Air pollution and traffic linked to deaths and organ rejection in lung transplant patients

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Researchers have shown for the first time that lung transplant patients in Europe who live on or near busy roads with high levels of air pollution are more likely to die or to experience chronic organ rejection, than those living in less polluted areas.

Dr David Ruttens, from the University of Leuven (Belgium) told the European Respiratory Society's International Congress today (29 September, 2015) that the risk of dying increased by 10% for patients living in an area where air pollution was above World Health Organization (WHO) recommended maximum levels, compared with patients living in areas with lower levels of pollution. However, this increased risk was not seen in lung transplant patients who were taking a class of antibiotics called macrolides, which include azithromycin and clarithromycin.

WHO estimates that 3.7 million people worldwide die prematurely every year as a result of exposure to small particulate matter measuring between 2.5-10 micrometers in diameter (known as PM10). Ten micrometers is less than the width of a human hair, and PM10 particles tend to be dust particles stirred up by vehicles on roads and some grinding operations. WHO recommends PM10 particles should not exceed 20 micrograms per cubic metre in the atmosphere.

Dr Ruttens said: "Short and long-term exposure to air pollution has been linked to an increase in deaths from respiratory diseases, particularly among vulnerable populations. Lung transplant patients are among the

most vulnerable because they have weakened immune systems due to the immunosuppressive drugs they have to take to prevent organ rejection."

Around 50% of lung transplant patients survive for five years or more after their operation; a rate that is lower than for other organ transplants and is due to a higher incidence of chronic organ rejection. Doctors have suspected for some time that this might be due to air pollution but, until now, there has been no confirmation that this is the case.

Dr Ruttens and a team of European researchers led by Professor Dr Bart Vanaudenaerde, also from the University of Leuven, collected data on 5,707 lung transplant patients from 13 major lung transplant centres in 10 European countries from 1987 to 2012, including follow-up data in 2013.

They estimated the patients' exposure to PM10 particles at their homes, and collected information on the density of roads around their home addresses. They also collected other information, including date and type of lung transplant, age, sex, underlying disease, socio-economic status, smoking status before the transplant and whether or not the patients were taking macrolides after the transplant. They matched this with outcomes, including chronic rejection and death.

In order to standardise the information on road density and air pollution for addresses all over Europe, the researchers collaborated with an environmental expert consortium (ESCAPE) to quantify annual mean concentrations of PM10 particles, the distance from patients' homes to the nearest main roads, and the amount of road length within a 50, 100, 200, 500 and 1000 metre radius of the home addresses (known as buffer zones).

During an average of 5.6 years of follow-up, 2577 patients (45.2%) died and 2688 (47.1%) developed chronic organ rejection. A total of 3511

patients (62.2%) took macrolides at some point in their treatment, and 2149 patients (37.7%) did not.

Chronic organ rejection was experienced by 61.5% of patients in the macrolide group and in 38.5% of patients not taking macrolides. "Macrolides, such as azithromycin, tend to be given only when organ rejection or inflammation occurs," explained Dr Ruttens. "As fewer patients taking macrolides died, this suggests that the drugs are working and protecting against further complications and death."

A total of 640 (29.8%) of patients died in the macrolide group and 1937 (54.5%) died in the macrolide-free group.

The researchers found a link between road length in the area around patients' homes and chronic rejection in the group of patients not taking macrolides. In the 200, 500 and 1,000 metre buffer zones there was an 11-13% increase in the risk of organ rejection for every 100-metre increase in road length. A similar increase in the risk of death was also seen in the 100, 200 and 500 metre buffer zones. No such associations were seen in the group of patients who were taking macrolides.

"Our results show that both deaths and chronic rejection in lung transplant patients are associated with air pollution and exposure to traffic," said Dr Ruttens. "Lowering the levels of air pollution in Europe would significantly improve the chances of these patients' survival and lower their risk of organ rejection. For instance, if levels of air pollution were reduced to below the maximum recommended by the WHO, there would be a 9.9% reduction in deaths among lung transplant patients who were not taking macrolides, and 6.4% reduction among all patients, regardless of whether or not they were taking macrolides.

"The use of macrolides, such as azithromycin or clarithromycin, seems to protect patients against the devastating effects of air pollution."

The researchers say their research is unique because it is the first time that lung transplant centres across Europe have collaborated to investigate the factors involved in deaths and organ rejection among patients.

Lung transplants are usually the final treatment option for patients with end-stage pulmonary diseases such as lung emphysema, pulmonary fibrosis and cystic fibrosis.

More information: Abstract: The impact of long-term air pollution and traffic on outcome after lung transplantation in Europe.

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