Diet could combat adverse side-effects of quinine

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(Medical Xpress)—Scientists at The University of Nottingham say adverse side-effects caused by the anti-parasitic drug quinine in the treatment of malaria could be controlled by what we eat.

The research, carried out by Nottingham scientists on the University's campuses in the UK and Malaysia, indicates that natural variation in our levels of the amino acid, tryptophan, has a marked bearing on how we respond to quinine treatment. It appears that the lower our levels of tryptophan the more likely it is that we would suffer side-effects. And because tryptophan is an essential amino acid the body cannot produce it—we get it from the food we eat.

Discovered back in the 1600s, quinine is still used for anti-malaria treatment. However, it is associated with a long list of side effects ranging from sickness and headaches to blindness, deafness and in rare

cases death. This latest study, published in the *Journal of Antimicrobial Chemotherapy*, could offer a cheap and simple way of combating our adverse reaction to quinine treatment and improving the performance of this important drug.

The study, funded by The University of Nottingham's doctoral award scheme, was led by Dr Simon Avery and Dr Kang-Nee Ting from the Schools of Biology in the UK and Biomedical Sciences in Malaysia, in collaboration with Professor Richard Pleass now at the University of Liverpool.

Reinforcing previous research

These findings reinforce a discovery they made three years ago.

Using a yeast model, which is a relatively close evolutionary neighbour of the human, they showed that quinine can block take-up of tryptophan, causing quinine toxicity in cells. This research, published in 2009, gave the scientific community a new insight into the way quinine behaves and led Dr Avery and his team to believe that a quinine/tryptophan combination therapy might allow the use of higher quinine dosages to improve the effectiveness of the drug and reduce the risk of adverse side-effects.

A year later the researchers received funding through the University's Intercampus Doctoral Award Scheme (MIDAS) and Malaysia's Ministry of Higher Education Scholarship for a PhD student, Ms Farida Islahudin, to screen malaria patients in several public hospitals in the Klang Valley in Malaysia.

They discovered that quinine levels in patients receiving treatment for Malaria were linked to the patients' levels of tryptophan. They were also able to show that the incidence of adverse reaction to quinine was

significantly lower in patients with high levels of tryptophan.

Diet or dietary supplements could avert the toxic effects of quinine

Dr Simon Avery said: "This new work with malaria patients shows that our earlier suggestions are largely borne out in the clinic. That is, natural variation in human levels of the amino acid tryptophan can have a marked bearing on patient responses to quinine therapy. One potential application stems from the fact that tryptophan levels can be modified by diet, possibly offering a cheap and simple way of manipulating adverse quinine responses in patients."

About 3.3bn people—half the world's population—are at risk of malaria. In 2010 there were about 216 million cases of malaria and an estimated 655,000 people died from the disease. In Africa, malaria is a leading cause of death in children.

The body uses tryptophan to make the brain chemical serotonin—which is thought to produce healthy sleep and a stable mood—so a lack of tryptophan, induced by quinine, could also explain why many of quinine's toxic effects are localised to the head region.

This on-going research fits well with evidence that quinine reactions are more severe in malnourished individuals. Tryptophan is abundant in meat but limited in yams, a staple food crop in the tropics where malaria is prevalent. If quinine severely reduces tryptophan uptake, then it follows that people with pre-existing tryptophan deficiency, a common occurrence in undernourished populations, would be especially at risk from this drug.

The paper is also a rare example of how yeast can be used as a model for

gaining clinically-relevant insights into anti-malarial action. This approach avoids the use of animal experimentation adding further value to the strategy.

Provided by University of Nottingham