦工作為獨立變項來預測尿液中 8-OHdG濃度顯示，煉焦工作人員其他危害因子，會影響DNA氧化傷害指標（尿液中8-OHdG濃度），例如：苯[17]與酚[18]的暴露危害。本研究也顯示爐頂煉焦勞工比爐側煉焦勞工有較高的氧化傷害情形，此氧化傷害情形的原因有尿液中1-OHP影響之外的原因。

吸菸對尿液中8-OHdG濃度的影響，國際間並沒有一致的研究結果，Loft等人的研究指出，吸菸者尿液中8-OHdG濃度會比不吸菸者高出30% -50%[19]。然而本研究結果發現吸菸對尿液中8-OHdG濃度並沒有顯著影響，此研究結果與先前有關煉焦勞工之流行病學研究，有一致的結果[14]。

綜合維他命中含有抗氧化劑，例如維他命C可保護DNA避免氧化傷害，Cooke等人對受測者每天供應500 mg的維他命C，發現血漿中8-OHdG濃度隨著維他命C的增加而顯著降低[20]。然而本研究結果發現，有經常服用綜合維他命者，其尿液中8-OHdG濃度並沒有顯著降低的趨勢，此研究結果與先前有關116名沒有吸菸的煉焦勞工之流行病學研究，有一致的結果[14]。

Cherng等的研究指出年齡與BMI和尿液中 8-OHdG 濃度會有相關，因為年老或體瘦的

人比年輕或肥胖的人有較佳的新陳代謝速率[21]。但本研究結果顯示年齡與BMI和尿液中8-OHdG 沒有顯著相關，此結果與一個針對消防隊員的研究，有一致的結果[22]。

本研究仍有一些研究上的限制，有些煉焦爐排放物質沒有測定，例如：氣相PAHs、苯[17]與酚[18]沒有測定，這些物質可能會干擾氧化傷害測定的結果。另一個研究的限制為缺乏來自非職業性暴露的測定數據，例如：交通污染的PAHs，但煉焦勞工每天花在交通的時間少於1個小時，而每天待在煉焦工廠的時間超過8個小時，因此非職業性的PAHs對氧化傷害的影響極為有限。此研究推論尿液中8-OHdG是一個良好的基因氧化傷害指標，因為其反應了PAHs內在暴露劑量（尿液中1-OHP）的影響，及顯示工作區域的影響。

結論

尿液中1-OHP、爐頂煉焦工作為PAHs暴露造成DNA氧化傷害的良好預測因子；本研究結果並指出煉焦勞工的DNA氧化傷害與暴露PAHs有顯著相關。

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Research Articles

Oxidative Stress Evaluation for Polycyclic Aromatic Hydrocarbons Exposed Coke-Oven Workers

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Abstract

Coke oven workers have long-term been exposed to coke oven emissions (COEs). PAHs are important components of COEs that caused most seriously health effects among coke oven workers. Long-term exposure to PAH concentrations has been associated with lung cancer, respiratory cancer, urinary system cancer, skin cancer, and neurological diseases. This study conducted a cross-sectional epidemiology research for coke oven workers in a steel company in Taiwan. Based on job titles obtained from responses to the questionnaire survey, the coke oven workers were classified into two groups, including topside-oven workers (high exposure group, N=110), and side-oven workers (low exposure group, N=182). We quantified human subject exposure to 16 PAHs by using personal dosimetry. Urinary 1-hydroxypyrene (1-OHP) was used as an internal dose of exposure to PAHs, and urinary 8-hydroxy-2'-deoxyguanosine (8-OHdG) was used as an oxidative DNA damage marker. The relationship between workers' 8-OHdG and 1-OHP levels was estimated using linear mixed-effects models. Airborne PAHs levels in topside-oven workers significantly exceeded those in side-oven workers. The topside-oven workers' geometric mean levels of urinary 8-OHdGand 1-OHP were significantly higher than those of side-oven workers, respectively. Urinary 1-OHP level, and work in topside-oven, gender were two significant predictors of urinary 8-OHdG levels, after adjustments are

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made for covariates. Oxidative DNA damage was associated with exposure of coke oven workers to PAHs.

