The future of asthma treatment: is a cure possible?

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For around 300 million people in the world, whipping out their inhaler – a medical device that delivers medicine to the lungs to open up narrowed airways – before

puffing medicine into their mouth, is a typical response to wheezing, worsened by an asthma attack.

While inhalers offer momentary relief, it is, however, no cure. But some recent studies have shown therapeutic promise. As we observe World Asthma Day on May 2, let us take a look at the recent progress in asthma treatment.

The disease, which is often triggered by factors such as allergies, sinus infections, pollen, and extreme weather conditions, presents itself through symptoms like breathlessness, tightening of the chest and persistent coughing.

And although current asthma treatments like inhaled corticosteroids and allergy shots, as well as the latest U.S. Food and Drug Administration (FDA)-approved inhalation aerosol Airsupra provide quick relief from these symptoms, Cliff Han, former biologist and founder of U.S.-based allergy lollipop manufacturing company AllerPops, believes that the microbiota may be the key to a cure.

The lung and the microbiome

"Microbiota associated with humans, is increasingly being recognized as an important part of our health," said Han. Eyeing the gut microbiome, people have proposed the gut-brain axis and the lung-gut axis, he added. "Recently, researchers have shown that it is not sterile deep in the lung and have identified different microbial compositions associated with asthma."

A study conducted by AllerPops explored the possible causes and microbiota-related treatments for allergic rhinitis – nasal inflammation caused by an allergen. It was found that common allergies may transpire when there is an oral probiotic deficiency. Simply put, restoring gut health can be crucial to tackling allergic asthma.

Results of the study indicated that the lack of beneficial bacteria like Streptococcus and Veilonella in the oral and nasal cavities causes allergies.

"Our study on oral microbiota in relation to allergic rhinitis shows close interaction between some bacteria and our immune system. Those beneficial bacteria tend to calm down our immune system so that they can live peacefully with us. That interaction also reduces inflammation against allergens," said Han, who has developed prebiotic lollipops, which is a concoction of supplements that not only ease allergy symptoms but also helps to control asthma in nearly 80% of cases.

Moreover, the study led to the Theory of the Negative Trigger (TNT), which postulates that oral probiotics are a negative trigger that results in the host and the microbiota making peace with one another. Therefore, modulating the microbiota with the immune system could treat, and more so, cure allergies as well as autoimmune disorders, according to the study.

Han said: “Managing microbiota will have huge potential to improve our health and, in many cases, cure our chronic suffering. The key is to identify which microbiota should be the primary target and how to manage it more efficiently and sustainably.”

Another recent study led by researchers at University of British Columbia in Canada validates Han’s research on the relationship between the lung and gut microbiota. As most studies highlight the link between gut bacteria and viruses with the immune system, this research also looked at how fungi and archaea could influence inflammation in the lungs, illustrating how different microbial compositions are associated with asthma.

Despite comprising less than one per cent of the gut microbiome, fungi have the potential to impact microbial ecology, according to the study. Although the mechanisms are yet to be confirmed, fungal dysbiosis – an imbalance in fungal composition – in infant gut microbiota have been connected to asthma symptoms.

Han expressed that the microbiota associated with humans is increasingly being recognized as an important part of our health.

Lifestyle changes and asthma prevention

As the saying “prevention is better than cure” goes, the risk of developing asthma could be curbed by enjoying a good night’s sleep, according to a study conducted by Shandong University in China. The study revealed that a healthy sleeping pattern along with a low genetic risk, could prevent about a fifth of total asthma cases. Having mapped the genetic makeup of all the participants as well as monitored their sleep schedules and the occurrence of insomnia and snoring at night, the risk of asthma had significantly reduced. For those with a healthy sleep pattern and a low genetic risk, the likelihood of developing asthma came down by 44%, for those with an intermediate risk, it decreased the chances by 41%, whereas for those with a high genetic risk, it was still cut down by 37%.

