BÖLÜM 44

HAYVAN DENEYLERİNDE GÖZ MODELLERİ

Doç. Dr. H. Tuba ATALAY[1]
Uzm. Dr. Serdar BAYRAKTAR[2]

Oftalmolojik hastalıklara neden olan risk faktörlerinin belirlenmesi, fizyopatolojide yer alan mekanizmaların aydınlatılması ve belirli bir tedavi protokolünün insanlar için güvenli ve etkili olup olmayacağının anlaşılması için, çeşitli hayvan modelleri kullanılarak birçok deneysel çalışma yapılmaktadır (1). Planlanan deneysel çalışmaların doğru sonuçlar vermesi ve klinik uygulamalarda yol gösterici olması için üzerinde durulması gereken en önemli nokta, kullanılacak modelin istenen amaca uygun olmasıdır. Bu nedenle deneysel hayvan çalışmaları planlanırken insan gözünün anatomisi ve fizyolojisine en yakın benzerliğe sahip hayvanların denek olarak seçilmesine dikkat edilmelidir (2). Üzerinde çalışılan hastalığın doğal olarak geliştiği hayvanların denek olarak kullanılması, fizyopatolojik sürecin daha iyi anlaşılmasına neden olur. Ancak bu koşulu sağlamak her zaman mümkün değildir.

İnsan göz hastalıklarının incelenmesi için çeşitli kemirgenler (fareler, ratlar ve kobaylar), memeliler (tavşanlar, köpekler ve primatlar), omurgasızlar (meyve sinekleri ve nematodlar) ve zebra balığı modelleri geliştirilmiştir. Bu modellerden en yaygın olarak kullanılanı faredir. Çünkü fare gözü yapısal olarak insan gözüne benzer ve insanlardaki birçok oküler bozukluk farelerde de gözlenir. Ayrıca insan ve fare genomları, kodlama bölgelerinde önemli bir deoksiribonükleik asit (DNA) dizi homolojisi sergiler. Böylece glokom ve yaşa bağlı makula dejenerasyonu

[1] Doç. Dr., Gazi Üniversitesi Tıp Fakültesi, Göz Hastalıkları AD. E-posta: tubaatalay@gazi.edu.tr, ORCID iD: 0000-0002-1847-615X
[2] Uzm. Dr., Ankara Etlik Şehir Hastanesi, Göz Hastalıkları AD. E-posta: drsbayraktar@yahoo.com, ORCID iD: 0000-0001-6521-9984

fare sınıfı II moleküllerinin silindiği ve insan muadilleriyle değiştirildiği HLA sınıf II transgenik farelerde retina antijeni ile aşılama yoluyla da indüklenebilir. HLA-DR3, HLA-DR4, HLA-DQ6 veya HLA-DQ8 transgenik fareler, bu sınıf II molekülleri taşıyan insanlar tarafından tanınabilecek antijenik epitoplar sunar ve bunlara yanıt verir (85). HLA-Tg fareleri, yalnızca IRBP ile değil, S-Ag ile aşılandıklarında da şiddetli üveit geliştirir. MHC sınıf II molekülleri antijen tanımada yer aldığından, HLA sınıf II Tg fareleri, insan hastalığına karışan retinal antijenlerin kritik bölgelerini belirlemeye yardımcı olabilir ve insan üveiti için antijene özgü tedaviler bulmak için önemli olabilir (81,85).

Prematüre Retinopatisi

Yenidoğanlarda prematüre retinopatisini (ROP) incelemek için geliştirilen "oksijenin neden olduğu retinopati modeli" ilk olarak Smith laboratuvarı tarafından kullanılmıştır (88). Bu modelde, doğum sonrası 7. gün hayvanlar (P7) 5 gün boyunca yüksek kısmi oksijen basıncına (~ %75 oksijen) maruz bırakılır, bunun ardından normal retina damar gelişimi durur ve VEGF azalmasına bağlı olarak merkezi retinada bulunan intraretinal kılcal damarlar dejenere olur. Hayvanlar daha sonra yüksek oksijen ortamından normal atmosferik koşullara (% 21 oksijen) çıkarılır, ardından yetersiz kan ve oksijen kaynağı nedeniyle retina şiddetli iskemiye maruz kalır ve retina öncesi neovaskülarizasyon meydana gelir (88). Retinal hipoksi, PDR gibi iskemik retinopatilerin bir özelliğidir ve oksijene bağlı retinopati modeli, bu durumu makulada oldukça belirgin bir şekilde sağlar (65). Retinada glia ve nöronların oksijen yoksunluğu, oksijene bağlı retinopatide pro-anjiyogenik büyüme faktörü ekspresyonunu yönlendirir ve ortaya çıkan neovasküler model vazojenik ajanların değerlendirilmesinde yaygın olarak kullanılmaktadır (65) .

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