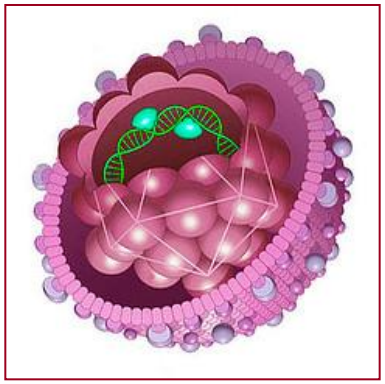

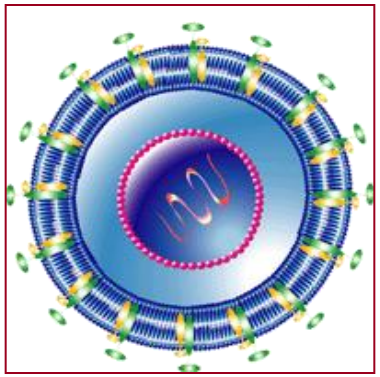

HBV/HCV KOİNFEKSİYONUNDA EPİDEMİYOLOJİ ve DOĞAL SEYİR OLASILIKLARI

Dr. Bilgehan Aygen

Erciyes Üniversitesi Tıp Fakültesi İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Anabilim Dalı, Kayseri

HBV/HCV koinfeksiyon sıklığı (1)

- Sıklık?
  - Büyük ölçekli epidemiyolojik araştırma yok
  - KHB veya KHC'de serolojik olarak "occult" infeksiyonların varlığı
- Dünyada 7-20 milyon koinfekte kişi olasılığı
  - Yaygın değil!
    - İki virusun da aynı yolla bulaşması nedeniyle endemisitenin yüksek olduğu bölgelerde ve parenteral infeksiyon açısından riskli gruplarda koinfeksiyon olasılığı fazla

Jamma S, et al. Curr Hepat Rep 2010;9(4):260-9.
Potthoff A, et al. Expert Opin Pharmacother 2010;11(6):919-28.

HBV/HCV koinfeksiyon sıklığı (2)

- Bulgaristan'da 2211 randomize olarak seçilmiş sağlıklı popülasyonda koinfeksiyon oranı %0.68
- HBsAg pozitifliği olanlarda HCV koinfeksiyon oranı %3-18
  - Asya-Pasifik ülkelerinde KHB varlığında HCV süperinfeksiyonu en sık saptanan klinik form
- KHC'li hastaların ~ %2-10'unda HBsAg pozitif
  - ABD'de HCV'li hastaların ~ %25'inde HBV serolojik göstergeleri pozitif

Atanasova MV, et al. Minerva Gastroenterol Dietol 2004;50(1):89-96.
Potthoff A, et al. Expert Opin Pharmacother 2010;11(6):919-28.
Jamma S, et al. Curr Hepat Rep 2010;9(4):260-9.

HBV/HCV koinfeksiyon sıklığı (3)

- HCV ile infekte olanlarda “occult” HBV infeksiyonu oranı %11.9-44.4
  - ↳ Karaciğer dokusunda HBV DNA pozitifliği %40-50
- KHC’li hastalarda izole anti-HBc pozitifliği %18.6-71
  - ↳ Aynı hasta grubunda HBV DNA pozitiflik oranı %15.8-22.5

Fukuda R, et al. J Med Virol 1999;58:201-7.
Fukuda R, et al. J Med Virol 2001;63:220-7.

Risk grupları

- Damar içi ilaç kullanma bağımlılığı olanlar
- Hemodiyaliz hastaları
- Organ transplantasyonu yapılanlar
- HIV ile infekte olanlar
- Hemofili hastaları

Chu CJ, Lee SD. J Gastroenterol Hepatol 2008;23(4):512-20.
Peters MG. Hepatology 2009;49(Suppl):S146-2S155.
Liaw YF, et al. Gastroenterology 2004;126(4):1024-9.

ELSEVIER

Journal of Hepatology 39 (2003) 1036–1041

Journal of Hepatology

www.elsevier.com/locate/jhep

Epidemiological and clinical burden of chronic hepatitis B virus/hepatitis C virus infection. A multicenter Italian study☆

Giovanni B. Gaeta[1,*], Gianfranca Stornaiuolo[1], Davide F. Precone[1], Salvatore Lobello[2], Maria Chiaramonte[3], Tommaso Stroffolini[4], Giuseppe Colucci[5], Mario Rizzetto[6]

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[2]*Department of Gastroenterology, University of Padua, Padua, Italy*
[3]*Chair of Gastroenterology, University of L'Aquila, L'Aquila, Italy*
[4]*ISS, Rome, Italy*
[5]*Scientific Affairs, Roche Molecular Systems, Rotkreuz, Switzerland*
[6]*Department of Gastro-Hepatology, A.O. S. Giovanni Battista, Turin, Italy*

- 14 merkez, prospektif
- HBsAg pozitif 837 hasta
- Anti-HCV pozitif hasta sayısı 59
- Koinfeksiyon için bağımsız risk faktörleri
  - > 42 yaş
  - Damar içi ilaç kullanımı ve/veya kan transfüzyonu yapılması
  - Ülkenin güney bölgesinde yaşama

KHB'de HCV süperinfeksiyonu için risk faktörleri

- Damar içi ilaç kullanımı
- Kan transfüzyonu yapılması
- Medikal girişim uygulanması
- Ev içi veya toplumda şüpheli temas varlığı

Liaw YF, et al. Gastroenterology 2004;126(4):1024-9.

TÜRKİYE'DE HBV/HCV KOİNFEKSİYONU

Türk Aile Hek Derg 2012;16(1):3-7

Araştırma | Research Article
doi:10.2399/tahd.12.003

Kronik Hepatit C hastalarında Hepatit B enfeksiyonu ile karşılaşma sıklığı: Geriye dönük bir çalışma*

The frequency of hepatitis B virus infection in patients chronically infected with hepatitis C virus: a retrospective study

Fatih Akca[1], Ayşe Semra Demir Akca[2], Selim Aydemir[3], Erol Aktunç[4]

- Ocak 2001-Haziran 2008 tarihleri arasında anti-HCV pozitif 223 hasta
  - HBsAg pozitifliği %4
  - Anti-HBs ve anti-HBc birlikte pozitifliği %14.9
  - İzole anti-HBc pozitifliği %17
  - HBV'ye karşı aşılanma oranı %26.2
- SONUÇLAR: HCV infeksiyonu olan hastaların HBV ile karşılaşma oranı yüksektir ve aktif bağışıklanma oranları düşüktür!

KHC hastalarında HBV infeksiyonu açısından serolojik araştırmalar yapılmalıdır!

AKADEMİK GASTROENTEROLOJİ DERGİSİ, 2007; 6 (1): 10-13

Şanlıurfa'da kronik C hepatitinde hepatit B virüs enfeksiyonu ile karşılaşma sıklığı

The rate of hepatitis B virus exposure in subjects with chronic hepatitis C infection in Şanlıurfa

Füsun F. BÖLÜKBAŞ[1], Cengiz BÖLÜKBAŞ[1], Mehmet ASLAN[2], Esen DOLGUN[2], Mustafa ULUKANLIGİL[3]

Harran Üniversitesi Tıp Fakültesi Gastroenteroloji Bilim Dalı[1], İç Hastalıkları Anabilim Dalı[2], Mikrobiyoloji Anabilim Dalı[3], Şanlıurfa

- Tedavi almamış 22 KHC hastası
  - HBsAg pozitifliği %9 (2 hasta)
  - Anti-HBc pozitifliği %68.2 (15 hasta)
    - 3 (%20) hastada HBV DNA pozitif
- SONUÇLAR: KHC'li hastalarda HBV ile karşılaşma oranı yüksektir

ve

HBV için endemik bölgelerde KHC'li hastalarda "occult" HBV infeksiyonu araştırılmalıdır!

Ankara Üniversitesi Tıp Fakültesi Gastroenteroloji Bilim Dalı verileri

- 1036 hepatit hastasının 42'sinde HBV/HCV koinfeksiyonu
  - 728 HBV infeksiyonlu hastanın 29'unda (%3.9) anti-HCV pozitif
  - 308 HCV infeksiyonlu hastanın 13'ünde (%4.2) HBsAg pozitif
    - Aktif HBV+ aktif HCV: 3 hasta
    - Aktif HCV+ taşıyıcı HBV: 11 hasta
    - Aktif HBV+ inaktif HCV: 6 hasta
    - Gizli HBV: 13 hasta
    - İnaktif HBV+ inaktif HCV: 9 hasta

Özkan H, Yakut M. Viral Hepatit 2009.

