India has the second highest number of people living with HIV/AIDS and it happened within a few years after identifying the first cluster of HIV infected sex workers in Chennai in 1986. The management of HIV infection evolved rapidly after 1994 when the triple therapy was introduced. Thereafter the disease was identified as a chronic manageable illness like hypertension and diabetes. Till now there is no curable treatment for HIV. Introduction of Zidovudine to positive mothers during antenatal period prevented transmission to babies and was considered as a great achievement. The National AIDS Control Organisation has successfully implemented strategies for diagnosis, treatment and prevention of this disease.

The initial WHO recommendation was to initiate ART when CD4 count is <350 and/or stage 3 or 4 disease. Later WHO changed the recommendation to CD4 less than 500 and/or stage 3 or 4 disease, acute HIV infection and combination therapy for mother to child transmission. Drug intolerance, early emergence of resistance, inconvenience to patients leading to poor adherence due to multiple drugs were factors contributed to delayed initiation of ART. However evidence from systematic reviews and cohort analysis indicated that earlier initiation of ART reduced the mortality, morbidity and transmission. Hence newer guidelines were issued regarding management of HIV infection.

WHEN TO START TREATMENT?

- All patients with detectable viremia regardless of CD4
Patients with undetectable vireamia if CD4 low

A/C HIV: - initiation prior to development of antibody reduces the size of latent HIV reservoir & reduces immune activation. Also protect central memory T cell from infection. Benefits maximal during first few weeks of infection, but up to 6 months is established.

RCT Data now confirms previous recommendations of early initiation of ART because of the clinical benefits like reduction in AIDS related events and non AIDS related events (cardiovascular diseases, renal disease, various cancers, liver disorders, and neurocognitive disorders).

WHAT TO START?

<table>
<thead>
<tr>
<th>INSTI based Regimen</th>
<th>NNRTI based regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dolutigravir/ABC/LAM</td>
<td>ZLN /ZLE</td>
</tr>
<tr>
<td>Dolutigravir/TAF/EMTRI</td>
<td>SLN/SLE</td>
</tr>
<tr>
<td>Elvitegravir/cobicistat, /TAF/EMTRI</td>
<td>TLN / TLE</td>
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<tr>
<td>Raltegravir/TAF/EMTRI</td>
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</table>

INSTI (Integrase strand transfer inhibitors) based regimens are optimal for the initial therapy. Tenofovir alafenamide (TAF) is a newer substitute for Tenofovir disoproxil fumarate (TDF) as the latter is associated with kidney injury, osteoporosis or osteopenia. However if TAF is not available TDF can be used. The available INSTI are DOLUTIGRAVIR, ELVITEGRAVIR-COBICISTAT and RALTEGRAVIR.

PREGNANCY

HIV infected pregnant women should be initiated on ART irrespective of CD4 count or clinical stage. The regimen includes NRTI backbone with INSTI or boosted PI. Raltegravir is the recommended INSTI for pregnancy. Recommended boosted PI include Atazanavir or Darunavir. The recommended NNRTI is EFV when initiated after first eight weeks of pregnancy. If an HIV infected woman who is taking EFV becomes pregnant the regimen may be continued.

<table>
<thead>
<tr>
<th>NRTI</th>
<th>INSTI</th>
<th>*PI</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABC/ LAM</td>
<td>RAL</td>
<td>r ATZ</td>
</tr>
<tr>
<td>TDF/EMTRI</td>
<td>Darunavir</td>
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</tr>
<tr>
<td>ZIDO/LAM</td>
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</tbody>
</table>

r denotes Ritonavir boosting

ART AND OI

ART should be initiated within first two weeks after diagnosis of opportunistic infection but there are two exceptions

1. Cryptococcal meningitis- ART should be initiated after five weeks of therapy

2. TUBERCULOSIS- If the CD4 count is less than 50 ART may be initiated in two weeks. But if CD4 is more than 50 treatment can be initiated within eight weeks. TAF is not recommended with Rifampicin.

WHEN AND HOW TO SWITCH THERAPY?

Earlier, the indications for switching therapy were ART failure and life threatening complications. Presence of any adverse effects, simplification of regimen, anticipation of drug –drug interaction, pregnancy or planning pregnancy, food restrictions, all are current indications to switch therapy. Drugs can be changed to a single pill regimen from any older regimen. Available single pill regimen are

- Dolutigravir /ABC/ LAM
- Elvitegravir© /Etmri/ TAF
- Elvitegravir© /Etmri/ TDF

However, switching should be done when there is a full virological suppression. A complete treatment history and a resistance testing should be obtained prior to switching. Within the class switching has the lowest risk. (TDF-TAF, EFV-RILPIVIRIN)
LABORATORY MONITORING

The recommendations promote screening for mutation prior to initiating treatment. Apart from the CD4 count, viral load is done initially and it is recommended that viral load may be done every 4 to 6 weeks till there is no detectable viremia (< 50 copies/ml). After suppression, viral load is done every 3 months till suppressed for 1 year. Thereafter every 6 months assay is done as long as viral load is stable. Newer methods for laboratory monitoring have also evolved. Cepheid Xpert HIV1 viral load assay is one such method where the result is ready within two hours. SAMBA-HIV - semi quantitative assay (simple amplification based assay) is a point of care viral load monitoring assay for resource limited setting. Here two groups can be distinguished, those with viral load > 1000 copies /ml and others with <1000 copies/ml. Virological failure should be considered when RNA copies are above 200 copies /ml (previously 1000 copies/ml).

PREVENTION

Offering ART to all positives is the first step in preventing transmission. Also it is recommended to high risk people from a population with an HIV incidence of > 2%/year. Sero negative partners of HIV positives are also offered prophylactic treatment. The drug given is Tenofovir + Etmricitabine.

POST EXPOSURE PROPHYLAXIS

This is an emergency intervention to prevent HIV infection following an occupational or non occupational exposure. Selection of drug depends on many factors, and an expert may be contacted. The recommended drugs are as follows:-

- TDF + EMTRI + RAL
- TDF + EMTRI + DOLUTIGRAVIR
- TDF + EMTRI + c ELVITEGRAVIR
- TDF + EMTRI + r Darunavir

Guideline still recommends PEP initiation within 72 hrs of exposure. PEP should be continued for 28 days.

As the newer drugs are having excellent potency, greater convenience and greater safety and tolerability, lifelong viral suppression is possible and it reduces the risk of resistance and transmission hence provides a good quality life to patients.

REFERENCES

1. Antiretroviral drugs for treatment and prevention of HIV infected adults- 2016 recommendations of the international anti viral society- USA panel JAMA July 12-2016
2. Initiation of antiretroviral therapy in early symptomatic HIV infection Lundgren JD, Babiker AG NEJM-2015-373(9)