KRONİK OBSTRÜKTİF AKCİĞER HASTALIĞINDA DENEY HAYVANI MODELLERİ

14 BÖLÜM

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Kronik obstrüktif akciğer hastalığı (KOAH) tüm dünyada morbidite ve mortalitenin önemli bir nedenidir ve kronik solunum yolu enflamasyonu, mukus hipersekresyonu, hava yolu yeniden şekillenmesi ve amfizem ile karakterizedir. Akciğer fonksiyonlarında azalmaya ve nefes darlığında artmaya neden olur [1-4]. KOAH gelişimi yavaş ve ilerleyicidir. Bazen Bakteriler veya virüsler gibi maddelerin tetiklemesiyle indüklenen inflamatuar yanıtların neden olduğu alevlenmeler olur [2].

KOAH için etkili bir tedavi yoktur, çünkü KOAH'ın altında yatan mekanizmalar moleküler düzeyde tam olarak anlaşılamamıştır. Belirli bir zaman diliminde hastalığın ayırt edici özelliklerini yeniden özetleyen küçük hayvan modelinin olmaması, KOAH çalışmasında önemli bir sınırlayıcı faktördür [1]. Bununla birlikte, hayvan deneyleri, solunum yollarını ve akciğerleri etkileyen tüm kronik hastalıkların tedavisi için yaklaşımlar sağlamaya devam etmektedir [5].

Hayvan modelleri kronik obstrüktif akciğer hastalığını incelemek için kullanılır [6], inflamatuar süreçleri araştırır [7] ve KOAH'ın temel mekanizmalarını belirler [8]. Kemirgenler, köpekler, kobaylar, maymunlar ve koyunlar da dahil olmak üzere birçok KOAH modeli kullanılmıştır [8], ancak uygun bir model çalışmanın amaçlarına bağlıdır [9].

KOAH'ın hayvan modellerinin farklı indüksiyon yöntemleri, bu amaç için kullanılan farklı hayvanlar ve çeşitli ölçülen parametreler bu makalede kapsamlı bir şekilde gözden geçirilmiştir. Bu nedenle, bu derleme araştırmacıların bir KOAH hayvan modelinin indüksiyonu için uygun bir yöntem seçmelerine ve çalışma tasarımlarına dayanarak bilgilendirici değişkenleri ölçmelerine yardımcı olacaktır.

ÇEŞİTLİ HAYVAN MODELLERİNDE KOAH İNDÜKLEYİCİLERİ

Hayvan modellerinde KOAH'ı taklit etmek için farklı yaklaşımlar vardır [10]. Bu yaklaşımlar laboratuvar hayvanlarını Sigara kullanımı (KOAH için birincil etiyolojik faktör), inflamatuar uyaranlar (örn. LPS), proteolitik enzimler (örn., Elastaz) ve genetik modifikasyona maruz bırakmayı içerir [7, 11]. Bu bölümde, çeşitli hayvanlarda kullanılan farklı KOAH indükleyicileri gözden geçirilmektedir

Sigara dumanı (CS)

Tütün kullanımı KOAH için en önemli risk faktörüdür [2, 4] in vivo çalışmalarda kullanılan en yaygın KOAH indükleyicisidir [12].

yolu duvarı inflamasyonu [10, 110] ve amfizemile akciğer elastik geri tepmesi kaybının [1, 10, 111, 112] bir kombinasyonunun sonucu olabilir. Amfizem ve küçük hava yolu remodelingi gibi akciğerin yapısal değişiklikleri KOAH'ın patolojik özellikleridir [113]. KOAH'ta küçük hava yolu yeniden şekillenmesi, alt epitelyal fibroz, mukus hücre hiperplazisi ve bazı durumlarda hava yolu düz kas (ASM) kitlesini arttırır [9, 113-117]. Ek olarak, hava yolu duvarındaki makrofajlar, nötrofiller, T ve B-lenfositler gibi enflamatuar hücrelerin sürekli infiltrasyonu, hava yolu duvarının yapısal hücrelerinin CS ve LPS'ye maruz kalmasının doğrudan neden olabileceği hava yolu yeniden modellenmesinin [115-117] özellikleridir ve inflamasyondan bağımsız [9].

Trakeal cevap verebilirlik (TR)

Havayolu aşırı duyarlılığı (AHR), KOAH'ta da bulunan astımın temel özelliğidir [54]. Ayrıca, farklı astımlara trakeal cevap (TR) sadece astımlı hayvanlarda değil, aynı zamanda CS'ye maruz kalan hayvanlarda da gözlenmektedir [118-119]. Bu parametre in vivo veya in vitro olarak bazı KOAH hayvan modellerinde değerlendirildi.

TR'nin in vivo ölçümü

TR'nin in vivo değerlendirilmesi genellikle artan metakolin (Mch) aerosol dozlarının teneffüs edilmesinden sonra herkesin pletismografı kullanılarak gelişmiş duraklama (Penh) ölçümü ile incelenmiştir [31].

İnflamatuar hücreler ve aracılar

Toplam ve diferansiyel beyaz kan hücresi (WBC) sayıları Nötrofiller, makrofajlar, CD8-Lenfositler ve eozinofiller (KOAH'ın akut alevlenmelerinde önemli bir rol oynayabilir) dahil olmak üzere KOAH'ın patofizyolojisinde çeşitli hücre tipleri yer alır. Doku yıkımını ve kronik iltihaplanmayı düzenleyebilen birkaç inflamatuar aracı ve doku parçalayıcı enzimler salgılarlar [10, 104, 130-135].

İnflamatuar aracılar ve sitokinler

KOAH patogenezinde birkaç enflamatuar aracı vardır [10, 138]. Örneğin, makrofajlar, interlökin 8 (IL8), tümör nekroz faktörü alfa (TNF-a), lökotrien B4 (LTB4) [120, 121], reaktif oksijen türleri (ROS), monosit kemotaktik protein 1 (MCP- 1) ve CS ve diğer uyaranlara yanıt olarak matris metaloproteinaz (MMP-2, MMP-9, MMP-12) ve katepsin K, L ve S gibi elastolitik enzimler [122]. Ayrıca nötrofiller, serin proteazların (nötrofil elastaz, katepsin G, proteinaz) ve metalloelastaz MMP-8 ve MMP9'un salgılanmasıyla KOAH patogenezine açıkça katkıda bulunur [135, 122]. Ek olarak, bir Th2 sitokini olan IL-13'ün KOAH patofizyolojisinde rol oynadığı ileri sürülmüştür [10, 123].

Sonuç

Hayvanlarda KOAH üzerine bir çalışmanın yapılabileceği birçok yöntem çeşitliliği vardır. Bu nedenle, değerlendirilecek parametreleri ve izlenecek prosedürleri (örneğin maruz kalma prosedürü) tanımlayan standart bir protokole ihtiyaç vardır.

Bir hayvanın gelişimi için KOAH model temsilcisi, KOAH indüksiyon yöntemleri, değerlendirme parametreleri ve insan KOAH özellikleri değerlendirilmelidir. Bu derlemede, farklı hayvanlarda deneysel KOAH modellerinin indüksiyonu, bu amaç için kullanılan çeşitli yöntemler ve ölçülmesi gereken farklı parametreler hakkında bilgi verilmiştir. Bu temel bilgiler, gelecekte KOAH üzerine yapılacak araştırmalarda uygun çalışmalar tasarlamak için değerlidir.

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