

## 大气污染对2型糖尿病相关指标影响的研究进展

张经纬<sup>1</sup> 冯利红<sup>1</sup> 侯常春<sup>1</sup> 顾清<sup>2</sup>

<sup>1</sup>天津市疾病预防控制中心环境与健康室 300011; <sup>2</sup>天津市疾病预防控制中心主任办公室 300011

通信作者:顾清, Email: guqing315@126.com

**【摘要】** 近年来,我国空气污染情况日渐严重,了解大气污染与糖尿病关系的相关研究势在必行。通过分析国内外相关文献,对大气污染和2型糖尿病血糖和血脂相关指标的关系进行综述,归纳两者间关系规律,并在此基础上对此领域的研究方向进行展望,旨在为我国制定控制大气污染和防治2型糖尿病的相关政策提供参考性依据。

**【关键词】** 大气污染; 糖尿病; 血糖指标; 血脂指标

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### Review on the relationship between major air pollutants and related indicators of type 2 diabetes mellitus

Zhang Jingwei<sup>1</sup>, Feng Lihong<sup>1</sup>, Hou Changchun<sup>1</sup>, Gu Qing<sup>2</sup>

<sup>1</sup>Institute of Environment and Health, Tianjin Center for Disease Control and Prevention, Tianjin 300011, China; <sup>2</sup>Office of the Director, Tianjin Center for Disease Control and Prevention, Tianjin 300011, China

Corresponding author: Gu Qing, Email: guqing315@126.com

**【Abstract】** The situation of air pollution has become increasingly serious and its relationship with diabetes becomes a new research concern, in China. After going through a large number of epidemiological studies published in recent years, this paper reviews the relationship between major air pollutants and both blood glucose and blood lipid, related to type 2 diabetes. It also summarizes the relationships among the main pollutants of the atmosphere so as to propose the research directions in this field. Hopefully, this paper can provide reference for forming policies on air pollution, prevention and treatment of type 2 diabetes in the country.

**【Key words】** Air pollution; Diabetes; Glycemic index; Blood lipid index

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空气污染已成为威胁发展中国家居民健康的主要原因之一<sup>[1]</sup>。随着工业化和城市化节奏的加快,能源消耗与日俱增,空气污染已成为我国公众健康的主要威胁<sup>[2-4]</sup>。研究表明,恶劣的空气环境可能导致严重的心血管、脑血管和呼吸系统疾病的发生<sup>[5-8]</sup>,也可能导致2型糖尿病的患病率和死亡率的升高<sup>[9-11]</sup>。

糖尿病是一种代谢紊乱性疾病,也是全球公认的造成疾病负担增高和过早死亡的主要原因之一<sup>[12]</sup>,根据其不同的临床表现可分为1型糖尿病(胰岛素抵抗)和2型糖尿病(高血糖)。有证据表明,空气污染可能会增加2型糖尿病患病风险<sup>[2,13]</sup>。其中可能的分子生物学机制包括:自主神经系统功能失衡<sup>[14]</sup>、脂质代谢紊乱<sup>[15-16]</sup>、内皮功能障碍、胰岛素敏感性改变、糖基化血红蛋白代谢紊乱等<sup>[10,14]</sup>。

关于空气污染与2型糖尿病发病关系的研究结论并不统一。有研究认为两者间存在关联<sup>[17]</sup>,也有研究得出两者间并没有显著性关联<sup>[18-19]</sup>。过往研究多为发达国家人群<sup>[2,13]</sup>,

少数是在发展中国家完成的<sup>[2-4]</sup>,且少有研究涉及空气污染物和2型糖尿病相关指标之间的关系<sup>[2]</sup>。本研究通过分析近年来国内外文献,对大气污染与2型糖尿病相关指标的关联进行综述,旨在为2型糖尿病预防策略方面提供参考性的依据。

