Tools for more accurate dosage of drugs against HIV/AIDS and malaria

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A doctoral thesis presented at the Sahlgrenska Academy, University of Gothenburg, Sweden, shows that it is possible to describe and quantify the relationships between dose, concentration and effectiveness of several drugs against HIV/AIDS and malaria. The method may allow improved treatment and fewer undesired effects for patients with these diseases.

Registered pharmacist Daniel Röshammar has in his thesis studied the optimal use of certain pharmaceutical substances that are used to combat HIV/AIDS and malaria. He has analysed, among other things, data from 121 healthy volunteers from Uganda using a mathematical model known as a pharmacometric model. The study showed that both sex and genetic differences between individuals influence the way in which the body metabolises efavirenz, which is part of some anti-HIV/AIDS drugs. Other studies have focussed on 74 people from Zimbabwe with HIV/AIDS, and showed that a reduction in the daily dose of efavirenz from 600 mg to 400 mg can reduce the risk of undesired effects in those affected who have a genetically conditioned poorer ability to catabolise the substance.

"Many HIV/AIDS patients are treated with efavirenz, and they should be genetically tested using a blood test before deciding on a dose. This is particularly important in Africa, where the fraction of patients with a poorer catabolic ability is greater than it is elsewhere", says Daniel Röshammar.

Repeated measurements of the drug concentrations and virus levels in 239 previously untreated Scandinavian patients with HIV/AIDS allowed a similar model to be used in order to study the antiretroviral effects of anti-HIV/AIDS drugs. Calculations showed that treatment in which efavirenz was combined with other pharmaceutical substances was more effective than two other frequently used combination treatments.

"It may be possible in the future to use the model to predict when the treatment will loose its effectiveness for an individual patient, and explain why", says Daniel Röshammar.

Further work involved using a model to describe how the catabolism of the anti-malarial drug artemisinin increases and the concentration of the drug decreases when patients take this drug. When artemisinin was given to 97 patients in Vietnam without other drugs, approximately 37% of them were affected by recrudescent malaria. The model showed that this could not be explained solely by low drug concentrations. Another anti-malarial drug, piperaquine, may be a suitable partner for artemisinin in the treatment of malaria. An investigation of 12 Vietnamese study subjects, however, allowed scientists to estimate that the levels of piperaquine that remain in the body are too low to be effective, and this increases the risk that the malaria parasite will develop resistance.

"Research shows that pharmacometric models can be adapted to patient data in order to understand the relationships between drug concentration, effectiveness and the progress of disease, while at the same time taking into consideration differences between patients such as, for example, weight, age, sex, genetic factors, other diseases and other drugs. We expect that these tools will be important in the fight against HIV/AIDS and malaria", says Daniel Röshammar.

Source: University of Gothenburg