BÖLÜM 79

MİTOKONDRİYAL HASTALIKLAR

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GİRİŞ

Mitokondriyal hastalıklar, mitokondriyal fonksiyon bozukluğu ile karakterize bir grup genetik bozukluktur.[1] Mitokondri vücutta eritrosit dışında bütün hücrelerde bulunur ancak her hücredeki mitokondri sayısı değişkendir.[1] Vücutta başlıca enerji üretiminden sorumlu olan mitokondri kalp, iskelet kası gibi daha çok enerji gerektiren dokularda daha fazla sayıda bulunur.[2] Bu durum da klinikte daha çok enerji gerektiren dokularda daha fazla klinik bulgu gelişmesi şeklinde karşımıza çıkar.[2] Mitokondri, oksidatif fosforilasyon, yağ asit oksidasyonu, Kreb's döngüsü, üre döngüsü, glukoneogenez ve ketogenez gibi önemli yolakların yer aldığı bir organeldir.[1]

MİTOKONDRİ YAPISAL ÖZELLİKLERİ VE FONKSİYONLARI

Mitokondri tüm ökaryotik çekirdekli hücrelerde bulunan, çift membranlı bir organeldir.[2] Mitokondrinin görevleri kalsiyum homeostazı, demir-sülfür kümelerinin biyogenezi, apoptozis, oksidatif fosforilasyon üzerinden hücresel enerji (ATP) üretimidir.[2] Mitokondri, dış membran, iç membran, membranlar arası boşluk ve matriks kısımlarından oluşur.[3] İç membran yapısından oluşan kristalar, matrikse doğru çıkıntılar şeklinde uzanır ve enerji dönüştürülmesinden sorumlu oksidatif fosforilasyonun ve solunum zincir kompleks reaksiyonlarının gerçekleştiği esas kısmı oluşturur.[3] Şekil 1'de mitokondri kısımları ve solunum zincir kompleksi reaksiyonları şematik olarak gösterilmiştir.[4]

Solunum zinciri (kompleks I-IV) ve oksidatif fosforilasyon sistemi (kompleks I-V) iç mitokondriyal membranda yerleşmiş olup aerobik metabolizma sonucu ATP üretiminden sorumludur.[4] Piruvat, yağ asitleri ve Krebs döngüsündeki indirgen maddeler NADH ve FADH2 aracılığı ile solunum zincirine transfer edilir.[4]

MİTOKONDRİYAL GENETİK

Mitokondriyal hastalıkların patofizyolojisinde nükleer DNA (nDNA) mutasyonları ve mitokondriyal DNA (mtDNA) mutasyonları rol alır.[1] Bu bilgiden yola çıkarak mitokondriyal hastalıklarda kalıtımın her şekilde (otozomal dominant, otozomal resesif, X'e bağlı kalıtım, de novo mutasyonlar ve maternal kalıtım)

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Mitokondriyal hastalıklarda görülen akut inme benzeri atakların, özellikle m.3243A>G mutasyonu olan hastaların tedavisinde L-arginin tedavisinin etkin olduğunu gösteren çalışmalar mevcuttur.[61]

MNGİE hastalarında allojenik hematopoetik kök hücre naklinin etkinliğinin gösterildiği çalışmalar olsa da bu tedavi şekli yüksek mortalite ve morbiditeye sahiptir.[62,63] Yeni tedavi yaklaşımlarından timidin fosforilaz içeren eritrositlerin transfüzyonu MNGİE hastalarında deneysel aşamada olan bir tedavi şeklidir.[64]

Gen tedavileri de özellikle LHON ve MNGİE hastalarında deneysel aşamada olan diğer tedaviler arasındadır.[65,66]

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