#### 一、大气污染对2型糖尿病发病、死亡的影响

多数关于环境中空气污染物和2型糖尿病患病风险关系进行的研究结论显示,二者间存在正相关关系<sup>[2-3,13]</sup>。北美洲和欧洲的关于空气污染物和2型糖尿病关系的Meta分析结果表明,大气中PM<sub>2.5</sub>和CO每升高10 μg/m<sup>3</sup>,其2型糖尿病患病的危险性分别上升10%和6%<sup>[2]</sup>;6种大气污染物(PM<sub>10</sub>、PM<sub>2.5</sub>、NO<sub>2</sub>、O<sub>3</sub>、硫酸盐和SO<sub>2</sub>)浓度每增加10 μg/m<sup>3</sup>,糖尿病患者的合并风险比和死亡风险比最高可达1.01和1.07<sup>[3]</sup>。一项双向病例交叉设计实验收集了4年内南京市因糖尿病死亡的3234人,观察到空气中每升高四分位数间距浓度的CO和SO<sub>2</sub>,糖尿病患者死亡的危险性就分别上升14%和13%<sup>[20]</sup>。

大气污染物致2型糖尿病发病的效应在不同的年龄组

中略有不同。PM<sub>2.5</sub>和CO在高龄组人群中致病作用更加明显<sup>[21]</sup>,可能因为随着年龄的增加,机体中与胰岛素抵抗密切相关的自主神经和交感神经的敏感性相应的降低<sup>[22-23]</sup>。但是,在我国东北对15 477名18~74岁正常人群进行的队列研究中发现,NO<sub>2</sub>使>50岁的老年人患糖尿病风险增加2%,低于<50岁的12%<sup>[24]</sup>,这可能是因为在老年人大部分时间是在家中度过,受到空气污染物暴露影响的可能性比年轻人低;还可能因为在老年人中,使用抗2型糖尿病药物的情况更加普遍,会削弱空气污染物对血糖的提升作用<sup>[25]</sup>。另有研究提示,由于年龄是2型糖尿病患病的危险因素之一,可能会掩盖空气污染物和2型糖尿病患者之间的关系<sup>[24]</sup>。

人群肥胖程度也可影响空气污染物致2型糖尿病效应,BMI较高的人群对空气污染物更加敏感。一项包括中国33个城市的15 000名非糖尿病人群的队列研究发现,在相同的空气污染条件下,PM<sub>2.5</sub>、CO和NO<sub>2</sub>的暴露可使超重或肥胖人群患糖尿病风险升高20%、12%和17%,高于体重正常人群(患病风险升高5%、1.3%和2.6%)<sup>[24]</sup>;另一项纳入11 847名正常人群的横断面研究显示,大气中每升高41.1 μg/m<sup>3</sup>的PM<sub>2.5</sub>,BMI>28 kg/m<sup>2</sup>的人群FPG浓度升高的可能性为29%,高于低BMI人群的22%,差异有统计学意义<sup>[10]</sup>。另一对中国551名正常人群的队列研究结果显示,超重人群与体重较轻人群相比,其2型糖尿病的发病率与SO<sub>2</sub>、NO<sub>2</sub>和PM<sub>10</sub>的浓度相关性更高;大气中污染物浓度每升高10 μg/m<sup>3</sup>,其患糖尿病的概率分别升高19%、55%、16%<sup>[26]</sup>。在德国一项纳入3 607例非患病人群的队列研究中,BMI>30 kg/m<sup>2</sup>且长期暴露于PM<sub>10</sub>和PM<sub>2.5</sub>的人群中,大气中污染物浓度每升高10 μg/m<sup>3</sup>,其患2型糖尿病风险分别增加19%和12%<sup>[27]</sup>。研究还发现,颈围和腰围均为2型糖尿病的危险因素,其OR值分别为1.15(95%CI: 1.01~1.58)和1.23(95%CI: 1.13~1.99),并且腰围较大的人群其胰岛素抵抗现象明显<sup>[28]</sup>,故腰围和大气污染物对2型糖尿病患病具有协同作用,可能因为超重或肥胖的人群更有可能发生系统性炎症,在空气污染物对机体产生危害的过程中,有些炎症通路会产生协同作用,加重其危害的程度<sup>[14, 29]</sup>。未来的相关研究或可将腰臀围比和BMI同时作为肥胖程度的指标。

