HIV ile enfekte hastalarda koenfeksiyonların yönetimi

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Olgu-1

- 71 yaş
- Erkek
- Emekli işçi
- Özgeçmiş
  - KAH+2 yıl önce anjiografi+stent uygulaması
  - Medikal tedavi alıyor
    - (beloc, asa)
- Soygeçmiş: özellik yok

Olgu-1 şikayet

6 aydır devam eden

- Halsizlik
- Tüm vücutta ağrı
- Anamnez
  - Şüpheli cinsel temas yok
  - Cerrahi-diş çekimi öyküsü yok
  - IV madde öyküsü yok

Olgu-1 patolojik muayene bulguları

- Servikal-inguinal 1-1,5cm'lik ağrısız mobil lenfadenomegali
- Diğer tüm sistem muayeneleri olağan

Olgu-1 tetkik

- WBC:5800/uL
- Hgb:14 g/dL
- Plt: 180.000/uL
- AST: 88 U/L (5-34)
- ALT: 102 U/L (0-55)
- AntiHIV: + (242)
- AntiHCV: +(15.3)

Olgu-1 tetkik

- VDRL-TPHA: negatif
- HbsAg: negatif
- AntiHBs: pozitif(728)
- AntiHBc IgG :pozitif
- AntiHAV IgG:pozitif
- AntiCMV IgG:pozitif
- AntiToxo IgG: negatif

Olgu-1 tetkik

- Pa Akciğer Grafisi
  - Normal
- Batın USG:
  - KC parankim ekosu hafif azalmış, hafif granüler görünüm
- Boyun-yumuşak doku USG:
  - Servikal-aksiller-inguinal 1,5 cm geçmeyen reaktif lenfadenomegali
- Eko:
  - LV çap ve sistolik fonks. normal EF%55
  - Septum mid ve bazali hafif hipokinetik 1+2 MY
- CD4 sayısı:1280/mm^3
- HIV RNA 353549 IU/ml
- HCV RNA: Negatif
- ART direnç ve HLA B5701 tetkikleri gönderildi

Olgu-1

- Kontrol muayene
- ART direnç: yok
- HLA B5701: negatif
- HCV-RNA: 138.768 IU/ML
- HCV-genotip: Genotip-1b
- Kc bx:
  - HAI:9/18
  - Fibrozis: 2/6

Olgu-1 özet

- HIV-HCV koenfeksiyonu kabul edildi
- Anti-HCV :pozitif
- Anti-HIV: pozitif
- HCV-RNA: 138.768 IU/ML
- HCV-genotip: Genotip-1b
- Kc bx:
  - HAI:9/18
  - Fibrozis: 2/6 (Modifiye ISHAK)
- HIV-RNA: 353549 IU/ML
- CD4 sayısı:1280/mm^3

Olgu-1

1-Antiretroviral tedavi(ART) başlarım

2-Kronik hepatit C tedavisi(DAA) başlarım

3-ART+DAA tedavisini birlikte başlarım

4-Tedavisiz takip ederim

GUIDELINES
Version 8.0
October 2015

GUIDELINES
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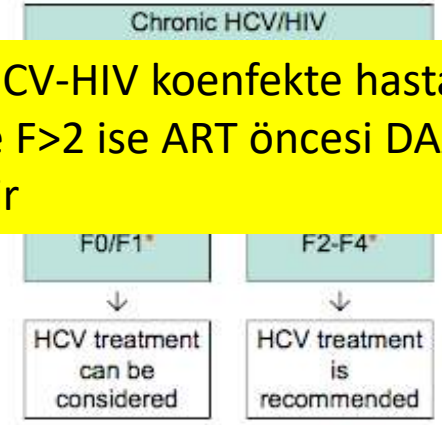
Management of Persons with Chronic HCV/HIV Co-infection

2. If chronic HCV and HIV infection are newly diagnosed at the same time with a CD4 count > 500 cells/μL treatment of HCV in presence of immediate HCV treatment indication (≥ F2 fibrosis) can be considered prior to ART initiation to avoid potential drug-drug interactions between ART and HCV DAAs, see Drug-drug Interactions between DAAs and ARVs.



Yeni tanı HCV-HIV koenfekte hastalarda CD>500 ve F>2 ise ART öncesi DAA başlanabilir

Treatment indication

1. Every person with HCV/HIV co-infection should be considered for IFN-free anti-HCV treatment regardless of liver fibrosis stage.
2. Due to similar HCV cure rates and tolerability in HCV/HIV co-infected persons as in HCV mono-infected persons under DAA therapy, treatment indication and regimens are to be the same as in HCV mono-infection.
3. Re-test for GT and sub-type should be performed in persons with tests

HCV-HIV koenfekte tüm hastalar karaciğer fibrozisine bakılmaksızın Anti-HCV tedavi değerlendirilmeli

* Metavir fibrosis score: F0=no fibrosis; F1= portal fibrosis, no septae; F2= portal fibrosis, few septae, F3=bridging fibrosis, F4=cirrhosis. FibroScan®: F0-F1 < 7.1 KPa; F2 7-10 KPa; F3/F4 > 10 Kpa

** Treatment must be considered independently from liver fibrosis in persons with low CD4 count (<200 cells/μL), ongoing HIV replication, HBV co-infection, debilitating fatigue, extrahepatic manifestations, high risk of HCV transmission (IVDU, prisoners, MSM with high risk behavior, fertile women who want to be pregnant).

HCV Treatment Options in HCV/HIV Co-infected Persons

IFN-free HCV Treatment Options				
HCV GT	**Treatment regimen**	**Treatment duration & RBV usage**		
		Non-cirrhotic	**Compensated cirrhotic**	**Decompensated cirrhotics CTP class B/C**
1 & 4	SOF + SMP +/- RBV	GT 4 only: 12 weeks with RBV or 24 weeks without RBV[i]		Not recommended
	SOF/LDV +/- RBV	8 weeks without RBV[ii] or 12 weeks +/- RBV[iii]	12 weeks with RBV[iv]	
	SOF + DCV +/- RBV	12 weeks +/- RBV[iii]	12 weeks with RBV[iv]	
	SOF/VEL	12 weeks		12 weeks with RBV
	SOF/VEL/VOX	8 weeks[viii]	12 weeks	Not recommended
	OBV/PTV/r + DSV	8[ix]-12 weeks in GT 1b	12 weeks in GT 1b	Not recommended
	OBV/PTV/r + DSV + RBV	12 weeks in GT 1a	24 weeks in GT 1a	Not recommended
	OBV/PTV/r + RBV	12 weeks in GT 4		Not recommended
	EBR/GZR	12 weeks[xi]		Not recommended
	GLE/PIB	8 weeks	12 weeks	Not recommended
2	SOF + DCV	12 weeks		12 weeks with RBV
	SOF/VEL	12 weeks		12 weeks with RBV
	SOF/VEL/VOX	8 weeks[viii]	12 weeks	Not recommended
	GLE/PIB	8 weeks	12 weeks	Not recommended
3	SOF + DCV +/- RBV	12 weeks +/- RBV[vii] or 24 weeks without RBV	24 weeks with RBV	
	SOF/VEL +/- RBV	12 weeks +/- RBV[viii] or 24 weeks without RBV		24 weeks with RBV
	SOF/VEL/VOX	8 weeks[x]		Not recommended
	GLE/PIB	8 weeks[xii]	12 weeks[xiii]	Not recommended
5 & 6	SOF/LDV +/- RBV	12 weeks +/- RBV or 24 weeks without RBV[ii]	12 weeks with RBV[iv]	
	SOF + DCV +/- RBV	12 weeks +/- RBV or 24 weeks without RBV[ii]	12 weeks with RBV[iv]	
	SOF/VEL	12 weeks		12 weeks with RBV
	SOF/VEL/VOX	8 weeks[viii]	12 weeks	Not recommended
	GLE/PIB	8 weeks	12 weeks	Not recommended

