PEP and PrEP
What the Heck?

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Definitions

- **PEP** – *Post* Exposure Prophylaxis
  - Often separated into occupational and non-occupational PEP (nPEP)
  - For this talk we will consider them together
- **PrEP** – *Pre* Exposure Prophylaxis

Risk of Acquiring HIV

- **Occupational**
  - Needle Stick 1/300
  - Mucosal Exposure 1/1143 (0.09%)
  - None from exposure to intact skin
- **Non-occupational (i.e. sexual)**
  - Receptive Anal 1/200
  - Receptive Vaginal 1/1,000
  - Insertive Anal/Vaginal 5-6/10,000
  - Receptive Oral 1/10,000
Additional Factors Influencing Risk

- Viral Load of the source patient
- If source is unknown can make estimates of odds of having HIV (0.43% males 18-39)
- Guidelines recommend against PEP for exposure via “found needles” unless there is visible blood or other reasons to think high risk exists

Studies “Proving” PEP Works

- No true randomized controlled trials
- Observational trial of 200 MSM given PEP to take after exposure: 11 seroconversions [10 failed to take PEP, 1 did]
- CDC needle stick registry showed taking AZT vs. not had an OR of 0.19 (older data)
- Much of the rest of this is extrapolated from MTC transmission studies

Giving PEP
Initial Evaluation

- Baseline Testing of Exposed Individual
  - HIV, Hep B and C status
  - CBC, CMP and BHCG (if appropriate)
  - Testing of the Source Patient (if available)
  - Rapid HIV, Hep B and C status
  - If known HIV +
    - Most recent Viral Load
    - Current HIV medications
    - If measureable, also need history of Genotype and Meds taken
Giving PEP Counseling

- Discuss Risk benefits of Treatment vs. Not
- Review lack of 100% protection
- Discuss how to avoid infecting others if they become infected
  - Avoid unprotected sex, donation of blood or other body tissues
- Discuss medications and adherence
- Arrange for f/u

Giving PEP The Meds

- If source is newly diagnosed HIV+ or not available for testing
  - Usual choice is Truvada (Emtricitabine/Tenofovir) + either Dolutegravir, Raltegravir or Darunavir
- If source is known HIV+
  - If never treated and no genotype available do as above
  - If on treatment and undetectable, use same regimen they are taking
  - If detectable and heavily pretreated, consult an expert, but do not delay initiation of one of the regimens above pending further information

Giving PEP Timing and Duration

- Strong Evidence that sooner is better, not usually recommended after 72 hours
- Duration of PEP 28 days
- Minimal Data to support this
- Some studies on SIV in Macques suggest it is better than 7 or 14 days for sexual acquisition
Giving PEP
Follow-up Testing

- CBC and CMP at 2-4 weeks after starting therapy
- HIV testing
  - If lab uses third generation testing (Ab only), do it at 6 weeks, 3 months and 6 months
  - If lab uses fourth generation testing (Ab/Ag combo), do it at 6 weeks and 4 months
- Don’t forget other BBP testing (Hep B and C)

PrEP

- In a sense it is PEP with zero time lag from exposure to starting the drugs
- Much like malaria prophylaxis
- Several studies have shown it works in trials
- Recently 2 papers have reviewed experience in the “real world”

PrEP iPrEx

- Participants randomized placebo vs. Truvada
- All received comprehensive counseling, condoms, etc
- Overall a 42% reduction in HIV infections in Truvada participants
- Post hoc analysis of those on Truvada with consistently + drug levels, protection was 93%
- 3 individuals were randomized who had acute HIV and 2 developed resistance
- No increase in “sexual risk taking”
PrEP
Other studies
- FEM-PrEP did not show benefit, but had a huge non-adherence problem
- TDF2 showed 62% protection (only statistically significant in men)
- Partner’s PrEP showed 66% efficacy in women and 84% in men
- Ipergay compared on demand to daily PrEP in MSM and showed 86% efficacy in each arm

PrEP
Controversies
- Does it lead to increased unprotected sex and does this negate efficacy of PrEP?
- Does it create resistant virus in those infected?
- Is it cost effective?
- Who should receive PrEP?