HEP-NET Erciyes Üniversitesi verileri
(16 Ocak 2013)

- Toplam hasta sayısı: 3212
  - HBV infeksiyonu: 1990
  - HCV infeksiyonu: 1137
  - HBV+HCV infeksiyonu: 52
  - HBV+HDV infeksiyonu: 31
  - HBV+HCV+HDV infeksiyonu: 2

THE PREVALENCE OF HEPATITIS B VIRUS AND HEPATITIS C VIRUS COINFECTION IN TURKEY

BİLGEHAN AYGEN[1], MUSTAFA KEMAL ÇELEN[2], İFTİHAR KÖKSAL[3], SELMA TOSUN[4], OĞUZ KARABAY[5], TANSU YAMAZHAN[4], ORHAN YILDIZ[1], CELAL AYAZ[2], FEHMİ TABAK[7]

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[2] DİCLE UNIVERSITY MEDICAL FACULTY, DEPARTMENT OF INFECTIOUS DISEASES, DIYARBAKIR, TURKEY
[3] KARADENİZ TECHNICAL UNIVERSITY MEDICAL FACULTY, DEPARTMENT OF INFECTIOUS DISEASES, TRABZON, TURKEY
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[6] EGE UNİVERSITY MEDICAL FACULTY, DEPARTMENT OF INFECTIOUS DISEASES, İZMİR, TURKEY
[7] İSTANBUL UNIVERSITY CERRAHPAŞA MEDICAL FACULTY, DEPARTMENT OF INFECTIOUS DISEASES, İSTANBUL, TURKEY

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E-Mail: baygen@erciyes.edu.tr

INTRODUCTION

Hepatitis B (HBV) and hepatitis C (HCV) virus infections are among the most common causes of advanced chronic liver disease worldwide. Patients coinfected with HBV and HCV have faster rates of fibrosis, progression, more severe liver disease, and are at markedly increased risk of developing hepatocellular carcinoma as compared to those with HBV or HCV monoinfection (1-3). The pathophysiology of HBV/HCV is complex, as different patterns of virological dominance may occur, which can even fluctuate over time (1,4-8).

Although HBV/HCV coinfection is not uncommon, its epidemiology is poorly defined (5,9). An estimated 7-20 million individuals affected worldwide (4). Dual chronic infection with HBV and HCV is common in areas endemic for either virus. HCV superinfection in patients with chronic HBV infection was the most common clinical features of coinfection in Asia-Pacific countries (5). To date, no standard-of-care recommendation exists for HBV/HCV coinfection (2,9,10) Pegylated interferon and ribavirin combination therapy demonstrated similar efficacy in suppressing HCV RNA in coinfected and HCV monoinfection. However, HBV reactivation during therapy can be challenge (9). Detailed serological and virological evaluations are required for HBV/HCV coinfected patients before initation of antiviral therapy (4,5). Coinfection accelerates liver disease progression (11, 12). Therefore, to determine the actual frequency of HBV/HCV coinfection is very important.

We aimed to determine prevalence and epidemiological characteristics of cases coinfected with HBV/HCV in Turkey.

MEDHODS

The data of this study was obtained from Turk-Hep-Net project. The project includes real-life cohort of HBV patients from 15 centers in Turkey and is supported by Viral Hepatitis Society.
In the study, 10.165 hepatitis cases were evaluated in 10 hospitals. The epidemiological and virological data of patients coinfected with HBV and HCV were analyzed. Serological markers (anti-HCV, HBsAg, HBeAg, and anti-HBe) have been tested with different enzyme immünoassay kits. HBV DNA and HCV RNA has been studied by using real-time polymerase chain reaction with dynamic range and sensitivity of different kits. All results were converted IU/ml.

RESULTS

Of the data evaluated were from nine academic and one was from public care hospital and had been distributed in six different regions. According to first visit results, HBV/HCV coinfection was detected in 99 patients. The ratio was 974/100.000. Fifty-six percent of the cases were male and 44% were female with the mean age of 40.9±21.7 years. Patients characteristics are summarized in Table 1.

The distribution of coinfected cases were; 31% in Mid Anatolian Region, 30% in Southeast Region, and 22% in Blacksea Region. The diagnosis was obtained in 8% during general health control, in 5% during blood donation, in 4% during military work, in 2% during pregnancy. The risk factors were dental therapy (10%), any surgical procedure (6%), hemodialysis (4%), and blood transfusion (2%).

Mean ALT level was 70.95± 49.12 IU/lt in coinfected patients. In 12% of patients HBeAg was positive. In 8% both HCV-RNA and HBV-DNA were positive and in 88% of cases HCV infection was dominant. In this group 3 patients had high ALT levels. HCV RNA levels were in the range of 150.000-2.400.000 IU/ml in seven patients. HBV DNA levels were in 10-51.900 IU/ml in these patients. In one patient, HBV DNA level was 12.271 IU/ml with low level of HCV RNA (50 IU/ml). In 2 of 8 cases (25%) the most important risk factor was hemodialysis.

CONCLUSIONS

- This is the most detailed study in Turkey evaluating the prevalence of HBV/HCV coinfection.
- Our results show that HBV/HCV coinfection prevalence is not higher than HBV or HCV monoinfections, but in majority of patients HCV infection was dominant. This is especially noticeable in hemodialysis patients in our study. This finding may be due to the high prevalence of HCV in hemodialysis patients.
- It is also revealed from the present study that HCV infection has a suppressive effect on the replication of HBV as seen by the loss of replicative markers like HBV DNA.
- More crowded populations must be examined and occult infections must be determined to detect the true prevalence of coinfection.
- Since the coinfection poses the risk of heavier liver disease, monoinfected cases must be followed with clinical and virologic means, and preventive strategies must be applied.

Acknowledgement

We thank to Gilead Sciences Medical Company for their definitive support to HEP-NET project (Hepatitis Registry Project).

Table 1. Characteristics of 99 Patients Coinfected with HBV/HCV

The mean age, years *	40.9±21.7
Sex, female/ male %	44/56
Distribution of patients %	
Mid Anatolian Region	31
Southeast Region	30
Blacksea Region	22
Other	17
Method of diagnosis %	
General health control	8
During blood donation	5
During military work	4
During pregnancy	2
Unknown	81
Risk factors %	
Dental therapy	10
Surgical procedure	6
Hemodialysis	4
Blood transfusion	2
Not found	78
HBV DNA and HCV RNA positivity %	8
Mean ALT level, IU/lt*	70.95±49.12

*Mean±standard deviation, ALT: Alanine aminotransferase

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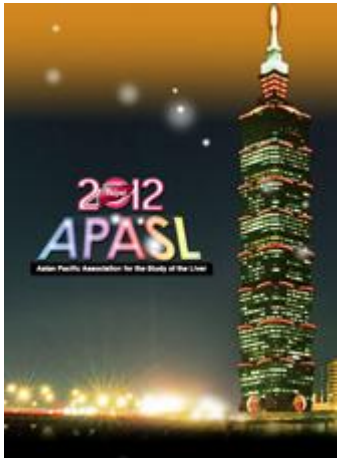

February 16-19 2012
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PP08-032

The Prevalence of Hepatitis B Virus and Hepatitis C Virus Coinfection in Turkey

Bilgehan Aygen1, Mustafa Kemal [2], Iftihar K[3], Selma Tosun[4], O Karabay[5], Tansu Yamazhan[6], Orhan Y[7], Celal Ayaz[8], Fehmi Tabak[9]

[1]Erciyes University; [2]Dicle University Medical Faculty; [3]Karadeniz Technical University, Medical Faculty; [4]Manisa Public Care Hospital, Manisa; [5]Sakarya University Medical Faculty; [6]Ege University Medical Faculty; [7]Erciyes University Medical Faculty; [8]Dicle University Medical Faculty

HEPATOLOGY
Official Journal of the Asian Pacific Association for the Study of the Liver
International

10.165 vaka değerlendirildi

On hastane katıldı… HBV/HCV KO-İNFEKSİYON ORANI 974/100.000

Background: The true incidence of HBV/HCV coinfection is not known in the world. Dual chronic infection with HBV and HCV is common in areas endemic for either virus. We aimed to determine prevalence and epidemiological characteristics of cases coinfected with HBV/HCV in Turkey.

Methods: The date of this study was obtained from Turk-Hep-Net project. The project includes real-life cohort of HBV patients from 15 centers in Turkey and is supported by Viral Hepatitis Society.

Results: In the project, 10.165 hepatitis cases were evaluated in 10 hospitals. Nine hospitals were academic care and one was public care hospital and had been distributed in six different regions. According to first visit results, HBV/HCV coinfection was detected in 99 patients. The ratio was 974/100.000. Fifty-six percent of the cases were male and 44% were female with the mean age of 40.9 + 21.7 years. The diagnosis was obtained in 8% during general health control, in 5% during blood donation, in 4% during military work, and in 2% during blood transfusion. The risk factors were dental therapy (10%), any surgical procedure (6%), hemodialysis (4%), and blood transfusion (2%). In 12% of coinfected cases HBeAg was positive. In 8% both HCV-RNA and HBV-DNA were positive and in 88% of cases HCV infection was dominant.

Conclusions: This is the most detailed study in Turkey evaluating the prevalence of HBV/HCV coinfection. Although these results show that HBV/HCV coinfection prevalence is not higher than HBV or HCV monoinfections, more crowded populations must be examined and occult infections must be determined.