Keywords: Polycyclic aromatic hydrocarbons, Coke oven workers, Urinary 1-hydroxypyrene, Urinary 8-hydroxy-2'-deoxyguanosine

Introduction

Coke is an indispensable raw material for steel smelting. Mainly coming from coal, coke is used in an iron and steel plant as a main reducing agent to refine the iron ore into iron. After coal is transported to a coke oven plant, it is added from the roof of coke oven and then pushed and leveled by the leveling bar at the side door. When the roof of coke oven is opened to add coal and during the process when coke is collected and transported, transient pollutant emissions are caused, while continual pollutant emissions are caused if there is any leak from the oven's door and roof and gas pipelines[1-3]. Emissions from a coke oven contain high concentrations of polycyclic aromatic hydrocarbons (PAH), mainly due to incomplete combustion of organic matters. Coke oven workers who have been long-term exposed to coke oven emissions, among which PAHs cause the most severe health effects, may suffer from lung cancer, respiratory cancer, urinary system cancer, skin cancer and neurological diseases. When PAHs enter into the human body, some species may form carcinogenic and mutagenic substances during metabolism[4]. It is found from animal experiments that carcinogenic PAHs are mainly of 4-7 rings, including such species as Pyrene, Benzo[a] anthracene, Chrysene,Benzo[a]fluoroanthene, Benzo[e]pyrene, Benzo[a]pyrene, Benzo[k] fluoroanthene, Indeno[1,2,3-cd]pyrene, Dibenz[a,h] anthracene, and Benzo[ghi]perylene. Among them, Benzo[a]pyrene is the most carcinogenic[5], and therefore the Benzo[a]pyrene concentration is often chosen by the scientific community to be the index for PAH as an urban air carcinogen.

As internal dose of exposure to PAHs for workers, urine metabolites are measured. Since a high level of pyrene is contained in PAHs, it is often used as an occupational and environmental indicator for PAHs. Pyrene can be absorbed by lungs or the skin of a human body and is then metabolized into 1-hydroxypyrene (1-OHP) and ultimately excreted as urinary1-OHP, which is thus considered to be a biological exposure Indices for PAHs[6] to reflect the recent exposure to PAHs for such occupations as firefighters, iron foundry workers, coke-oven workers and restaurant workers.

Damage to cells and genetic materials is an early process to induce cancers. 8-hydroxy-2-deoxyguanosine (8-OHdG) is the most abundant biological oxidative DNA pattern, which can be used to detect the biological mutation effects induced by environmental pollutants[7]. Detection of urinary 8-OHdG may reflect the effects of various carcinogens, including the impact of PAHs. By way of chemicals, 8-OHdG can cause damage to DNA and the repair mechanisms of in-vivo nucleic acid. As 8-OHdG is excreted into the urine without further metabolism, urinary 8-OHdG can be used to assess the damage and repair of oxidative DNA. Adequate amounts of research have been conducted on the use of urinary 8-OHdG levels to assess aging and cancer-causing diseases[8]. For example, a research has proved that firefighters exposed to high levels of carcinogens, like PAH, will lead to the rise of urinary 8-OHdG concentration levels[9].

Exposure to PAHs causes harm to human health. It is thus necessary to assess the relationships

between PAH exposure and health effects. In this study, the airborne PAH concentrations were measured in the coke oven plant, the urinary 1-OHP was used to indicate the internal dose of exposure to PAHs, and the urinary 8-OHdG was used to assess the oxidative DNA damage levels on the oven coke workers. The aim is to assess how exposure to PAHs affects the health of oven coke workers.

Methods

1. Objects of study

292 male workers from a coke oven plant who did not have cardiovascular disease (defined as the chest, the heart, and cardiovascular parts are free of diseases), cerebrovascular disease, high cholesterol, diabetes, and kidney disease were selected as the objects of study. Based on the airborne PAH concentrations measured in the coke oven plants in the past,[10] the workers were divided into two groups, namely the topside-oven workers (high PAH exposure group, including feeding car operators, feeding assistants, pipeline staff and topside-oven operators) and side-oven workers (low PAH exposure group, including coke-pushing car operators, coke-guiding car operators, quenching car operators and the fuel adjustment operators and foreman). The Institute Review Board of the Tri-Service General Hospital, National Defense Medical Center in Taiwan approved this study. Informed consent was obtained from all subjects.

