



BÖLÜM 52

Dislipidemi Tedavisinde Antioksidan Etkili Tedaviler

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GİRİŞ

Nefes alıp verme, terapötik ajanların metabolizması, besinlerin sindirilmesi, lipidlerden enerji üretilmesi gibi insan vücudunda gerçekleşen biyolojik süreçler reaktif oksijen (ROS) ve reaktif nitrojen türleri (RNS) olarak bilinen zararlı bileşikler üretebilir. Bu ajanlar genellikle serbest radikaller ya da kolayca serbest radikaller üretebilen türlerdir. Düşük ve orta konsantrasyonlarda ROS'lar patojenik mikroorganizmalara karşı savunma gibi birçok biyolojik yolakta önemli rol oynarken, yüksek konsantrasyonlarda lipid, protein ve DNA hasarı oluşturarak normal hücre sinyal mekanizmalarını bozabilir (1). Ekzojen ve endojen serbest radikallerin oluşumu engellenemez bir süreç olup hem metabolik işlevler (hücre solunum) hem de çevresel oksidanların (ilaçlar, sigara dumanı, alkol kullanımı, ultraviyole radyasyon, hava kirliliği, yoğun fiziksel aktivite gibi) etkisi ile sürekli olarak üretilir.

Stres koşulları altında, ROS oluşumu antioksidan savunmaları alt eder;

böylece hücre bileşenlerinde geri dönüşümsüz değişiklikler ve oksidatif strese neden olan bir redoks dengesizliğine yol açar (2). Oksidatif stres, hücrel membranlar, proteinler, lipidler ve DNA

gibi yapılarda hasar oluşturan faktörlerin başında gelmektedir. Bu tür hasarlar nedeni ile hücre fonksiyonları bozulabilir, ikincil reaktif türleri ortaya çıkartabilecek hücrel yanıtlar oluşabilir ve hücre sağlığı tehlikeye girebilir.

“Antioksidan” (AO) terimi, oksijenin organizmalara neden olduğu hasarı yavaşlatan kimyasal maddeleri tanımlar. Antioksidanlar, oksidatif stresin olumsuz etkilerini dengeleyerek oksidatif hasara karşı korunmak için vücudun kullandığı mekanizmalardan biridir (3). AO'lar; vücudun kendisi tarafından üretilenler (endojen antioksidanlar) ve diyet kaynaklarından türetilenler (ekzojen antioksidanlar) olarak iki ana sınıfa ayrılabilir. Endojen AO'lar ise kendi aralarında enzimatik ve enzimatik olmayan antioksidanlar olarak ikiye ayrılır.

Oksidatif strese karşı esas savunma mekanizması, ROS'ları hücrel biyomoleküllere zarar vermeden ortamdan temizleyen enzimatik endojen antioksidanlardır. Hidrojen peroksidi (H_2O_2) su ve oksijene parçalayan katalaz (CAT), indirgenmiş glutatyon (GSH) ile H_2O_2 'nin indirgenmesini katalize edip başka bir glutatyon molekülü ile glutatyon köprüsü oluşturan (GSSG) glutatyon redüktaz (GRx), glutatyon peroksidaz (GPx) ve süperoksit anyon radikalının oksijen (O_2) ve hid-

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güvenlik ve biyoyararlanım çalışmaları da dahil olmak üzere bu alanda geniş çaplı ve uzun süreli verileri inceleyen klinik çalışmalara ihtiyaç duyulmaktadır. İn vivo, in vitro ve klinik deneylere dayanan testlerin sonuçlarına dayanarak, çeşitli antioksidanların obezite, dislipidemi ve diyabet gibi metabolik hastalıkların tedavisinde iyi bir potansiyele sahip olduğu öngörülmektedir. Ancak; uzun süreli kullanım, optimum doz ve güvenlik açısından daha fazla araştırmaya ihtiyaç duyulmaktadır.

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