The Prevalence of Hepatitis B Virus and Hepatitis C Virus Coinfection in Turkey
Türkiye'de Hepatit B Virus ve Hepatit C Virus Koenfeksiyonu Prevalansı

Professor Dr. Bilgehan AYGEN[a], Associate Professor Dr. Mustafa Kemal ÇELEN[b], Professor Dr. İftihar KÖKSAL[c], Associate Professor Dr. Selma TOSUN[d], Professor Dr. Oğuz KARABAY[e], Professor Dr. Tansu YAMAZHAN[f], Associate Profesor Dr Orhan YILDIZ[a], Professor Dr. Celal AYAZ[b], Professor Dr. Fehmi TABAK[g]

DOI: 10.5336/medsci.2012-32319

Characteristics of 99 patients coinfected with hepatitis B virus/hepatitis C virus

The mean age, years	40.9±21.7
Sex, female/ male n (%)	43 (43.4)/ 56 (56.6)
Distribution of patients n (%)	
Central Anatolian Region	34.3
Southeastern Region	31.3
Black Sea Region	19.2
Agean Region	10.1
Marmara Region	5.1
Risk factors n (%)	
Surgical procedure+dental therapy	20 (20.2)
Dental therapy	15 (15.2)
Surgical procedure	14 (14.1)
Hemodialysis	6 (6.1)
Blood transfusion	5 (5.1)
Surgical procedure+ blood transfusion	2 (2.0)
Dental therapy+blood transfusion	2 (2.0)
Surgical procedure+dental therapy+blood trans.	1 (1.0)
Not found	34 (34.3)
Mean ALT level, IU/L	70.9±49.1
Virological characteristics	
HCV RNA positivity n (%)	43 (43.4)
Median (min-max) HCV RNA level, IU/mL	0 (50-2.18×10^{7})
HBV DNA positivity n (%)	56 (56.6)
Median (min-max) HBV DNA level, IU/mL	2.50×10^{2} (12-1.70×10^{8})
HBV DNA and HCV RNA positivity n (%)	8 (8.1)

Conclusion

This is the most detailed study in Turkey evaluating the prevalence of HBV/HCV coinfection. Our study demonstrates that most patients coinfected with HBV and HCV had a history of dental therapy, any surgical procedure, hemodialysis, and blood transfusion. HBV/HCV coinfection prevalence is not higher than HBV or HCV monoinfections. In cases where both HCV RNA and HBV DNA were positive, HCV was predominant. This is especially noticeable in hemodialysis patients in our study. Detailed serological and virological evaluations are required for HBV/HCV coinfected patients. More crowded populations must be examined and occult infections must be determined to detect the true prevalence of coinfection.

Viral etkileşim (1)

- Birbirlerini ve immün sistemi etkilerler
  - Eş zamanlı karşılıklı inhibisyon
    - HBV ve HCV replikasyon oranları düşer
  - Bir virusun replikasyonunun diğer virus tarafından baskılanması
    - Genellikle HBV HCV tarafından baskılanır
  - Birbirlerinin serokonversiyonunu indükleyebilirler
- Bazı hastalarda bir virus diğerinden bağımsız olarak replike olabilir

KRONOLOJİK SÜREÇ ÖNEMLİ!
PATOGENEZİ AÇIKLAYACAK NET MEKANİZMALAR?

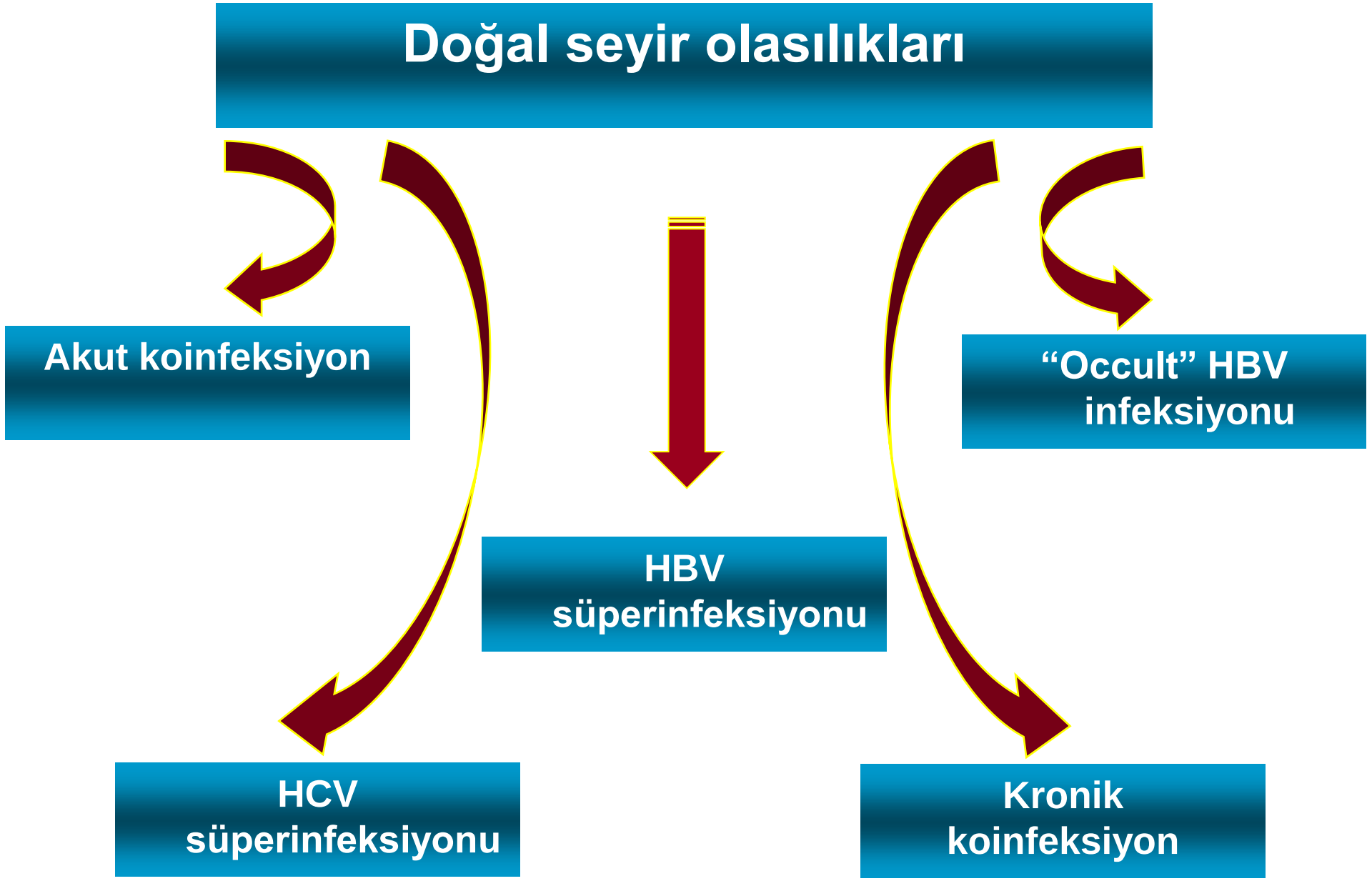
Chu CJ, Lee SD. J Gastroenterol Hepatol 2008;23(4):512-20.
Crockett SD, Keeffe EB. Ann Clin Microbiol Antimicrob 2005;4:13.
Jamma S, et al. Curr Hepat Rep 2010;9(4):260-9.
Peters MG. Hepatology 2009;49(Suppl):S146-2S155.

Hepatitis B and C Virus Coinfection: A Novel Model System Reveals the Absence of Direct Viral Interference

Pantxika Bellecave,[1] Jérôme Gouttenoire,[1] Markus Gajer,[2] Volker Brass,[2] George Koutsoudakis,[3] Hubert E. Blum,[2] Ralf Bartenschlager,[3] Michael Nassal,[2] and Darius Moradpour[1]

Hepatology 2009;50:46-55.

- Yeni hücre kültür modeli ("Huh-7 cell lines")
- *"In vitro"* olarak HBV ve HCV aynı hücrede direkt etkileşim olmadan çoğalabilir!
- Koinfekte hastalarda gözlenen viral etkileşim büyük olasılıkla konağın doğal ve/veya kazanılmış immün yanıtının rol aldığı indirekt mekanizmalara bağlıdır!


Doğal seyir olasılıkları
Akut koinfeksiyon
HBV süperinfeksiyonu
"Occult" HBV infeksiyonu
HCV süperinfeksiyonu
Kronik koinfeksiyon

Akut koinfeksiyon

- HBV/HCV'nin eş zamanlı akut infeksiyon yapması nadir
- Genellikle damar içi ilaç kullanıcılarında perkütan yaralanmalar ve kan transfüzyonu sonrası ortaya çıkar
- Akut koinfeksiyon sonrası
  - İki virustan biri veya her ikisi de tamamen temizlenebilir
  - Fulminan hepatit tablosu ortaya çıkabilir
  - Kronik koinfeksiyon tablosu gelişebilir
- Genomların "reciprocal" inhibisyonu bir virusun klirensine diğerinin kalıcılığına neden olur
  - Kesin immünolojik mekanizma?
  - İnkübasyon süreleri, viral inokülum konsantrasyonu veya genotiplerdeki farklar etkili olabilir

HCV süperinfeksiyonu

- HBV'nin endemik olduğu Asya-Pasifik ülkelerinde sık
- KHB'li olgularda süperinfeksiyon HBeAg serokonversiyonuna ve bazı olgularda HBsAg kaybına yol açabilir
  - ↳KHC tablosu kalıcı olur
- Fulminan hepatit tablosu (%3.1-23) ortaya çıkabilir
  - ↳Konak immün yanıtındaki ve viral faktörlerdeki farklar,

    çalışmalardaki hasta sayılarının azlığı…
- Mortalite oranı %10 kadar yüksek oranlarda bildirilmiştir

HCV süperinfeksiyonunun sonuçları

- Tipik akut ikterik hepatit tablosu
- Hastalığın ağırlığı akut HDV süperinfeksiyonuna benzer
  - Hastaların %34'ünde hepatik dekompansasyon, %11'inde hepatik yetmezlik ve %10'unda ölüm
- Uzun dönem komplikasyon oranı akut HDV süperinfeksiyonundan ve KHB'den yüksek
  - 10 yılda siroz için kümülatif insidans %48
  - Karaciğer kanseri kümülatif insidansı 10 yılda %14, 15 yılda %21 ve 20 yılda %32
- HBsAg kaybı erken
  - Seroklirensden sonra hepatit aktivitesi devam eder

Liaw YF, et al. Gastroenterology 2004;126(4):1024-9.