Drug-drug Interactions between DAAs and ARVs

	HCV drugs	ATV/c	ATV/r	DRV/c	DRV/r	LPV/r	EFV	ETV	NVP	RPV	MVC	DTG	EVG/c	RAL	ABC	FTC	3TC	TAF	TDF	ZDV
DAAs	daclatasvir	↑	↑110%	↑	↑41%	↑15%	↓32%	↓	↓	↔	↔	E33%	↑	↔	↔	↔	↔	↔	↑10% E10%	↔
	elbasvir/ grazoprevir	↑	↑	↑	↑	↑	↓54/83%	↓	↓	↔	↔	↔	↑	E43%	↔	↔	↔	↔	↓7/14% E34%	↔
	glecaprevir/ pibrentasvir	↑	↑553/64%	↑	↑397%/-	↑338/146%	↓	↓	↓	E84%	E	↔	↑205/57% E47%	E47%	↔	↔	↔	↔	E29%	↔
	parita-previr/r/ ombitasvir/ dasabuvir	↑	↑94%	↑	D	↑		↓E	↓E	E	E	↔	↑	E134%	↔	↔	↔	E	↔	↔
	paritaprev-ir/r/ombi-tasvir	↑	↑	↑	↑	↑		↓E	↓E	E	E	↔	↑	E20%	↔	↔	↔	E	↔	↔
	simeprevir	↑	↑	↑	↑	↑	↓71%	↓	↓	↑6% E12%	↔	↔	↑	↓11% E8%	↔	↔	↔	↔	↓14% E18%	↔
	sofosbuvir/ ledipasvir	↑	↑8/113%	↑	↑34/ 39%	↔	↓-/34%	↔	↔	↔	E	↔	↑36/ 78%E	D=20%	↔	↔	↔	E32%	E	↔
	sofosbuvir/ velpatasvir	↔	↑-/142%	↔	↓28%/-	↓29%/-	↓-/53%	↓	↓	↔	E	↔	↑	↔	↔	↔	↔	↔	E	↔
	sofosbuvir/ velpatasvir/ voxilaprevir	↑	↑40/93/331%	↑	↑-/ /143%	↑	↓	↓	↓	↔	E	↔	↑-/-/171%	↔	↔	↔	↔	↔	E	↔
	sofosbuvir	↔	↔	↑	↑34%	↔	↔	↔	↔	↔	↔	↔	↔	↓5%D27%	↔	↔	↔	↔	↔	↔

DAA ile RAL-DTG-ABC-FTC-3TC-ZDV etkileşim yok

DAA ile sofosbuvir etkileşim yok

Sofosbuvirli rejimler ile ELV/c etkileşim yok

DAA ile PI geçimsizlik

Legend

↑ potential elevated exposure of DAA
↓ potential decreased exposure of DAA
↔ no significant effect
D potential decreased exposure of ARV
E potential elevated exposure of ARV drug

no clinically significant interaction expected
these drugs should not be co-administered
may require a dosage adjustment or
potential interaction likely to be of weak intensity. Additional action/ monitoring or dosage adjustment is unlikely to be required

Numbers refer to decreased/increased AUC of DAA
in drug interactions studies. First/second numbers r
EBR/GZR or GLE/PIB or SOF/LDV or SOF/VEL
First/second/third numbers refer to AUC changes for SOF/VEL/VOX

ical significance
eractions.org.

AIDSinfo

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV

Hepatitis C Virus/HIV Coinfection (Last updated October 17, 2017; last reviewed October 17, 2017)

HCV açısından riskli ve şüphe edilen tüm hastalar yıllık HCV açısından takip edilmeli

HCV-HIV koenfekte tüm hastalara CD4'e bakılmaksızın ART başlanmalı A1

HCV-HIV koenfekte CD4<200 hastalarda önce ART başlanmalı, HIV tedavisi açısından stabilleşene kadar HCV tedavisi geciktirilebilir C3

- All people with HIV shoul … of HCV infection should be screened annually and w…
- Antiretroviral therapy (ART) may slow the progression of liver disease by preserving or restoring immune function and reducing HIV-related immune activation and inflammation. For most persons with HCV/HIV coinfection, including those with cirrhosis, the benefits of ART outweigh concerns regarding drug-induced liver injury. Therefore, ART should be initiated in all patients with HCV/HIV coinfection, regardless of …
- Initial ART regimens reco… …commended for individuals without HCV infection. Ho… …reatment regimen should be selected with special cons… …scussion in the text below and in Table 12).
- In patients with lower CD4 counts (e.g., <200 cells/mm^3), ART should be initiated promptly **(AI)** and HCV therapy may be delayed until the patient is stable on HIV treatment **(CIII)**.
- All patients with HCV/HIV … …tage assessed to inform the length of their therapy, rib… …lular carcinoma and liver disease complications.
- Persons with chronic HCV … …/) infection by testing for the presence of hepatitis … …core (HBcAb total or IgG). Persons who are not immune to HBV infection (HBsAb-negative) should receive anti-HBV vaccination **(AIII)**.
- HBV reactivation has been observed in persons with HBV infection during interferon-free HCV treatment. Accordingly, persons with HCV/HIV coinfection and active HBV infection (HBsAg-positive) should receive ART that includes two agents with anti-HBV activity prior to initiating HCV therapy **(AIII)**.

