12.
BÖLÜM

PULMONER HİPERTANSİYON HAYVAN MODELLERİ

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Pulmoner hipertansiyon (PH) kronik ve ilerleyici hem kalbi hem de akciğeri beraber etkileyen bir hastalıktır. Tanımı ilk kez 1865 yılında A. Ayerza tarafından "pulmoner vasküler skleroz" olarak yapılmış olup o zamanlarda "Ayerza Hastalığı" olarak da isimlendirilmiştir. Devam eden süreçte hastalığın bazı nedenleri saptanmış olup bu grup "sekonder pulmoner hipertansiyon" olarak isimlendirilmiştir. Herhangi bir nedenin saptanamadığı grup ise "primer pulmoner hipertansiyon" olarak isimlendirilmiştir. Hastalığın fizyopatolojisi son 25 yılda aydınlatılmış olup, bundan dolayı hastalığın sınıflamasında değişikler olmuş, tanı ve tedavisinde birçok ilerleme gösterilmiştir. İlk modern sınıflama 1998 yılında yapılmış olup tanı ve tedavi kılavuzu da bunu takiben yayınlanmıştır. Bundan sonra yapılan tüm sınıflamalarda amaç hastalığa neden olan durumların ortak fizyopatolojik özelliklerini ve ortak klinik bulgularını kullanarak bir gruplama yapmak olmuştur.

Sağlıklı bireylerde ortalama pulmoner arter basınçdeğeri (oPAB) dinlenme konumunda 11 ile 17 mmHg aralığında, normalin üst sınır değeri ise 20 mmHg olduğunu göstermektedir (1,2). Sağ kalp kateterizasyonu yapılması sonucunda oPAB'nin 25 mmHg üzerinde saptanması Pulmoner Arteryel Hipertansiyon (PAH) olarak kabul edilir (1). Pulmoner arter basıncında meydana gelen yükselme ya prekapiller ya da postkapiller hastalıklar sebebiyle meydana gelir. PH'da hangi bölümün etkilendiğinin saptanması ve hangi gruba (Dana Point) girdiğinin belirlenmesi için pulmoner kapiller uç basınç ve kalp debisi mutlaka ölçülmelidir (3). Dana point sınıflaması daha sonra Simonneau ve arkadaşları tarafından güncellenmişve tablo 2 de gösterilmiştir (3). Global düzeyde, literatürde PH insidansına yönelik veri yeterli seviyede değildir. İngiltere'de PH prevelansının milyonda 97, kadın/erkek PH oranının ise 1,8 olduğu bildirilmiştir

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fan hidroksilaz-1 enzimi tarafından sentezlenir (102). PASMC' ların hipoksiye maruz kalması, 5-HTT ekspresyonunda ve aktivitesinde hızlı bir artışa neden olur. Buda PASMC'lardahipertrofiye neden olur (103). Aynı zamanda idiyopatik PH'ı bulunan hastaların PASMC'larında 5-HTT ekspresyonunun arttığı saptanmıştır (101). Maclean ve arkadaşları yaptığı çalışmada, 5-HTT'yi over eksprese eden fareler KHP'ye maruz bırakılmış ve bunun sonucunda farelerde RVH ve pulmoner vasküler remodeling saptanmıştır (101). Bu modelde yapılan çalışmalar sonucunda, 5-HTT inhibitörlerinin (fluoksetin vb.) PH tedavisinde yerinin araştırılmasına başlanmıştır (104). 2009 yılında Zhu ve arkadaşları fluoksetin tedavisinin MCT modelinde PH'yı önlediğini ve uzun süreli sağkalıma katkıda bulunduğunu gösterdi (105). 5-HT reseptör antagonisti birçok ilaç hem hücre kültüründe hem de hayvan modellerinde test edilmiş ve başarılı olmuştur (105). Ancak yine bu modelin daha da geliştirilmeye ihtiyacı vardır.

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