2. Questionnaire survey on health

Study objects (including those in the high exposure group and the low exposure group) were interviewed through a face-to-face questionnaire survey to collect their basic information (including age, height, weight, and so forth), working conditions (including seniority), lifestyle (including smoking habits, drinking habits, and multivitamin-taking habits), and disease status.

3. Personal dosimetry of airborne particulate PAHs[10]

Glass fiber filters were used as sampling media. Automatic harvesting pumps were used to collect airborne PAH particulate matters in the work environment. IOM (Institute of Occupational Medicine, England) samplers with glass fiber filters (diameter: 25mm, pore size: 0.7μm) at a flow rate of 2.0 L/min were used for the particulate PAH sampling for 8 hours. Thereafter, the collected glass fiber filters were added to 2ml n-Hexane and ultrasonically extracted for 20 minutes. Then, 4 ml of 5% NaOH was added in and centrifuged at 3,000rpm for 10 minutes. 1.5 ml of supernatant was extracted and replaced with dimethyl sulfate. Then, nitrogen was used to concentrate the solvent and Gas Chromatography-Mass Spectrophotometer (GC-MS) was used to analyze the 16 kinds of PAHs, including naphthalene, acenaphthylene, acenaphthene, fluorene, phenanthrene, anthracene, pyrene, fluoranthene, benzo(a)anthracene, chrysene, benzo(b)fluoranthene, benzo(k) fluoranthene, BaP, indeno(1,2,3-cd)pyrene, dibenzo(a,h)anthracene, and benzo(ghi)perylene. The detection limit of this analytical method was in the range between 6.1 ng (dibenzo(a, h)anthracene) and 9.0 ng (phenanthrene).

4. Detection and analysis of urinary 1-hydroxypyrene (1-OHP)[11, 12]

10mL of supernatant was taken from the urine and placed in a conical flask. 10 mL of acetate buffer solution was added in to adjust the mixture to pH 5.0. 20μl of β-glucuronidase/sulfatase enzyme was added in to make hydrolysis, which was then cultured in a 37℃ shaking water sink for 24 hours. To purify the concentrated solution, 5 mL of methanol was put through the solid phase extraction tube for purification purpose. Then, 10 mL of deionized water was added in to rinse and activate the cultured urine, which was then extracted by the solid phase extraction tube at a filtration flow rate of less than 3mL/min controlled by a vacuum-assisted device. After the urine sample was completely filtered, 10 mL of deionized water was added in to rinse the solid phase extraction tube and the filtrate was discarded. 6 mL of isopropanol was used to wash and collect the filtrate into a test tube. The tube was put into a nitrogen-blowing concentrator and nitrogen gas was used to dry the solution at 50℃. 2 mL of isopropyl alcohol was added to dissolve the residue and the residue was placed in the ultrasonic shaker to shake for 4 minutes. Finally, a plastic syringe with a disc filter head was used to filter the concentrated solution and the filtrate was collected in a 1.8 mL glass vial. The Waters 2695 HPLC and Water 474 fluorescence detector were used to analyze the concentrated solution at excitation wavelength: 281 nm and Emission wavelength: 388 nm. Detection limit of the analytical method was to measure the 1.0 μg/L of 1-OHP standard solution for seven times in accordance with the optimum operating conditions used in the experiments. The calculated standard deviation was multiplied by three to get the detection limit of analytical method. Detection limit of 1-OHP analysis was 0.1 μg/L and the variation coefficient measured by repeating the analysis was less than 10%.

