Bölüm 25

AKUT RESPİRATUAR DİSTRES SENDROMUNDA KİŞİSELLEŞTİRİLMİŞ TIBBA DOĞRU

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TANIM, İLİŞKİLİ KAVRAMLAR VE EPİDEMİYOLOJİ

Akut Respiratuar Distres Sendromu (ARDS), akut solunum yetersizliği, aşikâr hipoksi (PaO2/FIO2 oranı ≤ 300 mmHg) ve konjestif kalp yetersizliğiyle açıklanamayan iki taraflı akciğer infiltrasyonlarıyla karakterize etyolojik, radyolojik ve biyokimyasal açıdan oldukça heterojen bir kritik hastalıktır (1-3). Yaklaşık 50 yıl önce ilk kez ortaya konduktan sonra prognozu iyileştirme adına birçok medikal ve girişimsel tedavi denenmişse de olumlu sonuçlar elde edilememiştir (4). Özellikle Berlin tanımlaması (Tablo 1) yapıldıktan sonra hastalığa yönelik farkındalık artmış; bu çalışmada hipoksi derecesine göre yapılan sınıflamayı takiben hastalığa yol açan sebepler, ortaya çıkış süresi, radyolojik ve biyokimyasal özellikler göz önüne alınarak farklı sınıflamalar getirilmiştir (1,5). Çok uluslu LUNG-SAFE çalışmasında yoğun bakım hastalarının %10'unun tanı kıstaslarını karşıladığı saptanmıştır ve bu hasta grubunda mortalite halen %41,6 gibi yüksek bir oranda gözlenmiştir (6).

İlginçtir ki, ne ARDS'ye yol açan temel sebep ne de hipokseminin ciddiyeti klinik sonlanımlarla direkt ilişkilendirilememiştir. İleri yaş, malignite ve akciğer dışı organ yetersizliği gibi modifiye edilemeyen faktörlerin prognoz üzerine daha etkili olduğu saptanmıştır (7). Ayrıca sağ kalanlar arasında da kalıcı fiziksel, psikolojik ve nörokognitif sekellerin sık gözlendiğini unutmamak gerekir.

Tablo 1. Berlin ARDS tanımlaması

Zamanlama		ARDS'ye yol açan klinik olaydan sonra bir hafta içinde gözlenen yeni ya da kötüleşen solunumsal semptomlar
Görüntüleme		Akciğer kollapsı, efüzyon ya da kitle ile açıklanamayan bilateral opasiteler
Akciğer ödeminin sebebi		Hipervolemi ya da kalp yetersizliği ile açıklanamayan solunum yetersizliği
Oksijenizasyon	Hafif	PaO_2/FiO_2 ≤300 mmHg, >200 mmHg
	Orta	PaO_2/FiO_2 ≤200 mmHg, >100 mmHg, PEEP≥5 cm H_2O
	Ciddi	PaO_2/FiO_2 ≤100 mmHg, PEEP≥5 cm H_2O

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tipleme söz konusu olmadığından klasik ARDS ile kanıta dayalı yaklaşımların tedavi yönetimine uyarlanması şu an için en mantıklı seçenek olarak görülmektedir (127). Hastalık ciddiyetiyle ilişkili risk faktörleri yaş, immün yetersizlik, diabetes mellitus, obezite, erkek cinsiyet, nörokognitif bozukluklar ve diğer kronik hastalıklar olarak sıralanabilir (17).

Tedavi heterojenitesi düşündüren tek modalite kortikosteroid kullanımı olup; RECOVERY çalışmasında deksametazondan en çok fayda gören grubun mekanik ventilatörle solutulan ciddi ARDS olguları olduğu bildirilmiştir. Solunum yetersizliği olmayan olgularda ise tedavinin potansiyel olarak zararlı bile olabileceği belirtilmiştir (128). Biyolojik belirteçler anlamındaysa IL-6 ve sTNFR-1gibi bazı moleküller sub fenotipleri tanımlamada kullanılmaya çalışılmıştır ancak keskin eşik değerleri elde edilemediğinden gerçek anlamda bir sınıflamadan söz etmek mümkün değildir (129).

SARS CoV-2 virüsünün genomik ve fonksiyonel özellikleri gözetildiğinde tedavi hedefi olarak görülebilecek yapıtaşları spike (S) proteini, ana viral proteaz ve RNA-bağımlı RNA polimeraz olarak sayılabilir (127). Khan ve ark. çözünebilir ACE-2 tedavisinin COVID-19 ilişkili ARDS'de iyi tolere edildiğini ve bu molekülün viral bağlanmayı ve ACE-2 eksprese eden Vero E6 hücrelerinde replikasyonu inhibe ettiğini belirtmiştir (130).

SONUÇ

ARDS'de tedavi cevabının iyileştirilmesinde artık heterojenitenin tanımlanması, doğrulanması ve sadeleştirilmesinin önemi netleşmiş olup; çalışma tasarımlarının patofizyolojik mekanizmalar veya biyolojik farklılıklar üzerine kurgulanmış sub fenotipleri esas alması gerektiği aşikârdır. Bu anlamda kişiselleştirilmiş tedavi hedeflerine uygun olarak pre-klinik ve katmanlı klinik çalışmalarda ortaya konan aday tedavi modaliteleri, prediktif zenginleştirme ile seçilen örneklemlerde test edilmeye devam edildikçe daha yüz güldürücü sonuçlar elde edileceğini öngörmek mümkündür. Bu alanda kişiselleştirilmiş tıbbın geleceğini ise derin öğrenme ve makine öğrenmesi gibi yapay zekâ sistemlerinin etkin entegrasyonuyla solunumsal parametrelere göre minimal akciğer hasarı için kendini her bir solukta yeniden programlayabilen ventilatörler, biyolojik verilere göre düzenlenmiş direkt hedefe yönelik spesifik tedaviler oluşturmaktadır. Tıbbi teknolojinin ulaştığı noktada artık bu hedeflerin çok da uzak olmadığını söyleyebiliriz.

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