## 二、大气污染对2型糖尿病血糖相关指标的影响

1. FPG和餐后2h血糖浓度值:FPG浓度和餐后2h血糖浓度的升高都是判断2型糖尿病的重要指标。在中国台湾地区进行的一项纳入1 023例非患病人群的队列研究提示,大气中每升高四分位数间距浓度的PM<sub>10</sub>、PM<sub>2.5</sub>、NO<sub>2</sub>、CO和O<sub>3</sub>,FPG的浓度就相应增加23.88、36.65、17.03、12.87和21.10 mg/dl<sup>[30]</sup>。另一项对象为11 847名中国成年人的队列研究提示,大气中每升高41.1 μg/m<sup>3</sup>的PM<sub>2.5</sub>,FPG浓度就相应的增加0.26 mmol/L<sup>[10]</sup>。在中国辽宁省进行的1万多名正常人群的队列研究也提示,大气中每升高四分位数间距浓度的PM<sub>10</sub>、PM<sub>2.5</sub>、NO<sub>2</sub>、CO和O<sub>3</sub>等主要大气污染物,FPG浓度就相应的增加0.04~0.09 mmol/L,餐后2h血糖浓度也相应的增加0.10~0.19 mmol/L,并发现长期暴露具有慢性的累积效

应<sup>[24]</sup>。但是相关机制尚不明确,还需加强此方面的研究。

2. 胰岛素抵抗指数(Homeostasis Model Assessment of Insulin Resistance):胰岛素敏感性降低是2型糖尿病的一个重要特征,而大气污染物已被证实可影响机体的胰岛素抵抗功能。Wolf等<sup>[25]</sup>对2 944名糖尿病患者的研究表明,长期暴露于4种主要的大气污染物(PM<sub>10</sub>、PM<sub>2.5</sub>、NO<sub>2</sub>和CO)中,会导致胰岛素抵抗指数升高13.2%~21.2%,空腹胰岛素浓度升高13.2~20.0 mU/L,类似关联也在墨西哥的1 023名正常人群队列中被观察到<sup>[31]</sup>。在辽宁省进行的1万多名正常人群的队列研究表明,相较于其他主要的大气污染物,NO<sub>2</sub>产生的胰岛素抵抗效应最为明显,大气中污染物浓度每升高10 μg/m<sup>3</sup>,可导致胰岛素抵抗指数升高24%<sup>[24]</sup>。

3. 胰岛β细胞功能指数(Homeostasis Model Assessment-β):胰岛β细胞功能紊乱是2型糖尿病发病的重要机制。但是关于大气污染物和β细胞功能之间关系的研究却很少。在墨西哥和中国进行的队列研究中<sup>[24, 30]</sup>,均对这两者的关系进行了探索,并且Chen等<sup>[31]</sup>还着重观察PM<sub>2.5</sub>和CO对胰岛β细胞功能的影响,但结论皆未显示出显著性关联。因此,还需继续加强对该方面的研究。

4. 糖化血红蛋白:糖化血红蛋白水平能够对糖尿病的早期诊断以及病情的早期判断起到积极作用,也能够进一步预测糖尿病发生发展的趋势<sup>[32]</sup>,在筛查糖尿病和糖耐受受损中具有重要的应用价值<sup>[33]</sup>,但该指标与空气污染之间关联的研究较少。在中国台湾地区进行的一项关于2 192名老年人的研究发现<sup>[34]</sup>,当大气中PM<sub>10</sub>和NO<sub>2</sub>的浓度是WHO设定的最高年平均均值(40 μg/m<sup>3</sup>和20 μg/m<sup>3</sup>)的3~7倍时,可显著升高人群中糖化血红蛋白和FPG浓度,但此效应在空气污染水平较低时并不明显。为了研究低污染水平时两者关联程度的大小,Riant等<sup>[35]</sup>在法国北部对2 895名成年人(40~65岁)进行横断面调查,采用多元logistic和广义线性回归模型分析后发现,长期暴露于低污染水平的PM<sub>10</sub>、NO<sub>2</sub>、CO和SO<sub>2</sub>等污染物的环境下,人群的糖化血红蛋白并未显著性升高。