HBV süperinfeksiyonu

- Nadir görülür
- Yeterli klinik veri yok
  - HCV ile infekte olanlarda HBV süperinfeksiyonu sürecinde anti-HCV kaybı ve karaciğer fonksiyonlarında akut bozulma (HCV'nin baskılanması)
  - Akut HBV infeksiyonuna göre hepatik ensefalopati ve asit gelişme olasılığı yüksek
- KHC'li hastalarda HBV süperinfeksiyonunun fulminan hepatite yol açabileceği akılda tutulmalı!

HBV Superinfection in HCV Chronic Carriers: A Disease That Is Frequently Severe but Associated with the Eradication of HCV

Evangelista Sagnelli,[1,2] Nicola Coppola,[1] Mariantonietta Pisaturo,[1] Addolorata Masiello,[1] Gilda Tonziello,[1] Caterina Sagnelli,[1,2] Vincenzo Messina,[2] and Pietro Filippini[1]

Hepatology 2009;49:1090-7.

- Grup I: Anti-HCV pozitif + akut HBV infeksiyonlu 29 hasta

  Grup II: Anti-HCV negatif + akut HBV infeksiyonlu 29 hasta

  5 yıl izlem

- Bulgular:
  - İki grupta da başlangıç HBV DNA düzeyleri ve HBV DNA'nın negatifleşme eğilimi benzer

- Süperinfeksiyon grubunda:
  - Ağır hepatit tablosu yüksek oranda (%34.5-%6.9)
  - 1 hasta kaybedilmiş, 5 yıl takip edilen 24 hastadan 22'sinde HBsAg negatif, 2'sinde KHB
  - AHB süresince HCV RNA negatif
    - 18 hastada (%75) 3-6 yıl sonra HCV RNA pozitif (reaktivasyon) ve 6 hastada negatif
    - Reaktivasyon grubunda ağır AHB görülme sıklığı yüksek (%83.3-%22.2, $p<0.05$)
- SONUÇ: KHC'de HBV süperinfeksiyonu yaşamı tehdit eder ve ağır AHB tablosunda HCV eradike edilebilir!

“Occult” HBV infeksiyonu

- Sıklık? Bazı serilerde %50
- Klinik tablolar tartışmalı
- Çalışmaların çoğunda HCV ile infekte olanlarda “occult” HBV infeksiyonu durumunda hepatik inflamasyon ağır, siroz ve HSK gelişme olasılığı yüksek
  - Sayı azlığı, kontrol gruplarının olmaması, farklı HBV DNA ölçüm yöntemlerinin kullanımı, farklı coğrafik bölgelerdeki konak ve viral faktörlerin etkileri…
- KHC’li hastalarda “occult” HBV infeksiyonu antiviral tedavi yanıtını olumsuz etkiler

KHC'de "occult" HBV infeksiyonunun sıklığı ve klinik önemi

- Portekiz, prospektif, Ocak 2008-Haziran 2011 tarihleri arasında takip edilen 100 hasta
- Hastaların %33'ünde geçirilmiş HBV infeksiyonuna ilişkin serolojik göstergelerde pozitiflik
- Karaciğerde HBV DNA %57 hastada pozitif
- KHC'li hastalarda "occult" HBV infeksiyonu olanlarla olmayanlar arasında epidemiyolojik, virolojik, histolojik ve tedavi yanıtları açısından istatistiksel olarak anlamlı fark yok
- SONUÇ: KHC'de "occult" HBV infeksiyonu sıklığı yüksektir, ancak klinik önemi yoktur!

Cardoso C, et al. Eur J Gastroenterol Hepatol 2013;25(2):142-6.

“Kronik koinfeksiyon

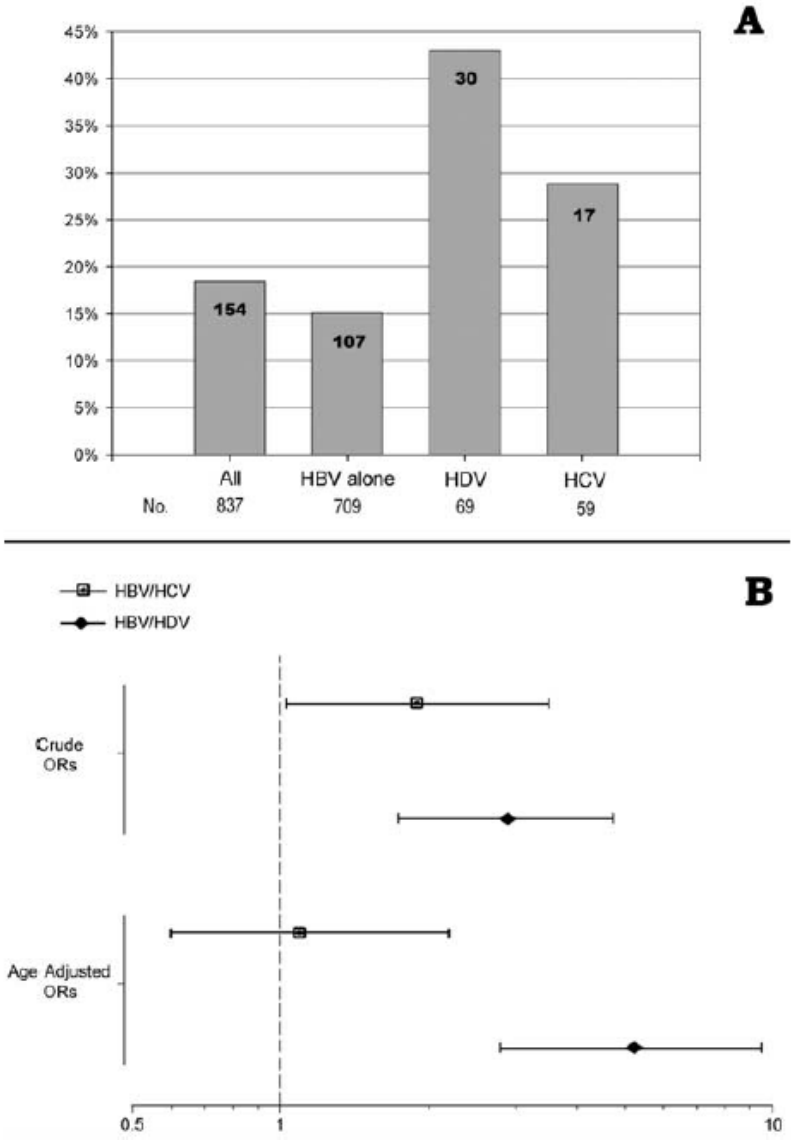
- Akut koinfeksiyon
- HBV süperinfeksiyonu
- HCV süperinfeksiyonu

} sonrasında gelişebilir

- HBV DNA ve HCV RNA birlikte pozitiftir
- Farklı derecelerde hepatik inflamasyon, sirozla sonuçlanan hepatik fibrozis, dekompanse karaciğer hastalığı ve HSK gelişebilir
- Monoinfeksiyonlara göre hastalığın progresyonu kötü ve HSK gelişme oranı yüksek
  - ↳Katkıda bulunan faktörler (genotipler, mutasyonlar, konak faktörleri, metabolik sendromlar, genetik yatkınlıklar)?

Koinfeksiyonda klinik bulgular

- HBsAg pozitif olan 837 hasta
  - Siroz oranları
    - Yalnızca HBsAg pozitif olanlarda (709 hasta) %15.1
    - HDV koinfeksiyonu olanlarda (69 hasta) %43
    - HCV koinfeksiyonu olanlarda (59 hasta) %28.8
- HBV/HCV koinfeksiyonu olan 36 hastanın
  - %44.4'ünde yalnız HBV DNA pozitif
  - %13.9'unda HBV DNA ve HCV RNA pozitif
  - %25'inde HCV RNA pozitif



Gaeta GB, et al. J Hepatol 2003;39:1036-41.

Koinfeksiyonda HCV bulaş yollarına göre klinik özellikler

- Koinfeksiyonu olan 133 olgu
- HCV bulaş yolları
  - 78 hastada damar içi ilaç kullanımı
  - 55 hastada kan transfüzyonu
- Kan transfüzyonu sonrası HCV bulaşı olanlar
  - İleri yaşta
  - Koinfeksiyon süresi uzun
  - AST, ALT, bilirubin düzeyleri düşük
  - Karaciğer hasarı hafif
  - Siroz oranı yüksek
- SONUÇ: HBV/HCV koinfeksiyonunda klinik özellikler HCV'nin farklı bulaş yollarına göre değişir!