PrEP
Kaiser of NoCal Experience
- 657 MSM in Bay area prescribed PrEP
- Mean duration of use 7.2 months, total of 388 person years
- No new HIV infections
- 187 developed at least one STI and 78 had multiple STI’s
- Previous data would suggest a rate of new HIV infections of 8.9/100 patient years (35 cases)
PrEP
The PROUD study
- 544 MSM randomized to immediate vs. deferred PrEP open label study (terminated deferred arm early)
- Immediate Arm had 3/243 HIV infections (1.2/100 patient years)
- Deferred Arm had 20/245 HIV infections (9.0/100 patient years) <in spite of 174 episodes of PEP>
- No difference in rate of STI’s but higher rate of reported unprotected sex in immediate arm

PrEP
Controversies
- Does it lead to increased unprotected sex and does this negate efficacy of PrEP?
- Yes it does seem to increase unprotected sex, especially the Kaiser data
- It did not result in loss of efficacy in preventing HIV infection

PrEP
Controversies
- Does it create resistant virus in those infected?
  - In Kaiser study no infections occurred
  - In PROUD study all three infections were in non-adherent patients
  - In iPrEX, resistance developed in 2 individuals infected at time of enrollment, who were randomized to active drug
PrEP
Controversies

- Is it cost effective?
  - Modeling suggests it is in a population with an annual rate of HIV infection of 2% (clearly met in Kaiser and PROUD studies)
- Who should receive PrEP?
  - MSM with syphilis, rectal gonorrhea or chlamydia in last 6 months or reports of unprotected anal sex in last six months
  - Sexual partners of HIV infected individuals, especially if they are either not taking ARV’s or taking ARV’s with incomplete viral suppression

Giving PrEP
Initial Evaluation

- Determine patient’s knowledge about PrEP
- Determine patient’s risk of HIV acquisition
- Discuss and assess barriers to adherence
- Jointly make decision regarding PrEP

Giving PrEP
Initial Testing

- Determine HIV status of patient
  - Unless abstinent for several weeks, do not rely on HIV antibody test alone
  - Usually do an HIV viral load or perhaps a 4th generation HIV test
- Screen for other STI’s
- Screen for Hepatitis status
- Check GFR and CBC
- Check BHCG if female of appropriate age
Giving PrEP Counseling

- Review critical importance of adherence
- Review strategies to improve adherence
- Discuss lack of protection for other STI’s and need to use condoms as much as possible
- Discuss side effects of medication
- Discuss importance of follow-up testing

Giving PrEP Medication

- Only approved medication is Truvada one tablet daily
- Cannot be given if GFR is < 60 (must use renally dosed individual components then)
- Do not prescribe more than a 90 day supply to facilitate follow up testing

Giving PrEP Truvada Side Effects

- GI intolerance early on
- Nephrotoxicity 0.2% in studies of PrEP
- Lower than that reported in HIV treatment
- No cases of Fanconi syndrome
- BMD loss of 1.5%
- Seen in first year of therapy, plateaus after that
- May be reversible with discontinuation
- No increase seen in rate of fractures
Giving PrEP
Follow-up Testing
- Guidelines recommend HIV testing every 3 months
- Testing for other STIs depends on level of risk
- CBC, BMP and UA once a year

Giving PrEP
Cost Considerations
- FDA approved
- Insurance coverage?
- Cost of PrEP vs. managing HIV care for entire lifetime of patient

Giving PrEP
Final Thoughts
- Withholding judgment about sexual practices
- Make decisions based on patient need and deciding on good candidates
- Spend the time for adequate counseling on medication, risk reduction, follow-up appointments
- Know your resources
  - PEP National Clinicians PEP Hotline 1-888-448-4911
  - PrEP
Questions?

References


