Action against AIDS Germany

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Viral load diagnostics

Background information

An HIV infection has to be treated on a life-long basis. According to the latest treatment recommendations of the World Health Organisation (WHO), anti-retroviral treatment should be started as early as possible while the immune system is still largely intact. In 2015, out of 37 million people living with HIV (PLHIV) globally, 17 million received lifesaving anti-retroviral treatment. (UNAIDS 2016)

It is not only anti-retroviral medicines (ARVs) which are needed for successful HIV treatment but also diagnostics.

So far the success of anti-retroviral treatment in countries of the Global South has mainly been measured by taking the CD4 count on a regular basis. The CD4 count determines the number of CD4 cells – or T-helper cells – per microliter blood. Yet a CD4 count is only a snapshot of the immune system's state at a particular moment. It can fluctuate according to the time of the day, concurrent infections, etc. The WHO therefore recommends the use of CD4 tests mainly for starting PLHIV on treatment. Until recently PLHIV were started on treatment at a CD4 count of 500 or 350 and many countries of the Global South still implement these older WHO recommendations. According to the latest treatment guidelines of the WHO of September 2015, however, any PLHIV who has tested HIV-positive should be started on treatment irrespective of their CD count. The determination of the CD4 count is therefore becoming less important but maintains its clinical significance, e.g. for risk evaluation of disease progression in case of first diagnosis or for indicating the prevention of infections.

However, to monitor treatment success, the WHO recommends the regular use a viral load tests. In determining the viral load, the number of HI virus particles (also called copies) in one millilitre of blood is measured.

Anti-retroviral treatment (ART) is treatment for life. One therefore has to ensure that ART continues to be effective. In cases where there is resistance to some medicines, the treatment regimen has to be changed to a different anti-retroviral regimen (with other groups of pharmaceutically active agents). In order to detect, when changes need to be made, viral load testing plays a central role. Yet, UNAIDS estimates that in 2014 less than a quarter of PLHIV receiving anti-retroviral treatment had access to viral load testing.

One speaks of a high viral load if it exceeds 50,000 virus copies per ml of blood. This can be the case of PLHIV who have not got access to treatment. Normally, the viral load should be undetectable after three to six months of anti-retroviral treatment. Today a viral load below 50 copies per millilitre is defined as undetectable.

Viral load testing. Part of UNAIDS fast track approach

In order to achieve an end to AIDS as a global health threat by 2030, UNAIDS came up with the fast track concept in 2014. It foresees that by 2020, 90 % of people living with HIV know their HIV-status, 90 % of those knowing their status have access to anti-retroviral treatment and 90 % of all PLHIV on treatment have an undetectable viral load. By 2030 this needs to be increased to 95 % respectively. As a means of control, regular viral load testing is essential. In 2015 only 38% of all PLHIV were virologically suppressed.

Viral load testing has various advantages:

- One important application of viral load testing is the detection of the HI-virus in new-borns. The use of antibody tests within the first 12-18 months does not produce accurate results in babies, as a baby has the antibodies of the mother for the first 18 months of its life. Antigen tests (p24) are unreliable in particular in the presence of antibodies since antigens are bonded to antibodies and evade testing. HIV-positive new-borns should, however, be treated as early as possible as HIV positive babies have a 50% risk of dying before the 2nd birthday. It is only through virological tests that one can determine an infection in babies. Yet, only 54% of the babies of HIV-positive mothers received virological tests within their first two months of life in 2015. In addition to scaling up the testing of babies, it is important that tests can be used as soon after birth as possible.
- A viral load tests demonstrates whether anti-retroviral treatment is successful in effectively suppressing the virus. If this is not the case, there may be problems with adherence to the treatment which can usually be overcome with better treatment counselling and comprehensive therapy support. If the viral load is detectable (more than 1000 copies/ml) despite accurate medication intake, this indicates that resistance has developed and that the anti-retroviral regimen has to be changed. A repeated viral load of more than 1000 copies is considered tantamount to treatment failure.
- If viral load increases, the risk of transmitting HIV to a sexual partner or to an unborn child also rises. If the viral load is undetectable, the risk of transmission from mother to child (during pregnancy, birth or breast feeding) or between sexual partners is negligible.

There are two kinds of viral load machines:

- On the one hand, we have laboratory based machines which can run a maximum of 300 tests per 24 hours. Some machines produce results within three, others after 48 hours. Approx. 30 – 100 tests can be carried out simultaneously depending on the machine used. Laboratory viral load machines are, however, complicated to handle and require trained laboratory staff.
- On the other hand, we have point-of-care diagnostics. They are easy to handle but can only carry out one to two tests at a time (duration: 45 minutes to 3 hours). Some point-of-care diagnostics work with an external battery supply and do not depend on electric power and are therefore well adapted to resource poor settings.

The method of transport most suitable for blood samples in developing countries is the use of dried blood spot technology (DBS). With DBS, one drop of capillary blood is dried on a filter paper which can be transported without cooling and can be stored for a long time. Many machines use blood plasma but can also determine the viral load from DBS provided sample preparation has been adapted. For point-of-care diagnostics DBS is less of a priority, as people usually reside close to health centres which use the machines.

Challenges

Cost

The cost per viral load test is between 10 and 60 US Dollar. In comparison, the CD4 tests cost on average about 5 US Dollar so that a changeover from CD4 to viral load tests represents a financial problem for many countries of the Global South.

Each test kit is designed for a specific type of viral load machine. Machines by different manufacturers are not compatible so that one has to purchase the test kits for a particular machine by that manufacturer.

Availability

So far viral load machines in the Global South are mainly available in large cities. In some countries their availability is limited to the capital city so that the changeover from CD4 to viral load tests causes logistical and financial problems in many countries of the Global South.

For babies the availability of virological HIV-tests which produce accurate results soon after birth needs to be improved.

Need for more DBS technology

Plasma samples are not suitable for long transport. This necessitates extensive use of dried blood spot technology (DBS) which is better suited to developing countries.

Turn-around time for results

Many laboratory staff are overworked due to staff shortages. Sometimes machines are not working. All of this results in a prolonged turn-around times before results are communicated to the PLHIV or the care-giver in terms of paediatric HIV. This in turn leads to some results not reaching the person who has been tested. All of this hampers timely and successful treatment.

Demands

On policy makers:

- Support countries financially and with know-how to implement WHO directives and provide suitable training for laboratory staff.
- Increase contribution to the Global Fund to Fight HIV/Aids, Tuberculosis and Malaria (GFATM) and ensure that access to viral load diagnostics including early infant diagnostics for new-borns forms part and parcel of grants.

On manufacturers of diagnostics:

- Widen the use of DBS technology across all viral load diagnostics.
- Development of early infant diagnostics (EID) which are sensitive enough to produce accurate results of HIV-status of babies as early as possible after birth.
- Price reduction for viral load machines, reagents and test kits.
- Better cooperation between manufacturers so that a platform technology can be developed which allows to the use of interchangeable test kits and materials rather than being bound to one manufacturer.
- Simplify the handling of the instruments.

Sources

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