Zhang K, et al. Zhonghua Shi Yan He Lin Chuang Bing Du Xue Za Zhi 2011;25(4):301-3.

Koinfeksiyonda fibrozisin ilerlemesi ve karaciğer kanseri

- Koinfeksiyonda karaciğer hasarı daha ağırdır
- Tartışmalı da olsa siroz ve hepatik dekompansasyon sıklığı monoinfeksiyonlardan yüksektir
  - ↳Fibrozis progresyonunu değerlendirmek için ardışık biyopsiler yapılmalı…
- Koinfekte olgularda HSK gelişme riski artar
  - ↳Hepatokarsinogenezde sinerjistik etki…

Chu CJ, Lee SD. J Gastroenterol Hepatol 2008;23(4):512-20.
Kew MC, et al. Gastroenterology 1997;112:184-7.
Chiaramonte M, et al. Cancer 1999;85:2132-7.
Donato F, et al. Int J Cancer 1998;75:347-54.
Benvegnu L, et al. Cancer 1994;74:2442-8.

Infection Clinical and Epidemiological Study

Influence of Chronic Coinfection with Hepatitis B and C Virus on Liver Histology

E. Sagnelli, G. Pasquale, N. Coppola, F. Scarano, C. Marrocco, C. Scolastico, T. Santantonio, A. Gentile, F. Piccinino

Infection 2004;32:144-8.

- 142 kronik hepatit hastasında karaciğer biyopsisi değerlendirilmesi (HAİ: Knodell, fibrozis: Scheuer's sistemi)
  - HBV/HCV koinfeksiyonu: 27 hasta
  - KHB: 57 hasta
  - KHC: 58 hasta
- Koinfeksiyon grubunda buzlu cam hepatosit oranı (%37) KHB'li gruba (%66.7) göre düşük ($p<0.01$)
  - Fibrozis skoru (2.1±1.2) KHC'li gruba (1.5±1.2) göre düşük ($p<0.05$)

- Koinfeksiyon grubunda
  - HCV RNA negatif olanlarda (10 hasta) pozitif olanlara göre HAİ ve fibrozis skoru yüksek bulunmuştur
    - HAİ: 8.5±4.4 ⟹ 5.4±2.4, $p<0.05$
    - Fibrozis: 3.0±1.3 ⟹ 1.69±1.0, $p<0.05$
- SONUÇ: HBV/HCV koinfeksiyonunda özellikle HCV replikasyonunun yetersiz olduğu durumlarda karaciğer histolojisi monoinfeksiyonlara göre daha ağırdır!

J Gastroenterol Hepatol 2007;22:515-7.

doi:10.1111/j.1440-1746.2006.04547.x

HEPATOLOGY

Comparison of liver histopathology between chronic hepatitis C patients and chronic hepatitis B and C-coinfected patients

Li-Po Lee,* Chia-Yen Dai,*,†,‡ Wan-Long Chuang,*,† Wen-Yu Chang,*,† Nei-Jen Hou,‡ Ming-Yen Hsieh,* Zu-Yau Lin,*,† Shinn-Cherng Chen,*,† Ming-Yuh Hsieh,*,† Liang-Yen Wang,*,† Tong-Jong Chen§ and Ming-Lung Yu*,†

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- 336 KHC hastası, 32 olguda (%59.8) HBsAg pozitif
- Karaciğer biyopsisi değerlendirilmesi (HAİ: Knodell, fibrozis: Scheuer's sistemi)
- İntralobüler nekroz koinfekte hastalarda (0.84±1.05) monoinfekte hastalara (0.53±0.89) göre yüksek
- Periportal nekroz, portal inflamasyon, total nekroinflamasyon ve fibrozis açısından gruplar arasında anlamlı fark yok
- SONUÇ: Koinfeksiyonda intralobüler nekroz izole HCV infeksiyonuna göre daha ağırdır!

The Gambia Liver Cancer Study: Infection With Hepatitis B and C and the Risk of Hepatocellular Carcinoma in West Africa

Gregory D. Kirk,[1,2] Olufunmilayo A. Lesi,[2,7] Maimuna Mendy,[4] Aliu O. Akano,[5,7] Omar Sam,[5] James J. Goedert,[1] Pierre Hainaut,[3] Andrew J. Hall,[6] Hilton Whittle,[4] and Ruggero Montesano[3]

Hepatology 2004;39:211-9.

- HSK tanılı 216 hasta ve 408 kontrol grubu
- HSK hastalarında %3.5 koinfeksiyon
- HBV veya HCV infeksiyonlarında HSK gelişme riski olasılığı 16.7, koinfeksiyonda 35.3
- SONUÇ: HBV ve HCV hepatokarsinogenezin çok aşamalı sürecinde önemli risk faktörleridir ve koinfeksiyonun varlığı olası riski artırır!

Int. J. Cancer: **112,** 1075–1080 (2004)

Publication of the International Union Against Cance

PROSPECTIVE STUDY ON THE RISK OF HEPATOCELLULAR CARCINOMA AMONG HEPATITIS C VIRUS-POSITIVE BLOOD DONORS FOCUSING ON DEMOGRAPHIC FACTORS, ALANINE AMINOTRANSFERASE LEVEL AT DONATION AND INTERACTION WITH HEPATITIS B VIRUS

Hideo TANAKA[1]*, Hideaki TSUKUMA[1], Hajime YAMANO[2], Akira OSHIMA[1] and Hirotoshi SHIBATA[2]

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[2]*Osaka Red Cross Blood Center, Osaka, Japan*

Int J Cancer 2004;112:1075-80.

- Anti-HCV pozitif, HBsAg negatif 1927 kan donörü, 9 yıl takip
- HSK'nın 9 yıllık kümülatif insidansı HCV ile infekte olanlarda %3, HBV/HCV koinfeksiyonunda %12
- SONUÇ: Japonya'da asemptomatik HCV infeksiyonunda HSK gelişme riski fazladır

ve

HBV/HCV koinfeksiyonu HSK riski için "superadditive" rol oynar!

Rate of incidence of hepatocellular carcinoma in patients with compensated viral cirrhosis

Chiaramonte M, Stroffolini T, Vian A, Stazi MA, Floreani A, Lorenzoni U, Lobello S, Farinati F, Naccarato R

Cancer 1999;85(10):2132-7.

- 259 hasta (66 hasta HBV, 166 hasta HCV ve 27 hasta koinfekte)
- Ortalama 64.5 aylık takip sonucu hastaların %19.7'sinde HSK
  - Beş yılda kümülatif HSK riski
    - HBV hastalarında %10, HCV hastalarında %21, koinfekte hastalarda %23
  - On yılda kümülatif HSK riski
    - HBV hastalarında %16, HCV hastalarında %28, koinfekte hastalarda %45
- SONUÇ: HBV/HCV koinfeksiyonu HSK gelişmesi için en yüksek riske sahip bağımsız faktördür!

uicc global cancer control

2011;128:176-84.

IJC International Journal of Cancer

Coinfection of hepatitis B and C viruses and risk of hepatocellular carcinoma: systematic review and meta-analysis

Lisa Y. Cho[1,2], Jae Jeong Yang[1,2], Kwang-Pil Ko[1,3], Boyoung Park[1,2], Aesun Shin[4], Min Kyung Lim[5], Jin-Kyoung Oh[5], Sohee Park[5], Yoon Jun Kim[6], Hai-Rim Shin[5,7], Keun-Young Yoo[1] and Sue K. Park[1,2,8]

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[3] Division of Epidemiology and Health Index, Korea Centers for Disease Control & Prevention, Seoul, South Korea
[4] National Cancer Center Research Institute, National Cancer Center, Goyang, Gyeonggi-Do, South Korea
[5] National Cancer Control Institute, National Cancer Center, Goyang, Gyeonggi-Do, South Korea
[6] Department of Internal Medicine and Liver Research Institute, Seoul National University College of Medicine, Seoul, South Korea
[7] Biostatistics and Epidemiology Cluster, IARC, Lyon
[8] Institute of Health Policy and Management, Seoul National University College of Medicine, Seoul, South Korea

- 1985-2009 yılları arası, 441 rapordan uygun bulunan 59'u
- Koinfeksiyonda subaditif veya supraaditif etki?
- HSK nedenleri:
  - İki virusun da endemik olmadığı bölgelerde subaditif etki
  - HBV'nin endemik olduğu bölgelerde aditif etki
  - HCV'nin endemik olduğu bölgelerde supraaditif etki

- SONUÇ: HBV/HCV koinfeksiyonu HSK için monoinfeksiyonlardan daha yüksek risk taşımaz (subaditif etki)

  ve

  HSK riski HBV veya HCV'nin endemik olmadığı bölgelerde endemik olduğu bölgelere göre daha yüksek orandadır!