5. Urinary 8-OHdG levels[11]

The urine sample was diluted by deionized water to one-fifth of its original concentration. The HPLC / MS / MS instrument was used to detect and analyze the urinary 8-OHdG levels. The measurement of reagent blank (water) was repeated for seven times in accordance with the optimum operating conditions used in the experiments. The calculated standard deviation was multiplied by three to get the detection limit of analytical method. Detection limit of 8-OHdG was 5.7ng/L, and the variation coefficient measured by repeating the analysis was less than 5%.

6. Urinary creatinine

Jaffe reaction method[11] was used to measure urinary creatinine. Both the urinary 1-OHP and 8-OHdG levels were adjusted by creatinine, respectively.

7. Sampling time

The personal dosimetry for particulate matters of polycyclic aromatic hydrocarbons was sampled and measured at the weekend. In other words, the urinary 1-OHP and 8-OHdG levels were sampled and measured after workers got off work at the weekend.

8. Statistical analysis

Data from health survey questionnaires and

the measurement results of work environment and biological specimen were collated, confirmed, coded and typed for computer filing. They were then analyzed by descriptive statistical analysis, chi-square analysis, Student's t-test, Mann-Whitney U test, and linear mixed-effects regression analysis. Spearman correlation analysis was used to assess the correlation between 1-OHP and 16 PAHs and the relationship between 8-OHdG and 16 PAHs. In this study, the statistical software package S-PLUS 2000 (MathSoft Inc., Cambridge, MA, USA) was used and the significant level was set at $\alpha = 0.05$.

Results

Basic information of 292 male coke-oven workers completing the questionnaire survey is shown in Table 1. The average age of topside-oven workers was 44.6 ± 8.9 years old, which was not significantly different from the average age of 44.9 ± 9.5 years old for the side-oven workers. The average BMI for topside-oven workers was 24.4 ± 3.7 kg/m^2, which was not significantly different from the average BMI of side-oven workers (24.9 ± 9.8 kg/m^2). The average work seniority of topside-oven workers at 13.1 ± 7.1 years was significantly lower than that of side-oven workers at 17.6 ± 12.4 years. 60.0% of topside-oven workers had a smoking habit. The ratio was significantly higher than that of side-oven workers at 44.5% (p=0.007). 17.3% of topside-oven workers had a drinking habit, which was not significantly different from that of side-oven workers. 27.2% of topside-oven workers had a habit of taking vitamin. The ratio was not significant different from that of side-oven workers.

Urinary 8-OHdG levels were used to assess oxidative DNA damage, while the urinary 1-OHP was a good internal dose index[11]. The urinary 8-OHdG and 1-OHP levels of the coke-oven workers are shown in Table 1. The topside-oven workers' geometric mean levels of urinary 8-OHdG and 1-OHP were significantly higher than those of side-oven workers.

Comparative analysis of coke-oven workers' median personal dosimetry of PAHs is shown in Table 2. Topside-oven workers' personal dosimetry of airborne acenaphthene, phenanthrene, anthracene, pyrene, fluoranthene, benzo(a)anthracene, chrysene, benzo(b)fluoranthene, benzo(k)fluoranthene, BaP, indeno(1,2,3-cd)pyrene, dibenzo(a,h)anthracene, benzo(ghi)perylene of was significantly higher than that of side-oven workers. Meanwhile, topside-oven workers' personal dosimetry of median airborne naphthalene, acenaphthylene, and fluorene was not significantly different from that of the side-oven workers.

Correlation analysis between coke-oven workers' urinary 1-OHP and 8-OHdG levels and the particulate PAHs is shown in Table 3. The 1-OHP levels were significantly positively correlated with the levels of acenaphthylene, acenaphthene, phenanthrene, pyrene, benzo(a)anthracene, benzo(b) fluoranthene, BaP, dibenzo(a,h)anthracene, benzo(ghi)perylene and total particulate PAHs. The 8-OHdG levels were significantly positively correlated with the levels of fluoranthene, anthracene, pyrene, benzo(b)fluoranthene, BaP, indeno(1,2,3-cd)pyrene and total particulate PAHs. The 1-OHP and 8-OHdG levels were significantly positively correlated with the levels of pyrene, benzo(b)

fluoranthene, BaP and total particulate PAHs, indicating that there was a significantly upward trend for benzo(b)fluoranthene, BaP, and indeno(1,2,3-cd) pyrene to increase oxidative damage.