Rating of Recommendations: *A = Strong; B = Moderate; C = Optional*

Rating of Evidence: *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

AIDSinfo

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV

HIV tedavisi alan ve HCV tedavisi planlanan hastada ilaç etkileşimi olmayan bir ART rejimine geçilmeli

Concurrent Tre

Guidance on the treatment and management of HCV in adults with and without HIV can be found at http://www.hcvguidelines.org/. Several ARV drugs and HCV DAAs have the potential for clinically significant pharmacokinetic drug-drug interactions when used in combination. Prior to starting HCV therapy, the ART regimen may need t 2 below provides recommendations o IIV infection. In patients on modifie e measured within 4 to 8 weeks after changing HIV therapy to confirm the effectiveness of the new regimen. After HCV treatment is completed, the modified ART regimen should be continued for at least 2 weeks before reinitiating the original regimen. Continued use of the modified regimen is necessary because of the prolonged half-life of some HCV drugs ar n is resumed soon after HCV treatmen

Modifiye ART başlandıktan 4-8 hafta sonra HIV-RNA bakılmalı

HCV tedavisi bittikten sonra orjinal ART rejimine geçmek için en az 2 hafta beklenmeli

British HIV Association
BHIVA

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV

8.2 Hepatitis B and C virus co-infection

8.2.1 When to st

HCV için acil tedavi planlanıyorsa ve CD4>500 ise ART tedavinin ertelenmesi kabul edilebilir

Table 8.1. Summary recommendations for the treatment of hepatitis B and C co-infection

HBV requiring treatment*	HBV not requiring treatment	HCV with immediate plan to start HCV treatment*	HCV with no immediate plan to start HCV treatment
Start ART promptly (1A) (include tenofovir and emtricitabine)	Start ART (1A) (include tenofovir and emtricitabine)	Start ART before HCV treatment commenced (1C); acceptable to defer if CD4 cell count >500 cells/μL. Discuss with HIV and viral hepatitis specialist	Start ART (1A)

*See BHIVA guidelines for the management of hepatitis viruses in adults infected with HIV 2013 [1] for indications to treat hepatitis B and C

British HIV Association
BHIVA

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV

8.2.3 Hepatitis C

8.2.3.1 When to start antiretroviral therapy in HCV co-infection

8.2.3.1.1 Recommendations

- We recommend all individuals with HIV and hepatitis C virus (HCV) co-infection be assessed for HCV treatment (GPP).
- We recommend commencing ART regardless of CD4 cell count (1A).
- We recommend HCV be considered an additional factor supporting ART in individuals with CD4 >500 cells/µL who are uncertain about commencing ART (2C).
- We suggest treating HCV before commencing ART is an option if there are concerns about drug–drug interactions or adherence (GPP).

HCV için acil tedavi planlanıyorsa ve CD4>500 ise ART tedaviden önce HCV tedavisi verilebilir

AIDSinfo

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV

Initiation of Antiretroviral Therapy (Last updated October 17, 2017; last reviewed October 17, 2017)

Panel's Recommendations

- Antiretroviral therapy (ART) is recommended for all individuals with HIV, regardless of CD4 T lymphocyte cell count, to reduce the morbidity and mortality associated with HIV infection **(AI)**.
- ART is also recommended for individuals with HIV to prevent HIV transmission **(AI)**.
- When initiating ART, it is important to educate patients regarding the benefits and considerations of ART, and to address strategies to optimize adherence. On a case-by-case basis, ART may be deferred because of clinical and/or psychosocial factors, but therapy should be initiated as soon as possible.

Rating of Recommendations: *A = Strong; B = Moderate; C = Optional*

Rating of Evidence: *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

While ART is recommended for all patients, the following conditions increase the urgency to initiate therapy:

- Pregnancy (refer to the Perinatal Guidelines for more detailed recommendations on the management of pregnant women with HIV)[10]
- AIDS-defining conditions, including HIV-associated dementia (HAD) and AIDS-associated malignancies
- Acute opportunistic infections (OIs) (see discussion below)
- Lower CD4 counts (e.g., <200 cells/mm^3)
- HIV-associated nephropathy (HIVAN)
- Acute/early infection (see discussion in the Acute/Early Infection section)
- HIV/hepatitis B virus coinfection
- HIV/hepatitis C virus coinfection

EACS European AIDS Clinical Society

GUIDELINES

Version 9.0
October 2017

Recommendations for Initiation of ART in HIV-positive Persons with Chronic Infection without prior ART Exposure

Recommendations take into account the level of evidence, the degree of progression of HIV disease and the presence of, or high risk for, developing various types of (co-morbid) conditions.

ART is recommended in a
irrespective of CD4 counts

Genotipik direnç testleri ART başlamadan bakılmalıdır

ART should always be recor
the lower the CD4 count, the
diately. Use of ART should a
order to reduce sexual trans
HIV (before third trimester o

- For best timing for start
  cryptococcal meningitis, see page 16 and page 89.
- A possible exception could be persons with high CD4 counts and HIV-VL < 1000 copies/mL, although even in such persons ART initiation has been shown to increase CD4 count, dampen inflammation and lower the risk of emerging infection with higher HIV-VL.
- Genotypic resistance testing is recommended prior to initiation of ART, ideally at the time of HIV diagnosis; otherwise before initiation of ART.
- If ART needs to be initiated before genotypic testing results are available, it is recommended to include a drug with a high genetic barrier to resistance in the first-line regimen (e.g. a PI/r, PI/c or DTG). Ideally, before starting treatment, the HIV-VL level and CD4 count should be repeated to more reliably assess the infection status and subsequent response to ART.

Direnç testi sonucundan önce ART başlamak gerekiyorsa PI/r, PI/c veya DTG gibi yüksek genetik bariyerli ART tercih edilmeli

Hangi ART?

1. TDF-FTC+DTG
2. TDF-FTC+RAL
3. TDF-FTC-COB-ELV
4. TAF-FTC-COB-ELV
5. ABC-3TC-DTG

Olgu-1

- Ombitasvir+Paritaprevir+Ritonavir+Dasabuvir
- TDF-FTC+DTG başlandı

1. TDF-FTC-COB-ELV → DAA ile etkileşim
2. TAF-FTC-COB-ELV → DAA ile etkileşim
3. ABC-3TC-DTG → KAH+Kalp yetersizliği

HLA B5701 sonucu gelmedi

Olgu-1

- ART direnç: yok
- HLA B5701: negatif

Olgu-1

	başlangıç	4. hafta	8. hafta	20. hafta
HIV RNA	353549	243	<100	negatif
CD4 sayısı	1280	1210	1190	1330
HCV-RNA	138768	negatif	Negatif(TSY)	Negatif(KVY12)