While lifestyle changes could benefit with managing the risk, environmental factors also play a significant role. And to expedite research, a study by Karolinska Institutet in Sweden has called attention to the importance of clean air and lung capacity. “Fortunately, we’ve seen a decrease in air pollutants and therefore an increase in air quality in Stockholm over the past 20 years,” said Erik Melen, co-author of the study, pediatrician and professor at the Department of Clinical Research and Education at Karolinska Institutet.

A 20% decline in risk of impaired lung function was observed in children in Stockholm, as a result of breathing in clean air.

Melen said: “It is ultimately of great importance since the lung function that children and adolescents develop as they grow up persists into adulthood,” adding that, “If you have reduced lung function as an adult, you run a greater risk of chronic lung diseases like

COPD (chronic obstructive pulmonary disease), cardiovascular disease and premature death. So by improving air quality, we reduce the likelihood of children developing chronic diseases later in life."

This could indicate a lower risk for asthma, although further studies need to take place. From the results of future studies, emission control measures could be taken into account for city planning policies to support the health of particularly urban communities.

Meanwhile, precision medicine is being heralded as an emerging approach for asthma care, let alone for different disease treatments. Digital asthma biomarkers like eNose can assess asthma control – the degree to which the symptoms of the disease is reduced by therapy – to tailor asthma treatment. A study proved that an eNose analysis is accurate, with it being able to differentiate between people diagnosed with the disease and those who aren't asthmatic, making it a non-invasive tool for the detection of asthma.

Another crucial biomarker is eosinophils. Eosinophils are white blood cells (WBC) that indicate an allergic reaction when high levels of it are in the blood. A high blood eosinophil count of more than 300 cells/μL can evaluate the efficacy of drugs like mepolizumab and omalizumab to treat asthma. This biomarker can predict the success of asthma treatments and in turn, drive treatment choices for patients.

An inhaler-free era for the treatment of asthma?

Another study progressing in asthma therapy research is being conducted by the U.S.-based Arrowhead Pharmaceuticals. In April 2023, the company announced interim results for an ongoing phase 1/2 clinical study of an investigational RNA interference (RNAi) ARO-RAGE, to reduce the production of the receptor for advanced glycation end products (RAGE) for the treatment of asthma.

"Reducing expression of the RAGE protein in pulmonary epithelial cells to the degree that ARO-RAGE has demonstrated to date in this study has the potential to treat patients with asthma and other inflammatory lung diseases in a fundamentally new way. RAGE represents a promising target for intervention as its activation has been implicated as a proximal regulator of the inflammatory cascade in the asthmatic airway, and thus RAGE silencing may result in potent anti-inflammatory effects," said Matthias Salathe, professor, Pulmonary, Critical Care and Sleep Medicine, and vice chancellor for Research at the University of Kansas Medical Center.

The trial demonstrated positive results which saw a mean maximum reduction of soluble RAGE by 90% with 92 mg dose, and for 10 to 44 mg dosages, the response ranged from 31% to 59%.

Furthermore, another more permanent asthma treatment, especially for those who do not respond well to steroids focuses on the movement of pericytes. Pericytes, which are

a kind of stem cell found in the lining of blood vessels, tend to travel to airway walls when an inflammatory reaction occurs. These pericytes develop into cells, thickening the airway walls and making it less flexible. As pericyte movement is controlled by the protein CXCL12, researchers at Aston University in England, have tested a molecule LIT-927, targeting the expression of the protein.

In a successful trial done on mice, the symptoms had completely disappeared after two weeks when treated with LIT-927, and noticeable airway size difference was observed, with those mice that were given LIT-927 developing thinner airway walls, when compared to those who were not treated with the drug candidate.

Despite this potentially being a long-lasting solution for asthma, more studies are required before the efficacy of the treatment is measured in human beings.

Although many still rely on corticosteroids – which can have adverse effects after long-term use in some people – with more research targeting various endotypes of asthma, we might just be close to a cure. And with developments with regard to its causative factors, preventive measures could be the answer as well.