Urinary 8-OHdG and 1-OHP levels analyzed by the linear mixed-effects regression analysis are shown in Table 4. The work area was significantly correlated with the urinary 1-OHP levels in that topside-oven work showed a significantly positive correlation with urinary 1-OHP levels. The work area was also significantly correlated with urinary 8-OHdG levels in that topside-oven work showed a significantly positive correlation with urinary 8-OHdG levels. Coke-oven workers' urinary 8-OHdG levels were significantly positively correlated with urinary 1-OHP levels. After urinary 1-OHP levels were adjusted, the work area was still a significant factor associated with urinary 8-OHdG levels.

Table 1 Descriptive statistics for coke-oven workers

Basic information, mean ± standard deviation[#]	Side-oven workers (n=182)	Topside-oven workers (n=110)	*p* value
Age (years old)	44.9±9.5	44.6±8.3	0.788
BMI (kg/m^2)	24.9±9.8	24.4±3.7	0.500
Work seniority (years)	17.6±12.4	13.1±7.1	0.001*
Lifestyle, n (%)†			
Smoking	81 (44.5%)	66 (60.0%)	0.007*
Drinking	39 (21.4%)	19 (17.3%)	0.368
Take vitamins	69 (37.9%)	30 (27.2%)	0.058
Urinary1-OHP, GM (GSD), g/g creatinine	9.4 (3.5)	66.7 (3.5)	<0.001*
Urinary 8-OHdG, GM (GSD), g/g creatinine	5.6 (3.1)	16.5 (2.4)	<0.001*

[#]Mean ± Standard deviation: Student's t-test is used to analyze the difference between side-oven workers and topside-oven workers.

[†]Number of persons (percentage): Chi-square is used to analyze the difference between side-oven workers and topside-oven workers.

* $p<0.05$

Table 2 Comparison of airborne PAH exposure for topside-oven workers and side-oven workers

PAH (ng/m^3)	Side-oven workers (n=28)		Topside-oven workers (n=28)		*p* value[#]
	median	geometric mean (geometric standard deviation)	median	geometric mean (geometric standard deviation)	
Naphthalene	594.8	401.9 (2.5)	725.7	505.3 (3.0)	0.479
Acenaphthylene	158.0	144.0 (1.7)	227.7	209.0 (2.0)	0.065
Acenaphthene	52.9	53.9 (1.3)	71.0	64.5 (1.3)	0.038
Fluorene	225.3	232.9 (1.9)	222.9	300.5 (1.9)	0.212
Phenanthrene	15.7	23.9 (4.8)	112.7	148.1 (8.2)	0.003*
Anthracene	211.6	139.5 (4.8)	410.6	406.1 (1.9)	0.001*
Fluoranthene	94.2	97.8 (2.8)	323.7	308.5 (2.0)	<0.001*
Pyrene	227.0	178.9 (2.7)	1220.0	543.4 (2.1)	<0.001*
Benzo(a)anthracene	2103.2	1568.6 (2.0)	3019.6	2707.6 (1.5)	0.005*
Chrysene	241.8	159.5 (2.6)	446.0	419.6 (1.4)	<0.001*
Benzo(b)fluoranthene	56.9	56.8 (5.0)	313.0	260.4 (1.2)	0.002*
Benzo(k)fluoranthene	139.1	130.7 (1.7)	260.6	213.0 (2.1)	0.021*
Benzo(a)pyrene	247.2	222.2 (2.2)	577.3	487.4 (1.7)	0.001*
Indeno(1,2,3-cd)pyrene	42.8	27.5 (7.2)	311.3	194.2 (3.4)	0.001*
Dibenzo(a,h)anthracene	72.7	24.9 (6.7)	216.2	196.0 (1.3)	<0.001*
Benzo(ghi)perylene	3.3	8.6 (4.6)	119.5	47.9 (5.4)	0.002*
Total PAHs	4942.8	4210.4 (1.6)	9210.9	8621.5 (1.5)	<0.001*

[#]Mann-Whitney U tests.