DAA tedavisi tamamlandı

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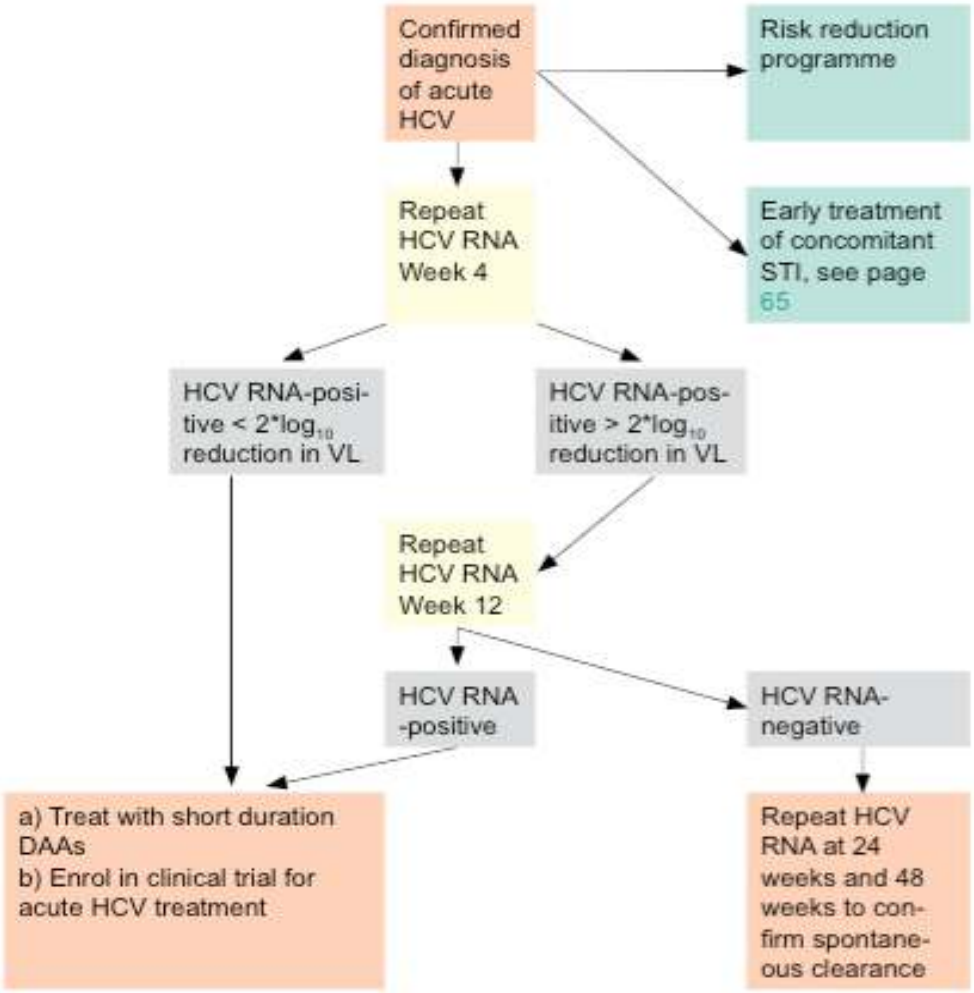
October 2017

Algorithm for Management of Acute HCV in Persons with HCV/HIV Co-infection



VIII. AKUT HEPATİT C TEDAVİSİ

İnterferon kullanılan dönemlerde, yüksek kronikleşme olduğu için ve erken tedavide kalıcı cevap oranı yüksek olduğu için olabildiğince erken tedavi yapılması, gene de spontan iyileşme için 3-4 ay beklenmesi öngörülürdü. Ancak doğrudan etkili antiviral tedavilerinde tedaviye başlama zamanı konusunda bir fikir birliği yoktur. Kronik infeksiyonun bile kalıcı cevap oranı >%95 olduğu için tedavide acele edilmemesi gerektiği de belirtilmektedir. Tedaviye başlamak için uygun zaman ALT yükselmesinin başladığı sıralar olabilir. Yeterli vakaya sahip çalışmalar olmamasına rağmen aşağıdaki tedavi şekilleri uygun görünmektedir.

- Sofosbuvir +Ledipasvir 8 hafta
- Sofosbuvir+Daclatasvir 8 hafta
- Sofosbuvir+Velpatasvir 8 hafta

HIV koinfeksiyonu varsa veya HCV RNA düzeyi> 1 milyon IU/ml ise süre 12 haftaya uzatılabilir.

Olgu-2

- 54 yaş
- Erkek
- Emlakçı
- Özgeçmiş: 30'lu yaşlarda Akut Hepatit A
- Soygeçmiş: özellik yok
- Anamnez
  - Çok partnerli MSM
  - Cerrahi-diş çekimi öyküsü yok
  - IV madde öyküsü yok

Olgu-2 şikayet

- Halsizlik
- Karın ağrısı
- Kas-eklem ağrıları
- Bulantı-kusma
- Göz, cilt ve idrar renginde sararma

Olgu-2 fizik muayene

- Cilt ve skleralar ikterik
- Kc kot altı 2 cm palpabl
- Flapping tremor yok

Olgu-2 tetkik

AST	1343 U/L (5-34)
ALT	1747 U/L (O-55)
D. bil	3.85 mg/dl (0-0,5)
T. bil	5.18 mg/dl (0,2-1,2)
ALP	243 U/L (40-150)
GGT	168 U/L (12-64)
PT	15,5 sn (11,5-15,5)
INR	1,23 (0,75-1,27)
WBC	7200/uL
HGB	13 g/dL
PLT	210.000/uL

Olgu-2 tetkik

- HbsAg: pozitif
- AntiHBs: negatif
- AntiHBc IgM :pozitif
- AntiHBc IgG :negatif
- AntiHAV IgG:pozitif
- AntiHIV: pozitif(357)

Olgu-2

- HIV RNA:569208 IU/ML
- CD4 sayısı:794/mm^3
- Üst batın USG: Kc parankimi olağan
- ART ve HLA B5701 gönderildi

Olgu-2 ne yapalım

1-Antiretroviral tedavi(ART) planlarım(Hep B etkin)

2-Antiretroviral tedavi(ART) planlarım (Hep B etkin olmayan)

3-Akut hepatit B tablosunun gerilemesini beklerim

4- Western Blot ve ART direnç sonuçlarını beklerim

Acta Gastroenterol Belg. 2010 Jul-Sep;73(3):389-91.

Seroconversion of acute hepatitis B by antiretroviral therapy in an HIV-1 infected patient.

Ikeda-Kamimura M[1], Horiba M.

Author information

Abstract

A 33-year-old man with human immunodeficiency virus type1 (HIV-1) infection was admitted because of acute hepatitis B. His serum alanine aminotransferase level was 1200 IU/mL and CD4 cells count was 268/mm3. Antiretroviral therapy including tenofovir and emtricitabine, which suppresses both HIV and hepatitis B virus (HBV) replication, was initiated. The liver enzymes decreased dramatically. The viral loads of both HIV-1 and HBV were suppressed below detectable limits. Seroconversion from hepatitis B surface antigen to hepatitis B surface antibody was acquired 19 weeks later. In this case, the initiation of antiretroviral therapy with anti-HBV activity during the acute phase of hepatitis B had a favourable effect on HBV serostatus.

