**Major advance in sleeping sickness drug made by Glasgow scientists**

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Scientists have made a key advance in developing a safer cure for sleeping sickness.

Sleeping sickness – or human African trypanosomiasis (HAT) – is a neglected tropical disease of major importance.

Transmitted by the tsetse fly and caused by the trypanosome parasite, sleeping sickness is invariably fatal if left untreated.

Once the disease has crossed the blood-brain barrier and entered the central nervous system the most commonly-used treatment is an intravenous course of the arsenic-based drug melarsoprol.

Treatment is protracted, excruciatingly painful and often deadly itself, killing one in 20 patients due to its brain toxicity.

Now researchers at the University of Glasgow’s Institute for Infection, Immunology and Inflammation have created a safer version of the drug that could be administered orally in pill form.

The research, funded by the Medical Research Council and led by Professor Peter Kennedy, Burton Chair of Neurology, is published online on the Public Library of Science Neglected Tropical Diseases website.

Prof Kennedy said: “Sleeping sickness is endemic in 36 sub-Saharan countries, exposing 60 million people to the risk of infection. Around 30,000 people at least are currently infected.

“Infection can last several weeks to several years before it crosses the blood-brain barrier and causes brain inflammation and swelling, always resulting in death if left untreated.

Even treated patients can be left with severe residual brain damage’

Because melarsoprol has a low solubility in water, it is dissolved in propylene glycol and administered intravenously.

The result is a highly-toxic drug that kills five per cent of patients receiving it and leaves many others permanently brain damaged.

The researchers at the University combined the melarsoprol with cyclodextrins – molecules that surrounded the drug allowing it to be administered orally, increasing its solubility and releasing the drug more slowly in the gut.

Prof Kennedy said: “Melarsoprol is very effective at killing the parasites but when given intravenously it probably does this too quickly, which is in part why we think it so dangerous.

By controlling the rate of release of the drug with this new oral formulation, we believe we make it safer.”

In laboratory tests the altered drug was shown to retain its ability to kill the infection, and was able to cure mice infected with the parasite after a seven-day daily oral dosing schedule.

The drug cleared parasites from the brain and restored normal blood-brain barrier integrity.

Prof Kennedy said: “This new research is the most clinically important in the 20 years of our trypanosome research group.

It has the potential of a major therapeutic advance and if it is equally effective in humans then it would also have a significant socio-economic impact because the duration of inpatient treatment would be shorter and some patients might even be eventually treated at home.”

The researchers hope to secure more funding soon in order to progress to Phase 2a trials in Uganda in around 18 months which would ascertain whether it is indeed effective in curing in human subjects with Trypanosome brucei rhodesiense brain infection.

Prof Kennedy added: “You always have to be very cautious when extrapolating results from mouse models to the human disease but there are several reasons why we are quietly optimistic that this may very well work in humans too.

“The mouse model reproduces the pathology of human sleeping sickness extremely well, and furthermore we are using a drug which is already effectively used to treat humans with the disease.”

There are two forms of the HAT: Trypanosome brucei gambiense, which accounts for 95 per cent of reported cases of sleeping sickness, and can infect a person for years without any major symptoms, often already having progressed to an advanced stage when signs do appear.

Trypanosome brucei rhodesiense accounts for five percent of cases and progresses rapidly with symptoms apparent a few weeks or months after infection and quickly crossing the blood-brain barrier.

The disease progresses in two stages, the first characterised by fever, headaches, joint pain and itching, before progressing to the second phase when the parasites invade the central nervous system.

This stage results in reduced coordination, confusion, weakness, tremors and disruption of the sleep cycle resulting in insomnia and bouts of daytime sleeping from which the disease takes its name.

Uganda is the only African country where both forms of HAT are known to co-exist.

If and when these eventually occur in the same patient then a safer form of melarsoprol will be essential as it is the only drug that can cure both types of brain infection.

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