* $p<0.05$

Table 3 Correlation analysis between coke-oven workers' urinary 1-hydroxypyrene(1-OHP) and 8-hydroxy-2'-deoxyguanosine (8-OHdG) and PAHs (n=56)

	1-OHP		8-OHdG	
PAHs	r	*p* value[#]	r	*p* value[#]
Naphthalene	0.098	0.546	0.004	0.981
Acenaphthylene	0.541	<0.001[*]	0.276	0.085
Acenaphthene	0.312	0.048	0.292	0.067
Fluorene	0.012	0.942	0.253	0.073
Phenanthrene	0.592	<0.001[*]	0.025	0.880
Anthracene	0.189	0.244	0.787	<0.001[*]
Fluoranthene	0.306	0.055	0.394	0.012[*]
Pyrene	0.330	0.038[*]	0.290	0.042[*]
Benzo(a)anthracene	0.354	0.025[*]	0.252	0.117
Chrysene	0.126	0.438	0.295	0.065
Benzo(b)fluoranthene	0.314	0.048[*]	0.340	0.032[*]
Benzo(k)fluoranthene	0.063	0.701	0.150	0.355
Benzo(a)pyrene	0.414	0.008[*]	0.357	0.024[*]
Indeno(1,2,3-cd)pyrene	0.160	0.323	0.330	0.038[*]
Dibenzo(a,h)anthracene	0.320	0.044[*]	0.252	0.116
Benzo(ghi)perylene	0.343	0.030[*]	0.040	0.805
Total PAHs	0.452	0.003[*]	0.374	0.017[*]

[*] $p<0.05$

[#] *p* value calculated using Spearman correlation analysis.

Table 4 Urinary 8-hydroxy-2'-deoxyguanosine (8-OHdG) and 1-hydroxypyrene (1-OHP) levels analyzed by linear mixed-effects regression analysis (=292)

Predictors	Log_{10} 1-OHP (μg/g creatinine)	Log_{10} 8-OHdG (μg/g creatinine)
	Regression coefficient (95% confidence interval)	Regression coefficient (95% confidence interval)
Work area (Topside-oven vs. side-oven)	0.736 (0.603 to 0.869)[*]	0.238 (0.109 to 0.367)[*]
Smoking (yes vs. no)	0.058 (-0.066 to 0.182)	0.066 (-0.035 to 0.167)
Drinking (yes vs. no)	0.020 (-0.138 to 0.178)	0.052 (-0.077 to 0.180)
Taking vitamins (yes vs. no)	-0.056 (-0.183 to 0.072)	-0.014 (-0.118 to 0.089)
work seniority (years)	0.003 (-0.002 to 0.009)	0.001 (-0.004 to 0.005)
Age (years old)	-0.003 (-0.010 to 0.004)	0.001 (-0.005 to 0.006)
BMI(kg/m^2)	-0.001 (-0.009 to 0.006)	-0.003 (-0.009 to 0.003)
Log_{10} 1-OHP(μg/g reatinine)	–	0.264 (0.168 to 0.360)[*]

[*] $p<0.001$

Discussion

The results showed that airborne BaP, total PAHs concentration, and urinary 1-OHP levels in the work environment were significantly positively correlated with the pyrene levels. The results from Student's t-test and linear mixed-effects regression analysis also showed that the urinary 1-OHP levels of coke-oven workers varied significantly when they were exposed to different PAH levels. This finding showed that urinary 1-OHP was an appropriate internal dose biological indicator for coke-oven workers under PAH exposures. Notably, such factors as smoking, drinking, taking vitamins, work seniority, age, and BMI were not significantly correlated with the urinary 1-OHP level ($p > 0.05$). This finding was consistent with the result of a previous research paper that studied the urinary 1-OHP levels of male restaurant workers[12].

