Göteborg, 2021

ANTIRETROVIRAL TREATMENT OF HIV-1 IN SWEDEN WITH FOCUS ON VIROLOGICAL ASPECTS

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i hörsal Arvid Carlsson, Medicinaregatan 3, Göteborg,

Torsdagen den 4 mars 2021 klockan 09.00
av Erik Sörstedt

Fakultetsopponent:

Niels Obel

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Avhandlingen baseras på följande delarbeten:

I. Sörstedt E, Nilsson S, Blaxhult A, Gisslén M, Flamholc L, Sönnerborg A, Yilmaz A. **Viral blips during suppressive antiretroviral treatment are associated with high baseline HIV-1 RNA levels**. BMC infectious diseases. 2016 Dec 1;16(1):305.

II. Sörstedt E, Carlander C, Flamholc L, Hejdeman B, Svedhem V, Sönnerborg A, Gisslén M, Yilmaz A. **Effect of dolutegravir in combination with nucleoside reverse transcriptase inhibitors (NRTIs) on people living with HIV who have pre-existing NRTI mutations.** International Journal of Antimicrobial Agents. 2018 May 1;51(5):733–8.

III. Sörstedt E, Nilsson S, Nowak P, Treutiger CJ, Månsson F, Ånghagen L, Gisslén M, Yilmaz A. **Less than half of patients with chronic HIV-infection and baseline HIV- RNA > 500,000 copies/mL reach treatment goal of < 50 copies/mL within six months.** Submitted manuscript.

IV. Sörstedt E, Nilsson S, Sönnerborg A, Svedhem-Johansson V, Treutiger CJ, Månsson F, Ånghagen L, Berggren H, Gisslén M, Yilmaz A. **Viral blips are more common in patients on antiretroviral therapy containing protease inhibitors in comparison to integrase inhibitors and non-nucleoside reverse transcriptase inhibitors – a retrospective nationwide study in Sweden 2007–2020**. In manuscript.

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Abstract

From a clinical standpoint, there are many factors to consider when optimizing the care for people living with HIV (PLWH). With help from clinical guidelines, most obstacles can be addressed. Expanded knowledge is however in constant demand, from local conditions to universal processes. This thesis emerged from a demand for both clinical and virological data about the effect of antiretroviral treatment (ART) in Sweden. All data were derived from the national InfCareHIV database.

The current goal of ART is to achieve lasting suppression to < 50 HIV RNA copies/mL. Transient episodes of viremia up to 500 copies/mL, so-called viral blips, are not uncommon. We sought to investigate the clinical importance and outcome of this phenomenon. Through two large retrospective studies, **Paper I and IV**, we concluded that it is more common with blips in PLWH with higher baseline viral load and ART based on boosted Protease Inhibitors (PI). Blip incidence during Integrase Strand Transfer Inhibitors (INSTI) and Non-Nucleoside Reverse Transcriptase Inhibitor-based ART was lower at a similar level. In PLWH who reached HIV RNA suppression after initiating their first ART, blips were relatively common (10–20% of all participants) but not associated with an increased risk of virological failure.

Before the introduction of the INSTI dolutegravir, PLWH with resistance mutations to Nucleoside Reverse Transcriptase Inhibitors were often restricted to PI-based treatment. PIs are characterized by many drug interactions and often tolerability issues. **In Paper II**, 244 participants with either dolutegravir or traditional PI-based ART were retrospectively studied. Dolutegravir has pharmacological benefits and we concluded that it was an equivalent alternative.

Treatment recommendations are not affected by different levels of baseline viremia. Most clinical studies compare the outcome in participants with higher or lower than 100,000 HIV RNA copies/mL. Considerably higher levels of viremia are sometimes observed. In **Paper III**, we included 2,956 PLWH of whom 394 (13%) had baseline > 500k HIV RNA copies/mL. We found that participants with that high initial viremia needed longer time to reach viral suppression. Initial treatment with INSTIs was associated with faster viral decline. Higher baseline viral load was not associated with an increased risk of virological failure.

Keywords: HIV-1, antiretroviral therapy, transient viremia, viral blip, nucleoside reverse transcriptase inhibitor resistance, dolutegravir, baseline viral load, HIV RNA, virological failure

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