Case Rep Med. 2010;2010:820506. doi: 10.1155/2010/820506. Epub 2010 Nov 7.

Acute Hepatitis B and Acute HIV Coinfection in an Adult Patient: A Rare Case Report.

Bansal R[1], Policar M, Mehta C.

⊕ Author information

Abstract

Acute HIV and acute hepatitis B coinfection is extremely rare. A 23-year-old homosexual man was admitted to our hospital with 5-day history of fever, malaise, and back pain with initial laboratory values showing severe transaminitis. The clinical picture was initially suggestive of acute viral hepatitis, which on further testing revealed acute hepatitis B and acute HIV coinfection. Although the patient was asymptomatic, a decision was made to start antiretroviral therapy. At 2-month followup, liver function tests were normal with undetectable viral loads. The early treatment of acute HIV/HBV coinfections likely contributed to eventual seroconversion with immunity to HBV in a severely immunocompromised host. To the best of our knowledge, this is the first case report of acute Hepatitis B and acute HIV coinfection and its management. In conclusion, early treatment of acute hepatitis B in immunocompromised patients may be beneficial.

Antivir Ther. 2017 Oct 12. doi: 10.3851/IMP3201. [Epub ahead of print]

Primary HIV infection in patients with acute hepatitis B: a report of two cases.

Binda F[1], Monge E[1], Simonetti FR[2], Zanchetta N[3], Galli M[1,4], Milazzo L[4], Corbellino M[4], Antinori S[1,4].

⊕ Author information

Abstract

We describe two patients admitted to our institution with a diagnosis of sexually acquired acute hepatitis B who also had underlying hyper acute HIV infection. Both individuals reported high rates of condomless sex. Antiviral therapy active against HBV and HIV was started within days after diagnosis. Treatment was well tolerated and led to a rapid control of both infections and hepatitis B surface antibody seroconversion. The efficacy and safety of contemporary antiretroviral drug combinations suggest that treatment of acute HIV infection is feasible in patients with acute hepatitis B.

PMID: 29022881 DOI: 10.3851/IMP3201

Olgu-2

	başlangıç	3. gün	7. gün	14. gün	28. gün	4. ay
ALT	1747	2122	1855	210	14	24
CD4 sayısı	794				822	988
HIV RNA	569208					<100
HBsAg	pozitif					negatif
AntiHbs						Pozitif(35)

TDF-FTC+DTG başlandı

Olgu-2

- ART direnç: yok
- HLA B501: Negatif

Olgu-3

- 27 yaş
- Erkek
- Öğrenci
- Özgeçmiş: özellik yok
- Soygeçmiş: baba dm+
- Anamnez
  - Çok partnerli MSM
  - Korunmasız cinsel temas öyküsü mevcut
  - Cerrahi-diş çekimi öyküsü yok
  - IV madde öyküsü yok

Olgu-3 şikayet

- Halsizlik
- Kilo kaybı

Olgu-3 patolojik muayene bulgusu

- Servikal, axiller, inguinal 1-1,5 cm lenfadenomegali
- Kc nonpalpabl
- Skleralar hafif ikterik

Olgu-3 tetkik

- AST: 240 U/L (5-34)
- ALT: 362 U/L (0-55)
- T.bil:1.62 mg/dl
- D.bil:0.86 mg/dl
- WBC:6200 u/L
- HB:13.9 g/dl
- PLT: 260000 u/L

- AntiHCV: negatif
- HBsag: pozitif
- HBeag: negatif
- AntiHBe:pozitif
- AntiHBcIgM:negatif
- AntiHBc IgG : pozitif
- AntiHIV: pozitif

Olgu-3 tetkik

- HIV RNA: 2.803.110 IU/ML
- CD4 sayısı: 316/mm^3
- HBV DNA: >20.000.000 IU/ML
- HBeag: negatif
- AntiHBe: pozitif
- Anti-Delta: negatif
- Batın USG: normal

Olgu-3 özet

- 27 yaş Erkek
- Halsizlik şikayeti
- Kronik hepatit B ?
- AntiHIV: pozitif
- HIV RNA: 2.803.110 IU/ML
- HBV DNA: >20.000.000 IU/ML
- CD4 sayısı: 316/mm^3
- ART direnç ve HLA5701 gönderildi

Olgu-3

- ART direnç: yok
- HLA B5701: negatif

Olgu-3 ne yapalım?

1. Kronik hepatit B açısından KC Bx yaparım
2. Hepatit B kapsayacak ART başlarım
3. 1+2

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Part IV Clinical Management and Treatment of HBV and HCV Co-infection in HIV-positive Persons

Every person with HCV/HIV co-infection should receive IFN-free DAA therapy to eradicate HCV, regardless of liver fibrosis stage in the context of faster liver fibrosis progression in co-infected persons and the availability of DAAs with excellent tolerability and efficacy. DAAs achieve similar cure rates and tolerability in HCV/HIV co-infected compared to HCV mono-infected persons. Therefore, treatment indication and regimens are the same as in HCV mono-infected persons. All persons with HBV/HIV co-infection should receive ART including TDF or TAF, unless history of tenofovir intolerance. Life-long therapy is recommended if anti-HBV nucleos(t)ides are given as part of ART. In HBsAg-positive persons without HBV active ART (including 3TC), TDF/TAF should be added as prophylaxis regardless of baseline HBV-DNA levels in case of chemotherapy or other immunosuppression (e.g. rituximab treatment) [1].

Tüm HBV-HIV koenfekte hastalar tenofovir intoleransı öyküsü yok ise TAF-TDF içeren ART başlanmalı

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Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV

Considerations for Antiretroviral Use in Patients with Coinfections

Hepatitis B/HIV Virus C… last reviewed October 17, 2017)

Tüm HBV-HIV koenfekte hastalar TAF-TDF içeren ART başlanmalı

- Before initiation of antiretrovira… B surface antigen (HBsAg) should be tested for hepatitis B virus (HBV) DNA using a quantitative assay to determine the level of HBV replication **(AIII)**.
- Because emtricitabine (FTC), lamivudine (3TC), tenofovir disoproxil fumarate (TDF), and tenofovir alafenamide (TAF) have activity against both HIV and HBV, an ART regimen for patients with both HIV and HBV should be include (TAF or TDF) plus (3TC or FTC) as the nucleoside reverse transcriptase inhibitor (NRTI) backbone of a fully suppressive antiretroviral (ARV) regimen **(AI)**.
- If TDF or TAF can… …lly suppressive ARV regimen **(BI)**. …al infection may result in the selection of the M184V mutation that confers HIV resistance to 3TC and FTC. Therefore, entecavir must be used in addition to a fully suppressive ARV regimen when given to patients with HBV/HIV-coinfection **(AII)**. Peginterferon alfa monotherapy may also be considered in certain patients **(CII)**.