A cigarette contains about 50-200 ng of pyrene[13]. A number of papers doing research on the correlation between smoking and urinary 1-OHP levels showed inconsistent results. This study and some other studies (like that of Wu) showed the same conclusion that smoking has no significant effect on the urinary 1-OHP levels[14]. Meanwhile, this study finds that PAH exposure in coking operation is a significant factor affecting the urinary 1-OHP levels and the exposure to occupational PAHs has a higher effect on coke oven workers than exposure to PAHs via smoking. On the contrary, studies of Kang et al indicated that in a steel factory, its workers who smoke had a significantly higher urinary 1-OHP level than no-smokers[13]. Thus, we need more researches to clarify how much impact smoking and occupational exposure to PAHs have on the urinary 1-OHP levels.

Urinary 8-OHdG comes from three sources: (1) repair product of DNA oxidation; (2) dG of nucleotide removed of oxidization; and (3) cell turnover. It is thus displayed that urinary 8-OHdG can represent the average state of oxidative DNA damage to a human body. This study showed that the urinary 8-OHdG levels in coke-oven workers were proportional to the personal dosimetry of airborne BaP and benzo(b)fluoranthene levels in the work environment, that BaP and benzo(b) fluoranthene were major carcinogens of PAHs and that BaP and benzo(b)fluoranthene would increase oxidative DNA damage. This finding is consistent with the result of a previous animal study that proves PAHs (BaP and benzo(b)fluoranthene) will amplify oxidative DNA damage[15].

Urinary 1-OHP level and work in topside oven are two significant factors correlated with urinary 8-OhdG, and they (urinary 1-OHP level and work in topside oven) are good predictors for oxidative DNA damage caused by exposure to PAHs. The finding indicates that the urinary 1 -OHP levels are significantly positively correlated with the urinary 8-OHdG levels is consistent with the result of another study that discusses the dose-response relationships between PAH exposure and oxidative DNA damage to the coke-oven workers[16]. When work in topside oven was used in the linear mixed-effects regression analysis as an independent variable to predict urinary 8-OHdG levels, it was showed that other hazardous factors (like benzene[17] and phenol[18]) would affect the coking staff’s oxidative DNA damage indicator

(urinary 8-OHdG levels). This study also showed that topside-oven workers had a higher oxidative damage than side-oven workers, and the oxidative damage was caused by factors other than urinary 1-OHP.

There is no international consensus on how smoking affects urinary 8-OHdG levels. The study of Loft et al pointed out that smokers had a urinary 8-OHdG level 30% - 50% higher than that of non-smokers[19]. However, this study found that smoking did not significantly affect the urinary 8-OHdG levels. This finding is consistent with that of a previous epidemiological study related to coke-oven workers[14].

Multivitamins contain antioxidants. For example, vitamin C may protect DNA from oxidative damage. Cooke et al pointed out that those subjects who were served 500 mg of vitamin C daily had their 8-OhdG levels in plasma significantly decreased as the amounts of vitamin C increased[20]. However, this study found that regular multivitamin users did not significantly decrease their urinary 8-OHdG levels. This finding is consistent with a previous epidemiological study on 116 coke-oven workers who did not smoke[14].

The studies of Cherng, et al. indicated that age and BMI were correlated with the urinary 8-OHdG levels, because the elderly or the thin persons had a better metabolic rate than younger people or the obese persons[21]. However, this study found that age and BMI were not significantly correlated with urinary 8-OHdG. This finding is consistent with a study for firefighters[22].

There are some restrictions to this study. For example, some emissions (such as gas PAHs, benzo[17] and phenol[18]) from the coke oven were not measured, but these substances may interfere with the determination of oxidative damage. Another limitation to this study is the lack of measurement data from non-occupational exposure, like traffic pollution of PAHs. However, non-occupational PAHs may cause very limited oxidative damage to the coke-oven workers, because they spent less than one hour on traffic every day but more than 8 hours every day in the coke oven plant. It is inferred by this study that the urinary 8-OHdG levels are a good indicator for oxidative damage to gene, because it reflects the internal dose of exposure to PAHs (urinary 1-OHP) and the impact of work area.

Conclusion

The urinary 1-OHP level and work in topside oven are good predictors of oxidative DNA damage due to PAH exposure. This study indicates that there is a significant relationship between oxidative DNA damage to coke-oven workers and their PAH exposure.

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