HEPATITIS B VIRUS AND HEPATITIS C VIRUS COINFECTION: AN EVALUATION OF 82 PATIENTS IN TURKEY

BİLGEHAN AYGEN[1], ÖZGÜR GÜNAL[2], ORHAN YILDIZ[1], MUSTAFA KEMAL ÇELEN[3], SILA AKHAN[4], ŞENER BARUT[2], CELAL AYAZ[3]

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INTRODUCTION

Hepatitis B virus (HBV) and hepatitis C (HCV) virus infections are among the most common causes of advanced chronic liver disease worldwide. Patients coinfected with HBV and HCV have faster fibrosis, higher rates of progression, more severe liver disease, and are at markedly increased risk of developing hepatocellular carcinoma as compared to those with HBV or HCV monoinfection[1-6]. The pathophysiology of HBV/HCV is complex, as different patterns of virological dominance may occur, which can even fluctuate over time[4-6].

Although HBV/HCV coinfection is not uncommon, its epidemiology is poorly defined[7,8]. An estimated 7-20 million individuals are affected worldwide[4]. According to study reports approximately 5-7% of HBV-infected patients also were positive for anti-HCV and 2-10% of chronic hepatitis C patients were positive for HBsAg[9,10]. HBV and HCV coinfection is overwhelmingly common in several high risk populations, including intravenous drug users, patients on hemodialysis, recipients of organ transplantations, and human immunodeficiency virus positive patients[7]. In endemic areas, however, the incidence of coinfection provides the basis for an appreciable rate of HBV and HCV co-infection in the general population[10]. In our a study, 10.165 hepatitis cases were evaluated in 10 hospitals and coinfection ratio was 974/100.000[11]. Dual chronic infection with HBV and HCV is common in areas endemic for either virus. HCV superinfection in patients with chronic HBV infection was the most common clinical features of coinfection in Asia-Pacific countries[9].

To date, no standard-of-care recommendation exists for HBV/HCV coinfection[1,8,12]. Pegylated interferon (peg IFN) and ribavirin combination therapy demonstrated similar efficacy in suppressing HCV RNA in coinfected and HCV monoinfection. However, HBV reactivation during therapy can be challenge[8,9,12,13]. Detailed serological and virological evaluations are required for HBV/HCV coinfected patients before initiation of antiviral therapy [4,5].

This retrospective, multicenter study aimed to investigate the epidemiological, virological, clinical, and histopathological charecteristics and treatment results and the change in the status of HBV or HCV infection following the treatment of 82 coinfected patients with HBV/HCV in Turkey.

MATERIALS AND METHODS

Study population and data collection

A total of 82 HBV/HCV coinfection cases who over 18 years of age were retrospectively evaluated from four university hospitals. Ethical approvel was not required as the study was retrospective. This study included patients who were followed between 1998-2012 and records of regularly. The HBV and HCV coinfection patients were diagnosed by serum HBsAg, and antibodies to HCV-positive and detectable serum HCV RNA and/or HBV DNA and compensated liver disease. Data collection was performed using a case record form in the charge of doctors in the individual hospital. Baseline clinical and virological characteristics and results of treatment were obtained by retrospective review of medical records, and when available histological data before the treatment were also recorded. Participant's demographic data, year of diagnosis, the possible transmission routes of viruses, alanine aminotransferase (ALT) levels, markers of hepatitis, results of HCV RNA and HBV DNA and the liver biopsy, and treatment results were all evaluated. The epidemiological, virological, clinical, histopathological data and the results of treatment in patients coinfected with HBV and HCV were analyzed.

Laboratory tests were performed at each hospital's own. ALT tests were performed with automatic devices. Serological markers (anti-HCV, HBsAg, anti-HBs, HBeAg, anti-HBe and anti-HBc) have been tested with different enzyme immunoassay kits. HBV DNA and HCV RNA have been investigated by using real-time polymerase chain reaction (RT-PCR) with different kits (Cobas Ampliprep/Cobas TaqMan HBV/HCV assay [Roche, Molecular System, Pleasanton, CA], Abbott RealTime HBV/HCV assay [Abbott Diagnostics, Chicago, IL], HBV/HCV QS-RGQ [Qiagen, Hilden, Germany]). All results were converted to IU/mL. Liver biopsy specimens were scored according to Ishak Scoring System[14]. The mean grade of necroinflammation and stage of fibrosis were evaluated. The HCV genotype was determined by different methods (sequence analysis [Pyromark Qiagen- Germany], RT-PCR [Fluorion HCV genotyping 1.0, Iontek AŞ, İstanbul, Turkey]) in patients receiving HCV treatment.

Definition, treatment and evaluation of the treatment responses

Peg IFN-a 2a plus ribavirin or peg IFN-a 2b plus ribavirin treatment was given patients with HCV dominant. Initial dosage and dose modification of treatment drug was determined based on the current guidelines[15,16]. The patients with genotype 1 or genotype 4 were treated for 48 weeks. All subjects were followed up at least for 24 weeks after cessation of therapy. Serum HCV RNA was measured at baseline and week 12 during therapy and at the end of the treatment and at week 24 of follow-up. An early virological response (EVR), an end of treatment response (ETR) and sustained virological response (SVR) of patients were observed. The categories and severity of adverse events were registered. HBV DNA was measured at baseline and week 24 and week 48 during therapy in all patients. We evaluated the results of patients receiving different treatments for HBV. All patients continue with the antiviral therapy and are followed at three to six month intervals.

Statistical analysis

The clinical and biochemical characteristics of the patients were expressed as mean ± standard deviation (SD). Statistical analysis were performed with Mann-Whitney test and χ2 test. P-values less than 0.05 were considered as statistically significant. The SPSS (version 16.0) software package was used to perform statistical analysis.

RESULTS

Demographics and baseline characteristics

Of the data evaluated were from four academic care hospitals and had been distributed in four different regions. The mean age of the patients was 44.3±14.7 years and 52.4% were female. The distribution of coinfected cases were; 41.5% in Mid Anatolian Region, 37.8% in Southeast Region, 18.3% in Black Sea Region, and 2.4% Marmara Region. The major risk factors were dental therapy, any surgical procedure, hemodialysis, and blood transfusion. In 14.6% of patients HBeAg was positive. HCV RNA levels were between 170-1.62x10^7 IU/mL (mean 1.36x10^6±3.06x10^6 IU/mL). Twenty-eight of the 36 patients (77.8%) had HCV RNA level less 600.000 IU/mL. HBV DNA levels were between 50-1.70x10^8 IU/mL (mean 1.55x10^7±4.83x10^7 IU/mL). Twenty-two of the 46 patients (47.8%) had HBV DNA levels less 2.000 IU/mL. Patients characteristics are summarized in **Table 1.**

Table 1. Characteristics of 82 patients coinfected with hepatitis B virus/hepatitis C virus	
The mean age, years*	44.3±14.7
Sex, female/ male n (%)	43 (52.4)/ 39 (47.6)
Distribution of patients n (%)	
Mid Anatolian Region	41.5
Southeast Region	37.8
Black Sea Region	18.3
Marmara Region	2.4
Risk factors n (%)	
Surgical procedure+dental therapy	14 (17.1)
Dental therapy	12 (14.6)
Surgical procedure	10 (12.2)
Hemodialysis	7 (8.5)
Surgical procedure+dental therapy+blood transfusion	5 (6.1)
Blood transfusion	3 (3.7)
Dental therapy+blood transfusion	3 (3.7)
Dental therapy+suspected sexual transmission	2 (2.4)
Surgical procedure+ blood transfusion	1 (1.2)
Surgical procedure+hepatitis in the family	1 (1.2)
Hepatitis in the family	1 (1.2)
Suspected sexual transmission	1 (1.2)
Not found	22 (26.8)
Mean ALT level, IU/L*	47.8±50.0
Virological characteristics	
HCV RNA positivity n (%)	36 (43.9)
Mean HCV RNA level, IU/mL*	1.36x10^6±3.06x10^6
HBV DNA positivity n (%)	46 (56.1)
Mean HBV DNA level, IU/mL*	1.55x10^7±4.83x10^7
HBV DNA and HCV RNA positivity n (%)	7 (8.5)
Histopathological results (n=25)*	
Mean grade of necroinflammation	4.0±2.4
Mean stage of fibrosis	1.7±1.3
*Mean±standard deviation ALT: Alanine aminotransferase	

In 8.5% (seven patients) both HCV-RNA and HBV-DNA were positive and in 85.7% of cases HCV infection was dominant. In HCV RNA and HBV DNA-positive group, five patients had high ALT levels. HCV RNA levels were in the range of 1139-2.40x10^6 (mean 6.24x10^5±8.38x10^5) IU/mL in seven patients. HBV DNA levels were 211-5.60x10^6 (mean 8.09x10^5±2.12x10^6) IU/mL in these patients. In one patient, HBV DNA level was 5.607.835 IU/mL with low level of HCV RNA (1139 IU/mL). In two of seven cases (28.6%) the most important risk factor was hemodialysis. Serum HCV RNA levels were compared between patients with and without detectable serum HBV DNA. HCV RNA levels were higher in the patients with detectable HBV DNA (6.24x10^5±8.38x10^5 IU/mL) than in the patients without detectable HBV DNA (1.53x10^5±3.38x10^6 IU/mL). There was no statistical significance (P=0.969).