Entekavir alternatif tedavidir

- Other HBV treatment regimens, including adefovir alone or in combination with 3TC or FTC and telbivudine, **are not recommended** for patients with HBV/HIV coinfection **(CII)**.
- Discontinuation of agents with anti-HBV activity may cause serious hepatocellular damage resulting from reactivation of HBV; patients should be advised against stopping these medications and be carefully monitored during interruptions in HBV t…

Adefovir tek başına 3TC veya FTC kombinasyonu önerilmemekte

- If… active against HBV should be continued for HBV treatment in combination with other suitable ARV agents to achieve HIV suppression **(AIII)**.
- HBV reactivation has been observed in persons with HBV infection during interferon-free HCV treatment. For that reason, all patients initiating HCV therapy should be tested for HBV. Persons with HCV/HIV coinfection and active HBV infection (determined by a positive HBsAg test) should receive ART that includes two agents with anti-HBV activity prior to initiating HCV therapy **(AIII)**.

Rating of Recommendations: *A = Strong; B = Moderate; C = Optional*

Rating of Evidence: *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

British HIV Association
BHIVA

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV

8.2 Hepatitis B and C virus co-infection

8.2.1 When to start ART?

Table 8.1. Summary recommendations for the treatment of hepatitis B and C co-infection

HBV requiring treatment*	HBV not requiring treatment	HCV with immediate plan to start HCV treatment*	HCV with no immediate plan to start HCV treatment
Start ART promptly (1A) (include tenofovir and emtricitabine)	Start ART (1A) (include tenofovir and emtricitabine)	commenced (1C); acceptable to defer if CD4 cell count >500 cells/μL. Discuss with HIV and viral hepatitis specialist	

Tüm HBV-HIV koenfekte hastalar TAF/TDF-FTC içeren ART başlanmalı

*See BHIVA guidelines for the management of hepatitis viruses in adults infected with HIV 2013 [1] for indications to treat hepatitis B and C

Olgu-3

- Batın USG: Karaciğer parankimi doğal
- INR:0.88
- Platelet:238000
- Albumin:3.7
- Hastada karaciğer S düşünülmedi
- Karaciğer biyopsisi yapılmadı
- TDF-FTC+RAL başlandı

Olgu-4

- 35 yaş
- Erkek
- Öğretmen
- Özgeçmiş: 15 yaşında apendektomi
- Soygeçmiş: baba dm+
- Anamnez
  - Çok partnerli MSM
  - Korunmasız cinsel temas öyküsü mevcut
  - Cerrahi-diş çekimi öyküsü yok
  - IV madde öyküsü yok

Olgu-4 şikayet

- Halsizlik
- Kilo kaybı
- Başağrısı

Olgu-4 patolojik muayene bulguları

- Servikal-aksiller-inguinal 1-1,5cm'lik ağrısız mobil lenfadenomegali
- Diğer tüm sistem muayeneleri olağan

Olgu-4 tetkik

- AST:22 U/L (5-34)
- ALT: 32 U/L (0-55)
- T.bil:1.43 mg/dl
- D.bil:0.72 mg/dl
- WBC:5400 u/L
- HB:11.8 g/dl
- PLT: 255000 u/L
- AntiHCV: negatif
- Hbsag: negatif
- AntiHBs:negatif
- AntiHBc IgG : negatif
- AntiHAVIgG: negatif
- AntiHIV: pozitif(765)

Olgu-4 tetkik

- HIV RNA: 450.310 IU/ML
- CD4 sayısı: 242/mm^3
- VDRL: 1/256 +
- TPHA: 1/2560 +
- Kranial BT: normal

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Erken sifilizde tedaviye 3 gün 20-60 mg prednizolon eklenmeli.
Optik nörit, üveit ve Jarisch-Herxheimer rxn engellemek için

Syphilis	Penicillin is the gold standard for the treatment of syphilis in both pregnant and non-pregnant individuals. **Primary/secondary syphilis:** benzathine penicillin G (2.4 million IU im as single dose). In early syphilis adjunctive treatment with prednisolone (20–60 mg daily for 3 days) prevents optic neuritis, uveitis and Jarisch–Herxheimer reaction. **Late latent syphilis and syphilis of unknown duration:** benzathine penicillin (2.4 million IU im weekly on days 1, 8 and 15); the alternative doxycycline (100 mg po bid for 2 weeks) is considered less effective. **Neurosyphilis:** penicillin G (6 x 3 - 4 million IU iv for at least 2 weeks). There is no evidence to give a general recommendation on prednisolone use in this condition.	• Expect atypical serology and clinical courses • Consider cerebrospinal fluid (CSF) testing in persons with neurological symptoms (evidence for intrathecally-produced specific antibodies, pleocytosis, etc.) • Successful therapy clears clinical symptoms and decreases VDRL test four-fold within 6-12 months

Nörolojik semptomları olan hastalarda BOS incelemesi önerilir

Tedavi başarısı 6-12 ay sonra klinik iyileşme ve VDRL titresinde 4 kat azalma ile değerlendir

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Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV

Recommendations for Treating *Treponema pallidum* Infections (Syphilis) to Prevent Disease (page 1 of 2)

Empiric treatment of incubating syphilis is recommended to prevent the development of disease in those who are sexually exposed.

Indication for Treatment:

- Persons who have had sexual contact with a person who receives a diagnosis of primary, secondary, or early latent syphilis within 90 days preceding t[illegible] results are negative **(AIII)**.
- Persons who have h[illegible] early latent syphilis >90 days before the diag[illegible] not immediately available and the opportunity[illegible]

Primer,sekonder veya erken latent sifiliz tanılı bireyle 90 gün içerisinde cinsel teması olan hastalar seolojik testleri negatif olsada erken sifiliz tedavisi verilmeli

Treatment:

- Same as for early stage syphilis listed below

General Considera[illegible]

Hastalar Jarisch-Herxheimer reaksiyonu açısından uyarılmalı

- The efficacy of non-penicillin alternatives has not been well evaluated in persons with HIV infection and should be undertaken only with close clinical and serologic monitoring.
- The Jarisch-Herxheimer reaction is an acute febrile reaction accompanied by headache and myalgias that can occur within the first 24 hours after therapy. It occurs more frequently in persons with early syphilis, high non-treponemal antibody titers, and prior penicillin treatment. Patients should be warned about this reaction and informed it is not an allergic reaction to penicillin.

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All persons with syphilis and signs or symptoms suggesting neurologic disease (e.g., cranial nerve dysfunction, auditory or ophthalmic abnormalities, meningitis, stroke, altered mental status,) warrant evaluation for neurosyphilis. An immediate ophthalmologic evaluation is recommended for persons with syphilis ... cular syphilis. Ocular syphilis ... yphilis, regardless of CSF resu...

