İSKEMİ REPERFÜZYON HASARI

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BÖLÜM

Füsun BAYSAL

GİRİŞ

İskemi-reperfüzyon hasarı patofizyolojisinin iyi anlaşılmasının miyokardiyal hibernasyon, akut kalp yetmezliği, serebral disfonksiyon, gastrointestinal disfonksiyon, sistemik inflamatuar yanıt sendromu(SIRS) ve çoklu organ yetmezliği (MOD) gibi hekimler için önemli sorunlara yeni tedavi girişimlerinin geliştirilmesine imkan sağlayacağına inanıyoruz.[(1)] Bu derlemede, iskemi-reperfüzyon hasarının temel patofizyolojisinden, özellikle reaktif oksijen türlerinin ve hücre ölüm yollarının tutulumundan ve antioksidanlar üzerine odaklanan son gelişmelerden bahsedilecektir.

PATOFİZYOLOJİ

Arteryal kan akımında ki azalmaya bağlı oluşan iskemi hipoksiye ve mitokondrinin elektron transfer zincirinde fonksiyon bozulmasına öncülük eder. Mitokondrinin ATP üretimindeki düşüş anaerobik metabolizmayı, Na-K pompalarını ve ribozomların ayrılmasını uyarır. Anaerobik metabolizmaya bağlı olarak ATP ve antioksidanların az üretilmesi laktik asid retansiyonu ve metabolik asidoz ile sonuçlanır. Hücre zarındaki Na^+-K^+-ATP, Na–H ve kalsiyum pompalarının bozulması; hücre içinde sodyum, hidrojen ve kalsiyum birikmesine neden olur ki bu da hiperosmolariteyi arttırarak hücre içine su girişi ve hücre şişmesi ile sonuçlanır. Hidrojen retansiyonu da hücre PH'ını düşürerek enzim salınmasına ve nükleer kromotin kümelenmesine neden olur. Ribozomlardaki ayrılma, protein sentezini azaltır. Reperfüzyon aşamasıyla iskemik dokuya kan akışıyla oksijenizasyon sağlanır. İskemik dokudaki antioksidan ajanların düşük konsantrasyonlarına bağlı serbest oksijen radikalleri oluşumu artar. Serbest oksijen radikallerine bağlı oluşan oksidatif stres; endotelyal disfonksiyon, DNA hasarı ve lokal inflamatuar yanıt oluşmasıyla sonuçlanır. İnflamatuar kaskad ve oksidatif stres sitokin fırtınasına bağlı hücre yapısındaki hasar ve hücre ölümüyle sonuçlanabilir [(2)].(şekil-1)

OKSİDATİF STRESİN İSKEMİ REPERFÜZYON HASARINDA Kİ YERİ:

Oksidatif stres enzimatik yada enzimatik olmayan yollardan gelişebilir. En bilinen enzimatik kaynaklar ksantin oksidaz, NADPH oksidaz, mitokondriyal elektron transfer zinciri ve nitrik oksit sentazdır (NOS). Ksantin oksidaz, NADPH oksidaz, ve mitokondriyal elektron transfer zinciri, barsaklar akciğer, kalp, beyin, kas, mide, lendirebilir. Renal IR yaralanmasının yeni tanı biyolojik belirteçlerini temsil edebilirler[103]

Diyabetik böbrek, artmış oksidatif stres ve bozulmuş nükleer faktör eritroid 2 ile ilişkili faktör 2 (Nrf2)/heme oksijenaz-1 (HO-1) sinyalizasyonu ile ilişkili iskemi/reperfüzyon (I/R) yaralanmasına daha duyarlıdır.[102]

Sonuç

Şu anda, MI hastalarının I/R yaralanmasına karşı önlem olarak soğutulması, soğutma birkaç potansiyel reperfüzyon yaralanma yolunu değiştirdiğinden miyokard kurtarma için en büyük potansiyele sahip görünmektedir. Bu devam eden çabalar başarısız olursa, daha fazla müdahaleyi dahil etmeye cesaret eden adaptif tasarıma sahip daha büyük denemeler ileriye doğru olmalıdır.

Anahtar Kelimeler: iskemi, reperfüzyon,antioksidanlar

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