Drug resistance danger for sleeping sickness treatments

July 5 2010

(PhysOrg.com) -- Drugs used to treat the epidemic disease African sleeping sickness must be used prudently to prevent the parasite acquiring resistance to current medicines, a new study at the University of Dundee has shown.

Currently, the World Health Organisation estimates that around 400,000 people are infected with the disease each year, with an annual death toll of around 50,000.

Last year a new treatment was introduced for the disease, a combination therapy of the drugs nifurtimox and eflornithine, which has shortened treatment times from two weeks to one, reduced costs, and made it easier to administer drugs to patients in rural regions of sub-Saharan Africa, where the disease is most prevalent.

However, tests carried out by a team led by Professor Alan Fairlamb in the College of Life Sciences at Dundee has shown trypanosomes can quickly develop resistance to nifurtimox.

"This combination therapy has had some initial success but our tests have shown there is a danger, in that exposing the parasite to nifurtimox results in increased resistance to the point where the disease is no longer curable," said Professor Fairlamb.

"This means that nifurtimox should never be prescribed on its own, only as part of a combination therapy."

The Dundee team also tested an experimental drug, fexinidazole, which is currently in clinical trials as a new oral treatment for sleeping sickness, and found that it too can quickly cause the parasite to acquire resistance not only to itself, but also to nifurtimox.

"This is another potential treatment which should not be used on its own as we have seen the parasite can readily develop resistance. It is a very worrying issue because once resistance emerges, those drugs become redundant. We only have two treatments available for the late stage of the disease when the brain is infected: nifurtimox plus eflornithine or melarsoprol, an arsenic-based drug that kills 1 in 20 patients who receive it.

"This highlights important policy issues regarding drug treatment for this neglected disease and also points to the need for better and safer drugs which could be administered as combinations to reduce the risk of resistance emerging."

The Dundee team's research is published in the journal '*Antimicrobial Agents and Chemotherapy*'. The work was funded by the Biotechnology and Biological Sciences Research Council and the Wellcome Trust.

Professor Fairlamb and colleagues in the Drug Discovery Unit at Dundee are already working on developing new compounds to treat sleeping sickness, among other neglected diseases. Earlier this year they announced a breakthrough in finding a new drug target for the disease, which shows promise for the development of effective, orally administered, low toxicity drugs to treat sleeping sickness.

African sleeping sickness (human African trypanosomiasis or HAT) is spread by the bite of a tsetse fly. The disease has two stages, the second of which is particularly difficult to treat in poverty-stricken rural areas, where many victims live.

Tragically for sufferers, African sleeping sickness is a neglected disease, one which has simply not been on the radar of large pharmaceutical companies. The shareholder value driven model of big drug companies, which works so effectively in the developed world, is not relevant to areas such as sub-Saharan Africa, where patients cannot afford to pay for their medicines.

The Drug Discovery Unit at Dundee was formed in 2005 specifically to fill the void of research and development of drug targets for diseases of poverty like African sleeping sickness, leishmaniasis, and Chagas' disease that afflict the developing world.

Provided by University of Dundee