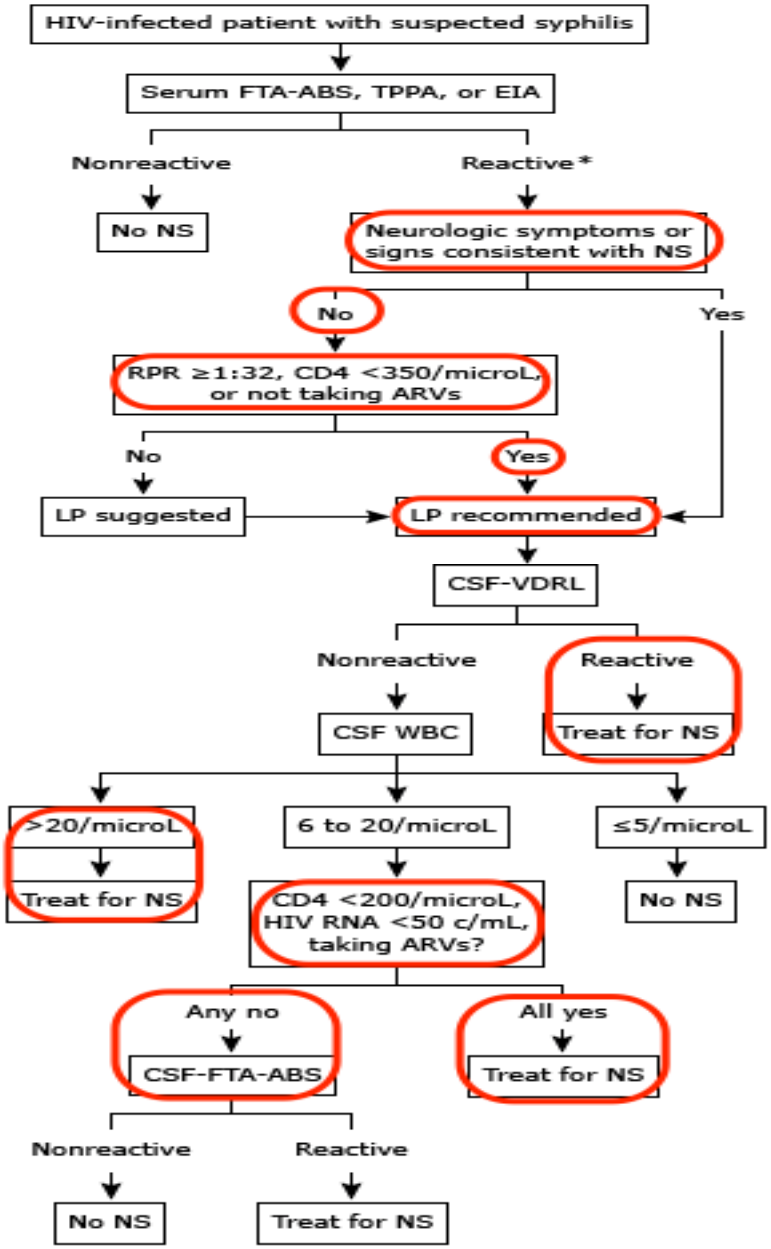
Nörolojik bulgu olmayan HIV-sifiliz koenfekte hastalarda CD4<350 ve RPR>1/32 ise BOS bulgularında anormallik olduğunu gösteren birçok çalışma mevcut

CSF abn... early stage syphilis[48] and in pe... cal and prognostic significa... ut neurologic symptoms is unknown. Several studies have demonstrated that in persons with syphilis and HIV infection, CSF laboratory abnormalities are associated with CD4 counts ≤350 cells/mm^3 or in combination with RPR titers ≥1:32.[31,32,49,50] However, unless neurologic signs and symptoms are present, a CSF examination has not been associated with improved clinical outcomes.

Nörolojik bulgu ve semptomların olmadığı durumlarda BOS bulguları ile klinik bulgular ilişkili değil

CD4 sayısı: 242/mm^3
VDRL titresi:1/256 +

Algorithm for the diagnosis of neurosyphilis in a patient with HIV infection



Olgu-4 lomber ponksiyon

- BOS bulguları
  - Berrak
  - Basınç normal
  - Pleositoz yok
  - Glukoz:55 (ezkş:87)
  - Protein:36
  - VDRL: negatif
- Nörosifiliz saptanmadı
- TTE: Normal
- Göz dibi muayenesi: normal

Olgu-4

- Benzatin Penisilin 2.4 IU
- 0-6 Hepatit A
- 0-1-6 Hepatit B aşıları planlandı
- TDF-FTC-COB-ELV başlandı

Olgu-4

The Jarisch-Herxheimer Reaction

- An acute febrile reaction due to a rapid release of treponemal antigen with an associated allergic reaction in the patient
- Caused by antisyphilitic treatment, especially penicilline
- Accompanied by headache, myalgia, fever, exacerbation of inflammatory reaction at sites of localized spirochetal infection
- Usually occur within 6-8 hours of treatment
- Occurs most frequently among patients with early syphilis
- Antipyretics can be used to manage symptoms- not prevent
- Might induce early labor or cause fetal distress in pregnant women, but this should not prevent or delay therapy

Penisilin tedavisinin 4. saati

- Ateş yüksekliği 38.9 C
- Titreme-üşüme
- Gövde ve sırtta makülopapüler döküntü
- Parasetamol ile ateşi geriledi
- Penisilin tek doz uygulandı

Neurosyphilis in patients with HIV

Emily Hobbs,[1] Jaime H Vera,[1,2] Michael Marks,[3] Andrew William Barritt,[1,4] Basil H Ridha,[1,4] David Lawrence[2,3]

Table 1 How to interpret syphilis serology

	ELISA IgG/IgM	TPPA or TPHA	VDRL or RPR
Never	–	–	–
Early	+	+	–
Secondary	+	+	+
Late	+	+	–
Treated	+	+	–
Reinfected	+	+	+
False-positive ELISA	+	–	–
False-positive TPPA/TPHA	–	+	–
False-positive RPR	–	–	+

RPR, rapid-plasma reagin; TPHA, *Treponema pallidum* haemagglutination; TPPA, *Treponema pallidum* particle agglutination; VDRL, venereal disease research laboratory.

Box 1 Indications for a lumbar puncture

- Neurological signs
- Ocular involvement
- CD4 count <350 cells/μL*
- Venereal disease research laboratory/reactive plasma reagin titre>1:32*
- Antiretroviral therapy naïve*

*Consider.

Box 2 Factors suggesting neurosyphilis

- Neurological signs
- Ocular involvement
- Positive CSF test including: VDRL, RPR, TPHA, TPPA, PCR
- CSF pleocytosis: >20 cells if antiretroviral therapy naïve, >10 cells if antiretroviral therapy exposed.

CSF, cerebrospinal fluid; RPR, rapid plasma reagin; TPHA, *Treponema pallidum* haemagglutination; TPPA, *Treponema pallidum* particle agglutination; VDRL, venereal disease research laboratory.