Treatment efficacy

Thirty-four patients had received treatment and in 25 of these liver biopsies have been taken. Peg IFN plus ribavirin therapy was given to 27 patients with dominant HCV infection (peg IFN-a 2a in 12 patients and peg IFN-a 2b in 15 patients). Characteristics of patients treated with peg IFN and ribavirin are summarized in **Table 2**. HCV RNA and HBV DNA were positive in three patients. Two of the three patients had baseline HBV DNA level of less than 2000 IU/mL (292 and 403 IU/mL) and HBV DNA level was 2400 IU/mL in one patient. Disappearance of HBV DNA occurred in 1 of 3 (33.3%) patients with positive HBV DNA at baseline. HBV DNA level of above 2000 IU/mL (2400 IU/mL) and SVR was not observed in this patient. After the completion of treatment, serum HBV DNA levels were remained positive with the same baseline values in another two patients. Interestingly, seven of 21 (33.3%) patients with negative HBV DNA at baseline had reactivation of HBV DNA at the 24 weeks of follow-up, this was not accompanied by significant hepatic flares. The reactivation rate of HBV DNA (50%) with HCV SVR was the same that of patients without SVR (50%) (P=1). Serum ALT levels were normal in four patients. The serum ALT levels were elevated in three patients (mean value 124±30.0 IU/L, range 89-161 IU/L), and these three patients were given TDF. After three months, the serum HBV DNA of these patients become undetectable and ALT levels returned to normal. During the treatment of peg IFN and ribavirin, and oral antiviral agents, severe side effects were not observed.

Table 2. Characteristics of patients treated with pegylated interfon and ribavirin	
The number of patients	27
HCV genotype n (%)	
Genotype 1	25 (92.6)
Genotype 4	2 (7.4)
Mean ALT level, IU/L*	73.4±53.8
Mean HCV RNA level, IU/mL*	[illegible]
Histopathological results (n=18)*	
Mean grade of necroinflammation	5.5±1.8
Mean stage of fibrosis	1.8±1.3
Results of treatment n (%)**	
EVR	20 (83.3)
ETR	19 (79.2)
SVR	17 (70.8)
Nonresponder	7 (29.2)
Relapse	3(12.5)
Disappearance of HBV DNA	1 (33.3)
Reactivation of HBV DNA	7 (33.3)
*Mean±standard deviation **Three patients were excluded ALT: Alanine aminotransferase, EVR: Early virological response; ETR: End of treatment response; SVR: Sustained virological response	

Different treatment regimens were given to seven patients with dominant HBV infection. The mean ALT levels were 94.1±46.9 IU/L and the mean HBV DNA level was found 4.86x10^7±8.29x10^7 IU/mL in the group for the treatment of HBV infection. HCV RNA and HBeAg were negative in this group. The mean grade of necroinflammation was 6.9±1.2 and mean staging of fibrosis was 2.9±1.1 in seven patients. HBV DNA was found negative in all patients who had received oral antiviral therapy. HBV DNA was negative in two patients from 12th months of lamivudine therapy. HBV DNA was negative in four patients treated with entecavir or tenofovir, on 6th month and 12th month. None of these patients developed HBV reactivation by now. HBV DNA was positive in one patient treated with peg IFN 2a at 6th month and therapy was stopped. During the treatment, HBsAg clearance and HCV RNA positivity were not observed in the patients.

CONCLUSIONS

- Our study demonstrates that most patients coinfected with HBV and HCV had a history of dental therapy, any surgical procedure, hemodialysis, and blood transfusion.
- It is also revealed from the present study that HCV infection has a suppressive effect on the replication of HBV as seen by the loss of replicative markers like HBV DNA.
- The replication of HBV was suppressed, and HCV was the dominant virus strain. This is especially noticeable in hemodialysis patients. This finding may be due to the high prevalence of HCV in hemodialysis patients.
- Detailed serological and virological evaluations are required for HBV/HCV coinfected patients before initiation of antiviral therapy. At present, peg IFN plus ribavirin should be the treatment of choice in patients with dominant HCV replication. However HBV rebound may occur after elimination of HCV, and thus close monitoring for both viruses is recommended even for patients with suppressed HBV DNA.
- Oral antiviral agents may be useful, particularly in patients with HBV-dominant disease. However, the larger randomized, controlled trials are needed to clarify the optimal treatment for such patients and the role of newer antiviral agents.
- Since the coinfection poses the risk of heavier liver disease, monoinfected cases must be followed with clinical and virologic means, and preventive strategies must be applied.

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[illegible]

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HBV/HCV koinfekte 82 hastanın özellikleri

Yaş ortalaması, yıl	44.3±14.7
Cinsiyet, kadın/ erkek n (%)	43(52.4)/ 39 (47.6)
Risk faktörleri n (%)	
Cerrahi girişim + diş tedavisi	14 (17.1)
Diş tedavisi	12 (14.6)
Cerrahi girişim	10 (12.2)
Hemodiyaliz	7 (8.5)
Cerrahi girişim + diş tedavisi + kan transfüzyonu	5 (6.1)
Kan transfüzyonu	3 (3.7)
Diş tedavisi + kan transfüzyonu	3 (3.7)
Bilinmeyen	22 (26.9)
Ortalama ALT düzeyi, IU/L	47.8±30.0

Virolojik özellikler

HBeAg pozitifliği n (%)	12 (14.6)
HCV RNA pozitifliği n (%)	36 (43.9)
Ort. HCV RNA düzeyi, IU/mL	$1.36x10^6 \pm 3.06x10^6$
>600.000 IU/mL n (%)	28 (77.8)
HBV DNA pozitifliği n (%)	46 (56.1)
Ort. HBV DNA düzeyi, IU/mL	$1.55x10^7 \pm 4.83x10^7$
>2000 IU/mL n (%)	22 (47.8)
HBV DNA + HCV RNA pozitifliği n (%)	7 (8.5)

Histopatolojik bulgular

- Karaciğer biyopsisi bulguları (n=39)
  - ↳Nekroinflamasyon derecesi ⟹ 4.9±2.6
  - ↳Fibrozis evresi ⟹ 1.7±1.2
- HBV DNA ve HCV RNA'nın birlikte pozitif olduğu hastalarda HAİ ve fibrozis evresi yalnız HBV DNA veya HCV RNA'nın pozitif olduğu hastalara göre daha yüksekti!

HBV DNA ve HCV RNA birlikte pozitif olan hastaların özellikleri

- Ortalama HCV RNA düzeyi, IU/mL → $6.24x10^5 \pm 8.38x10^5$
- Ortalama HBV DNA düzeyi, IU/mL → $8.09x10^5 \pm 2.12x10^6$
- HCV RNA hakimiyeti → 6 hasta (%85.7)
- Yedi olgunun ikisinde (%28.6) en önemli risk faktörü hemodiyaliz
- HCV RNA düzeyi, HBV DNA pozitif bulunan grupta negatif bulunan gruba göre daha yüksek (p=0.969)

SONUÇLAR

- Koinfekte hastalarda en önemli risk faktörleri diş tedavisi, cerrahi girişim, hemodiyaliz uygulaması ve kan transfüzyonu öyküsüydü
- HCV RNA ve HBV DNA birlikte pozitif olan hastalarda HCV infeksiyonu baskındı
  - Bu durum özellikle hemodiyaliz hastalarında dikkat çekici bulundu
- HCV infeksiyonunun baskın olduğu hastalarda pegile İFN + ribavirin tedavisi etkindir
  - HBV reaktivasyonu açısından dikkatli olunmalıdır
- HBV infeksiyonunun baskın olduğu hastalarda oral antiviral tedaviler etkilidir

