AKUT RESPİRATUAR DİSTRES SENDROMU MODELLERİ

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Akut akciğer hasarı (Acute Lung Injury-ALI), yüksek mortalite ile ciddi bir heterojen akciğer bozukluğunu temsil eder, vasküler permeabilite artışıyla seyreden akut ve sürekli akciğer inflamasyonudur. ALI'nın daha ağır şekli akut solunum sıkıntısı sendromu (Acute respiratory distress syndrome-ARDS) olarak tanımlanmaktadır. Dünya genelinde yoğun bakım ünitelerine başvuran tüm hastaların %10'unda meydana gelen yaygın ölümcül ve engelleyici bir hastalıktır[1]. Berlin tanımlamasına göre, akut hipoksemik solunum yetmezliğinin başlangıcı (<1 hafta) ve göğüs radyografisinde kalp yetmezliği ile açıklanamayan bilateral pulmoner infiltratlar ARDS olarak tanımlanmıştır[2,3]. Altta yatan patofizyoloji, aşırı bir inflamatuar yanıt ile karakterizedir. Akciğer pnömoni veya mide asidi aspirasyonu ile direk hasarlanabilir veya sepsis gibi veya birden fazla kan transfüzyonu sonrası indirek hasarlanabilir[3]. İlk hasarın ardından; ARDS patogenezi eksüdatif, proliferatif ve fibrotik faz olmak üzere üç aşamada ilerler[4]. Bu evreler ARDS hastalarının prognozunu belirleyen farklı moleküler ve hücresel immün ve onarım mekanizmaları ile karakterizedir. ARDS hastaları için destekleyici bakım temel dayanak olmaya devam etmektedir; halen, ARDS için etkili bir farmakolojik tedavi yoktur, bu yüzden bu yıkıcı durum için yeni araştırmalara ihtiyaç duyulmaktadır[3].

Eksüdatif evrede doğuştan gelen immün yanıtın disregülasyonu ARDS'nin akut başlangıcına ve ilişkili solunum yetmezliğine katkıda bulunur[5]. Potent proinflamatuar mediyatör sinyal ilk bağışıklık yanıtlarını yönetir, alveolokapiller bariyer bozulmasına, diffüz alveoler ödeme ve hasarlanmış akciğer dokusuna nötrofil infiltrasyonuna yol açar[3]. ARDS'de, akut inflamasyon için inefektif frenleme sinyalleri akciğer yetmezliğine yatkınlık ve hasarlı akciğer dokusunun zamanında iyileşmesini geciktirebilir[5]. Gözlemsel çalışmalara göre aslında risk grubu hastalarının büyük kısmında ilk 72 saatte, hemen tamamında ise bir haftada ARDS gelişmektedir. Risk faktörleri nonspesifik ve çeşitlidir. Olguların %20'sinde ise hiç risk faktörü olmadan ARDS gelişebileceği bildirilmiştir[6].

Akciğer hasar mekanizmalarını modellemede hasara cevapta önemli farklılıklar saptanmaktadır.

Hasara immün cevapta türler arasında bazı değişiklikler vardır.

1. *Toll-like reseptör (TLR) farklılıkları;* insan ve faredeki TLR 4 farklı lipopolisakkarit (LPS) yapılarını tanımaktadır. Aynı zamanda TLR 2, 3, 7, 8 ve 9'da türler arasında değişiklik göstermektedir[7].

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