

HEPATİT C

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GİRİŞ

1970’li yılların başlarında hepatit A ve hepatit B virüslerinin keşfinden sonra, akut ve kronik hepatit vakalarının büyük bir kısmının bu ajanlardan herhangi biri ile açıklanamayacağı anlaşıldı. 1989 yılında, non-A, non-B hepatitis olarak adlandırılan, kronik ve akut enfeksiyona yol açabilen viral ajan saptandı. Bu virüsün genomunun klonlanması sonucu Hepatit C virüsü (HCV) olarak adlandırıldı (1). Tüm dünyada 200 milyondan fazla insanın HCV ile enfekte olduğu bilinmektedir (2,3). HCV ilişkili mortalite oranları 1995 sonrası dramatik artış gösterirken, 2002 sonrası plato çizmiş ve son yıllarda yeni bulunan tedaviler ile azalma eğilimine geçmiştir (4,5).

VİROLOJİ

HCV, Flaviviridae ailesinde yer alan Hepacivirus genusu içinde sınıflandırılan, 50 nm çapında sferik, lipid zarflı, pozitif iplikçikli, tek zincirli bir RNA virüsüdür (6,7). İkozohedral simetrisi olan nükleokapsid, genomik RNA ve birçok kor proteini kopyasından oluşmaktadır. Nükleokapsid; E1 ve E2 zarf glikoproteinlerinin gömülü olduğu, konak hücre kaynaklı çift-katmanlı lipid zarf ile çevrilidir. Kor proteini, E1 ve E2 zarf glikoproteinleri virionun ana protein komponentleridir (8,9).

HCV genomu, yaklaşık 9600 nükleotid içeren pozitif iplikçikli, tek zincirli bir RNA’dır. Genom, yüksek oranda korunmuş kısa bir 5’UTR (untranslated region, translasyon olmayan bölge), uzun bir açık okuma çerçevesi (ORF) ve kısa bir 3’UTR bölgesinden oluşur (7). Genomun 5’ UTR bölgesi, 341 nükleotid uzunluğundadır. Bütün HCV suşları arasında benzerlik gösterir. Bu nedenle vireminin saptanmasında hedef bölge haline gelmiştir. 5’ UTR bölgesi, viral genomun ökaryotik ribozomun 40S alt ünitesine bağlanarak translasyonunu sağlayan bölgedir. 5’ UTR bölgesinde bu bağlanmayı sağlayan kısım “internal ribosomal entry site” (IRES) olarak adlandırılmakta ve başlangıçtaki 29 nükleotid hariç, 5’ UTR’nin tamamı bu işlevde yer almaktadır. Buna karşılık ilk 23 nükleotidin, translasyonu baskılayıcı rolü olduğu sanılmakta ve bu bölgenin gelecekte antivirallere uygun bir hedef oluşturabileceği düşünülmektedir (10).

3’UTR bölgesi ise, poly-U ya da poly-A ile sonlanan yaklaşık 27 ila 54 nükleotidi içermektedir. Poly-U bölgesinden sonra, çok iyi korunmuş 98 baz uzunluğunda, 3’-X dizisi adı verilen bölge yer alır. Bu bölgenin, virüs replikasyonunda, negatif RNA zincirinin sentezinin başlamasında rol oynadığı düşünülmektedir. Bu bölge “replikaz tanıma bölgesi” olarak tanımlanmaktadır (11).

Tek iplikçikli RNA yaklaşık 3000 aminoasit içeren tek bir poliprotein sentezler.

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Yeniden herhangi bir tedavi şemasına dahil edilmeyecek hastalarda ise; 3-6 ayda bir karaciğer hastalığının ilerleyip ilerlemediğini takip amaçlı; biyokimya, hemogram, pıhtılaşma zamanı içeren testler yanı sıra, hepatoselüler kanser açısından 6 ayda 1 ultrason ve alfa fetoprotein takibi yapılmaktadır.

Sirozu olan hastalarda Üst Gastrointestinal sistem (gis) endoskopisi ile varis takibi yapılmalıdır.

Tedavi Başarısı Elde Edilen Hastaların Takibi:

Kalıcı viral yanıt elde edilen hastalarda, tekrar HCV enfeksiyon riski yoksa, HCVRNA takibi yapılmasına gerek yoktur. Ancak uyuşturucu kullanımı, intravenöz madde kullanımı, çok eşlilik, riskli cinsel davranışları olanlarda, yeniden bulaş açısından 6 ayda bir HCVRNA düzeyi takibi önerilir.

İleri fibrozisi olan hastalarda, 6 ayda 1 ultrason takibi ile hepatoselüler kanser açısından takibi bırakmamak gerekmektedir.

Siroz hastalarında, üst gis endoskopileri ile varis takibi yapılmalıdır.

Hasta kalıcı viral yanıt geliştikten sonra immunosupresif tedavi alacaksa tekrar HCV alevlenme riskine sahip değildir. Takip gerektirmez (143).

Sonuç

1990'lı yılların başında tanımlanan Hepatit C Virüsü, önceleri oldukça mortal bir virus olarak karşımıza çıkmasına rağmen günümüzde virüsün yapısının çözümlenmesi ve bunlara karşı geliştirilen direk etkili antivirallerin keşfi ile, tedavide %99' lara varan başarı oranı sayesinde tarih sayfalarından silinmeye yüz tutmuştur. Tedavide başarı oranı bu kadar yüksek olmasına rağmen hala dünya üzerinde hatırı sayılır oranda tedavi edilmemiş Hepatit C pozitif hastalar bulunmaktadır.

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