## 三、大气污染物对2型糖尿病血脂相关指标的影响

1. TG、TC、LDL-C、HDL-C:血脂水平异常是2型糖尿病患者中比较普遍的症状,并且是高血糖患者患心血管疾病的主要危险因素之一<sup>[36-37]</sup>,严重时可以导致2型糖尿病患者死亡。在美国进行的73 117名正常人的研究发现,空气污染可以导致暴露人群的血脂异常,进而导致糖尿病或者心血管疾病的发生<sup>[38]</sup>。美国健康及营养状况调查项目(National Health and Nutrition Examination Survey, NHANES III)对11 623名成年人进行跟踪分析,研究显示大气中每升高11.1 μg/m<sup>3</sup>的PM<sub>10</sub>,可导致人群TC、TG、LDL-C升高的风险也随之增加1.43%(95%CI: 1.21%~1.66%)、2.42%(95%CI: 1.09%~3.76%)、1.18%(95%CI: 0.81%~1.56%),但是对HDL-C降低的影响并不显著<sup>[39]</sup>。Cai等<sup>[40]</sup>对144 082例正常人群进行观察,发现每升高2 μg/m<sup>3</sup> PM<sub>10</sub>和7.4 μg/m<sup>3</sup> CO,可导致人群TG升高的风险也随之增加1.9%(95%CI: 1.5%~2.4%)和2.2%(95%CI: 1.6%~2.7%);只有SO<sub>2</sub>的浓度变化对HDL-C产生

显著影响,风险比为0.5%(95%CI:0.3%~0.8%)。

Poursafa等<sup>[41]</sup>在伊朗对14~18岁之间的1413名学生进行基于线性回归模型来探索空气质量指数(air quality index, AQI)与心血管代谢有关危险因素之间相关性的研究发现, AQI与TC、LDL-C和TG之间存在显著正相关关系,与HDL-C有显著负相关关系。Bind等<sup>[42]</sup>对美国1112名老年男性进行的一项队列研究显示,在LDL-C低于80 mg/dl的研究者中,每升高四分位数浓度浓度的PM<sub>2.5</sub>、NO<sub>2</sub>、CO和SO<sub>2</sub>,可导致LDL-C升高7(95%CI:5~10)mg/dl、8.2(95%CI:6~12)mg/dl、3.6(95%CI:2~8)mg/dl和5.9(95%CI:4~10)mg/dl,而在LDL-C水平接近160 mg/dl调查者中,每升高四分位数浓度浓度的PM<sub>2.5</sub>、NO<sub>2</sub>、CO和SO<sub>2</sub>,可导致LDL-C升高16(95%CI:13~20)mg/dl、12.6(95%CI:15~21)mg/dl、10.8(95%CI:9~15)mg/dl和10.1(95%CI:9~16)mg/dl。动物亚慢性毒性实验显示,长期暴露于SO<sub>2</sub>,可导致血浆中TG浓度升高3.63倍<sup>[43]</sup>。

空气污染物在不同的季节,对血脂水平的影响是不同的。一项在中国进行的对3912名糖尿病患者的研究显示,虽然PM<sub>10</sub>、CO和NO<sub>2</sub>的浓度在冬、春季较高,但每升高10 μg/m<sup>3</sup> PM<sub>10</sub>, LDL-C上升的危险性仅为0.16%,低于夏、秋季每升高10 μg/m<sup>3</sup> CO和PM<sub>10</sub>, 2型糖尿病患者的LDL-C上升的危险性为69.55%和0.92%<sup>[44]</sup>。

#### 四、总结与展望

综上所述,大量的流行病学和毒理学研究表明大气主要污染物与2型糖尿病相关指标存在着关系。大气主要污染物可以导致机体血糖水平不同程度的升高,胰岛素抵抗功能的增强,以及胰岛β细胞功能的减退,还可以导致机体血脂水平的紊乱。

我国是世界上大气污染比较严重的发展中国家之一,也是2型糖尿病人口大国,但是针对这两者关系的研究却在国内很少涉及,或者只停留于表面。我国的大气环境、人种特性与国外有很大的差异,我们应针对大气污染物导致2型糖尿病可能的分子生物学机制,研究其影响血糖和血脂相关指标的原理,为我国制定控制大气污染和防治2型糖尿病的相关政策提供参考性依据。

**利益冲突** 所有作者均声明不存在利益冲突

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