Box 3 Potential manifestations of neurosyphilis

- (Aseptic) meningitis
- Chronic headache
- Psychiatric illness
- Cognitive impairment
- Ischaemic stroke
- Seizures
- Mass lesion
- Cranial (poly)neuropathy
- Optic neuritis/optic atrophy
- Ataxia
- Transverse myelitis
- Myelopathy
- (Poly)radiculopathy
- Peripheral neuropathy

Key points

- When HIV-positive individuals develop neurological symptoms, always consider syphilis in the differential diagnosis.
- When people who are not known to be HIV positive develop neurosyphilis, always perform an HIV test.
- HIV-positive individuals with serological evidence of syphilis require a detailed history and examination for neurological signs.
- Consider lumbar puncture for all patients with HIV and syphilis coinfection who have neurological signs, or if the CD4 count is <350 cells/μL, serum reactive plasma reagin/venereal disease research laboratory (VDRL) titre is ≥1:32, or they are not on antiretroviral therapy.
- If cerebrospinal fluid (CSF) VDRL is negative, still consider neurosyphilis in patients with neurological signs and/or a CSF white cell count is >10 cells/μL in treated HIV infection, or >20 cells/μL in untreated infection

Olgu-4

- ARV 4. ay
  - HIV RNA: negatif
  - CD4 sayısı: 562/mm^3
  - VDRL titre: 1/16 +
  - TPHA titre: 1/2560 +

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Anti-HAV IgG ve Anti-HBs negatif tüm hastalar CD4 sayısına bakılmaksızın aşılanmalı

5. Persons lacking anti-HAV IgG antibodies or anti-HBs antibodies should be offered vaccination for the respective virus to prevent infection regardless of their CD4 count. The response to the HBV vaccine is influenced by the CD4

Izole Anti-HBcIgG + olguların aşılamasıyla ile ilgili veriler yetersiz

vaccination. Because of the lack of data on the impact of immunisation in isolated anti-HBc IgG positive persons (HBsAg negative, anti-HBc positive and anti-HBs negative profile), vaccination is not presently recommended in this population. Additional data awaited.

Rutin aşılama sonrası aşı yanıtı oluşmayan hastalarda 0,1,6,12 çift doz aşı yanıtı daha yüksek

6. In anti-HB µg) at 3-4 time points (months 0, 1, 6 and 12) may help to improve response rates to the HBV vaccine. Persons who fail to seroconvert after HBV vaccination and remain at risk for HBV should have annual serological tests for evidence of HBV infection. TDF based cART has been associated with prevention of HBV infection in these persons and ART including TDF or TAF is recommended

Aşı yanıtı oluşmayan hastalardaTDF/TAF içeren rejim önerilir

The magnitude and duration of immunogenicity to hepatitis B vaccination in HIV-infected adults is significantly low -seronegative healthy adults.[53,56-58] Factors ass r response to vaccine include counts,[56,59-64] presence of detectable HIV RNA with HCV, occult HBV infection, and the general health status of the host.[23,36,66-70] Based on these data, early vaccination is recommended in HIV-infected patients before CD4 cell counts decline to <350 cells/mm^3 **(AII)**. However, in patients who present to care at a lower CD4 ccination should not be deferred until CD4 counts increase to >350 cells/mm^3 because som ed patients with CD4 counts <200 cells/mm^3 do respond to vaccination **(AII)**. Of HIV-infected persons who did not respond (anti-HBs titers <10 IU/mL) to a primary 3-dose vaccine series, 25% to 50% responded to an additional vaccine dose, and 44% to 100% responded to a 3-dose s who did not respond to a complete hepatitis B va eries **(BIII)**,[53] although some specialists might delay revaccination until after a sustained increase in CD4 cell count is achieved on ART **(CIII)**. Two randomised controlled trials have shown that using 4 doses of double-dose vaccine produces higher anti-HBs titers than 3 doses of standard-dose vaccine,[75,76] and 1 study also showed a higher overall response rate.[76] Some specialists consider that this approach—4 vaccinations—improves immunologic response in HIV-infected individuals either as an initial vaccination schedule or in patients who are non-responders (BI). However, whether a schedule of 4 double-dose vaccines is superior to 4 single-dose or 3 double-dose vaccines is still unclear. Another study suggested that HIV-infected patients with CD4 counts >350 cells/mm^3 had improved responses when vaccinated with a double-dose vaccine on a 0-, 1-, and 6-month schedule.[59] Although other approaches have been investigated to improve responses, such as the use of combined hepatitis A and B vaccine[77,78] or the use of adjuvants,[79] data are insufficient to support a broad recommendation for these approaches at this time. While additional studies are needed to determine optimal vaccination strategies in patients with advanced immunosuppression, the vaccination series for HBV should

4 tek doz

3 çift doz

4 çift doz

Hangi aşı rejiminin üstün olduğu net değil

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Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV

Preventing Disease

All family members and sexual contacts of patients with HBV should be screened and all susceptible contacts should receive HBV vaccines regardless of whether they are HIV- infected **(AII)**. Hepatitis B vaccination is the most effective way to prevent HBV infection and its consequences. All HIV-infected patients susceptible to HBV should be receive hepatitis B vaccination **(AII)** or with the combined hepatitis A and hepatitis B vaccination **(AII)**.

İzole AntiHBc IgG + vakalarda HBV DNA – ise
Tek doz aşı sonrası (1-2 ay) Anti-HBs>100 yeterli
AntiHBs <100 ise 1-2 doz aşıla

All HIV-infected patien , anti-HBs, and anti-HBc.[9,16,1 ction and does not need vaccinati tent with seroprotection, usually from vaccination,[52] and no further vaccinations are required.[53] The interpretation is less clear in individuals with the isolated anti-HBc pattern (HBsAg negative, anti-HBc positive, anti-HBs negative). Aside from false-positive results, this pattern may signify infection in the distant past with subsequent loss of anti-HBs.[54] Most HIV-infected patients with isolated anti-HBc are HBV DNA-negative and not immune to HBV infection;[36] therefore, routinely checking HBV DNA is not recommended. However, they should be vaccinated with one standard dose of HBV vaccine and anti-HBs titers should be checked 1 to 2 months afterward. If the anti-HBs titer is >100 IU/mL, no further vaccination is needed, but if the titer is <100 IU/mL, a complete series of HBV vaccine (single-dose or double-dose) should be completed followed by anti-HBs testing **(BII)**.[55] The cut-off of 100 IU/mL is used in this situation because one study demonstrated that patients with isolated anti-HBc who achieved a titer of 100 IU/mL after a booster dose maintained an anti-HBs response for >18 months compared to only 23% of those who achieved a titer of 10 to 100 IU/mL.[55]


sabrınız için teşekkür ederim