Original Paper

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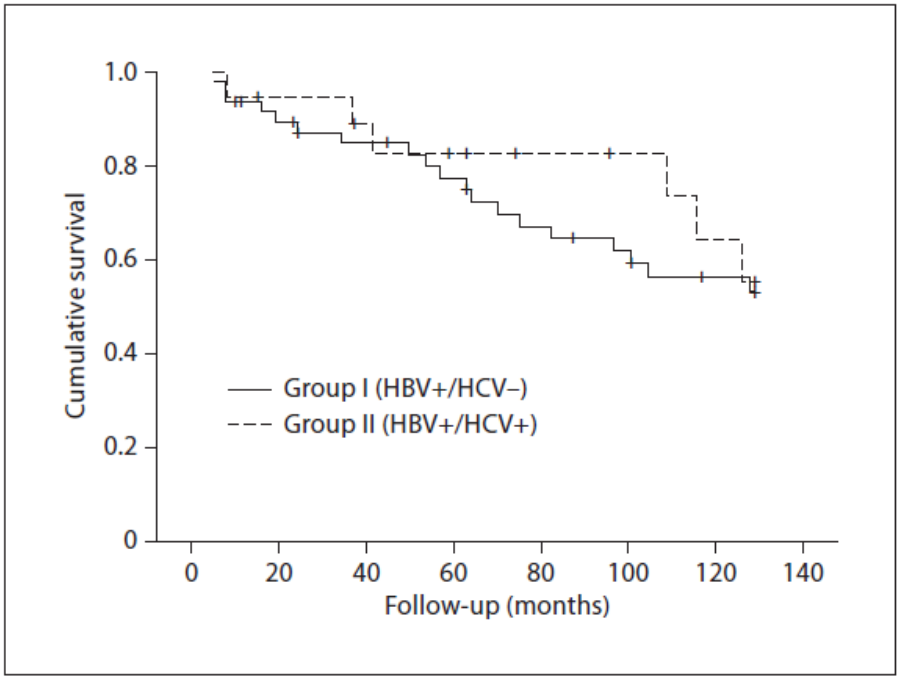
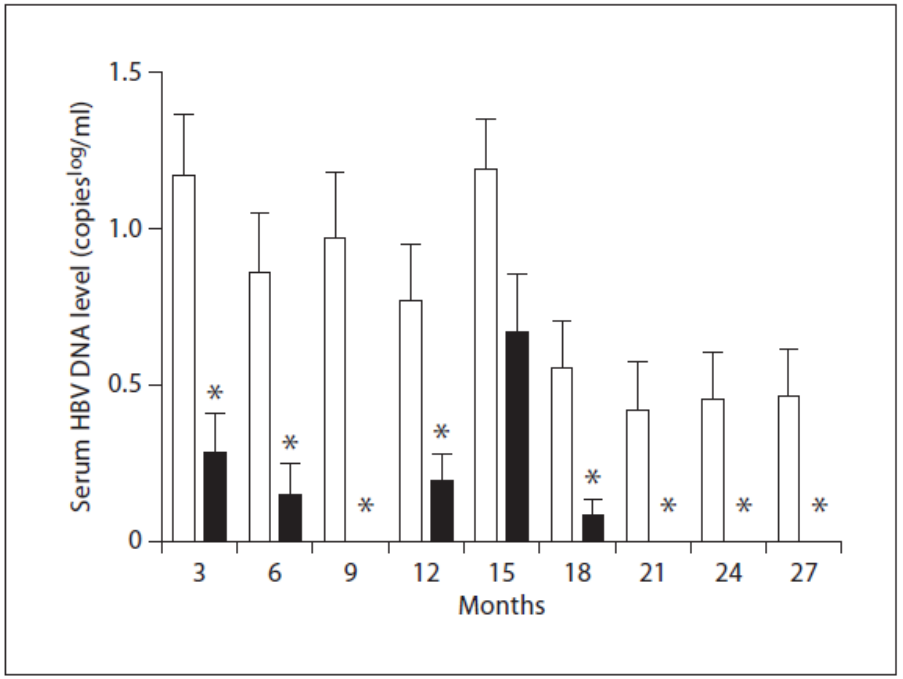
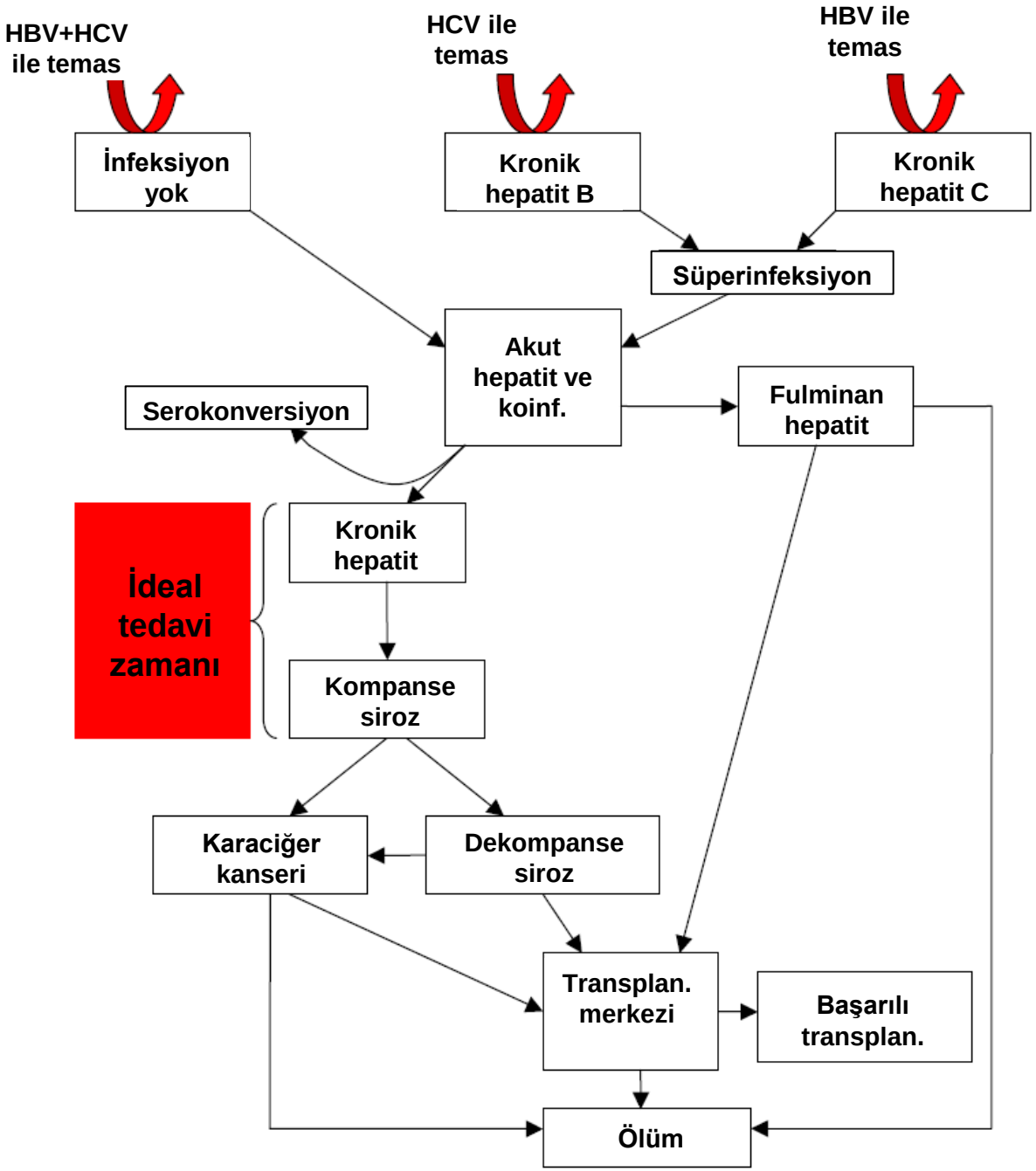
Comparable Ten-Year Outcome in Hemodialysis Patients with Hepatitis C Virus and Hepatitis B Virus Coinfection and Single Hepatitis B Virus Infection

- HBV infeksiyonu olan 48, koinfeksiyonu olan 19 hasta,1996-2006 yılları arasında takip
- Akut hepatit epizotları, yüksek ALT düzeyi periyotları, siroz-HSK gelişme olasılıkları ve yaşam süreleri açısından gruplar arasında fark yok
- Koinfekte olan hastalarda ilk 27 aylık süreçte HBV DNA düzeyleri yalnız HBV infeksiyonu olanlara göre anlamlı olarak düşük





- SONUÇLAR:
  - Hemodiyaliz hastalarında HBV/HCV koinfeksiyonunda HCV infeksiyonu HBV DNA düzeyini baskılar
  - Koinfeksiyon yalnız HBV infeksiyonuna göre daha ağır karaciğer hastalığına ve sağ kalım süresinin kısalmasına yol açmaz!



HBV/HCV koinfeksiyonunda infeksiyon senaryoları ve tedavi zamanlaması

HBV/HCV koinfeksiyonunda APASL uzlaşı raporu önerileri

- KHC'li hastalarda damar içi ilaç kullanımı veya diğer risk faktörlerinin varlığında HBsAg testine rutin bakılmalıdır
  - HBsAg negatif ise HBV'ye karşı bağışıklama yapılmalıdır
- KHC tanılı ve HBsAg'si negatif olan hastalarda rutin HBV DNA testi yapılması önerilmemektedir
- Koinfekte olgularda HSK açısından tarama testleri (USG ve alfa feto protein) yapılmalıdır
- Antiviral tedavi kararı için hangi virusun baskın olduğu araştırılmalıdır

APASL. Hepatol Int DOI: 10.1007/s 12072-012-9342-y

ÖZET

- HBV prevalansının yüksek olduğu bölgelerde koinfeksiyon oranı yüksek değildir
- Koinfeksiyonda karaciğer hastalığına ilişkin komplikasyon oranı yüksektir
- Hangi virusun baskın olduğunu saptamak tedavi kararı açısından önemlidir

Viruslar arasındaki kompleks etkileşim infeksiyon yönetimi ile ilgili ön görülemeyen sorunlarına yol açmaktadır!

GELECEK (1)

- Viral replikasyonu etkileyen
  - ↳İmmün yanıt
  - ↳Diğer konak faktörleri

    araştırılmalı!

- Hastalığın doğal seyri ve tedavi kararı için
  - ↳HBV ve HCV genotiplerinin rolü
  - ↳Viremi düzeylerinin önemi
  - ↳HBV mutantlarının etkisi
  - ↳Konağa ilişkin faktörler

    değerlendirilmeli!

GELECEK (2)

- HBV DNA ve HCV RNA düzeylerini ölçmek için standardize edilmiş RT-PCR yöntemleri kullanılmalı!
- Serolojik ve virolojik profilleri dikkate alan yeni terminolojik kavramlar geliştirilmeli!

Teşekkürler…