Alican BARIŞ

GİRİŞ

Düşük kemik mineral yoğunluğu (KMY) ve yüksek osteoporotik kırık riski ile karakterize olan osteoporoz dünya genelinde en yaygın görülen kemik hastalığıdır. Osteoporozda kemik yapım ve yıkım arasındaki denge bozulmuştur. Yıkım lehinde işleyen bir süreç ortaya çıkmıştır (Şekil-1). Dünya Sağlık Örgütü'ne (DSÖ) göre genç sağlıklı kadınlar için ölçülen kemik mineral yoğunluğu (T skoru) değerinden -2.5 veya daha düşük standart sapma değerleri osteoporoz olarak tanımlanmaktadır. Aynı tanıma göre -1'den yüksek değerler normal KMY, -1 ile -2.5 arasındaki değerler ise osteopeni olarak kabul edilmektedir [1, 2]. Sık görülen osteoporotik kırıkların yüksek maliyetli tedavileri nedeniyle bu hastalığın dünya nüfusunun geneline ekonomik ve sosyal büyük etkileri vardır [3]. İki yüz milyondan fazla insanın osteoporotik olduğu tahmin edilmektedir. Artan yaşam süresi ile beraber bu sayının 2040 yılı civarında ikiye katlanması beklenmektedir [4].

Osteoporozun birçok nedeni vardır. Postmenopozal östrojen hormonunda azalma, ileri yaş, uzun süreli immobilizasyon, yerçekimsiz ortam, kronik hastalıklar ve bazı ilaçların kullanımı bunlardan bazılarıdır [6, 7]. Nedenleri farklı olsa
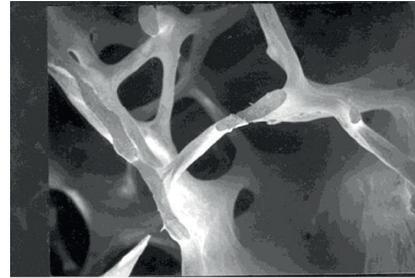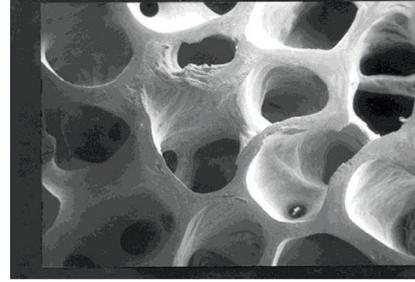
Şekil 1: Normal ve osteoporotik kemiğin mikrografik görüntüleri [5]

da sonuçta osteoporoz iskelet sisteminin fizyolojik dengesinin bozulmasıyla neticelenmektedir. Bu dengesizliğin altında yatan süreçler ve mekanizmalar hala tam olarak aydınlatılamamıştır. Hastalık ile ilgili kemiğin davranışını daha iyi anlamak, potansiyel tıbbi tedavileri ve bu tedavilere kemiğin cevabını incelemek, osteoporotik kırık ve onarım süreçlerini anlamak için birçok

grubu, diyabet + ovariektomi (D+O), diyabet + ovariektomi + alendronat (D+O+A), diyabet + ovariektomi + raloksifen (D+O+R) olmak üzere beş sıçan grubu oluşturulmuştur. Bu gruplarda, osteokalsin ve tip I kollajenin C-telopeptidi (CTX-1) gibi kemik döngüsünün serumdaki biyokimyasal belirteçleri analiz edilmiştir. Ayrıca dördüncü lomber vertebra histomorfometrik parametreleri ve mikro-BT ile kemik mineral yoğunluğu değerlendirilmiştir. Kompresyon (sıkıştırma) testi ile vertebra mekanik gücü test edilmiştir. Diyabet ve D+O gruplarında 8. haftada osteokalsin düzeyinin kontrol grubu ile kıyaslandığında önemli ölçüde azaldığı görülmüştür. Çalışmanın 12. haftasında D+O+A ve D+O+R gruplarında serum CTX-1 düzeyinin D+O grubu ile kıyaslandığında önemli ölçüde azaldığı, osteokalsin düzeylerinde ise farklılık olmadığı gözlenmiştir. Ayrıca alendronat ve raloksifen tedavisi alan gruplarda KMY ve kemik mekanik gücünün diğer diyabetik gruplara göre anlamlı derecede arttığı görülmüştür. Sonuç olarak hem bifosfonatların hem de SERM'lerin diyabetin eşlik ettiği postmenopoazal osteoporozda antirezorptif etkileri ile kemik yıkımını azalttıkları, kemik gücünde önemli iyileştirme yaptıkları kanıtlanmıştır [64].

Sonuç

Osteoporozun demografik değişimlere bağlı olarak gelecekte daha çok insanı etkileyeceği tahmin edilmektedir. Bu kritik hastalığın patofizyolojisinin tam olarak aydınlatılamaması ve tedavi seçeneklerinin tatmin edici bir şekilde çözüme kavuşturulamaması nedeniyle osteoporoz araştırmalarına hala büyük oranda ihtiyaç duyulmaktadır. Bu araştırmaların "olmazsa olmazı" deneysel hayvan modelleridir. Bu modellerdeki en önemli sorun insanın durumu ile tam olarak karşılaştırılabilir bir osteoporoz modelinin oluşturulamamasıdır. Uygun model seçimi yapılırken hayvanın ömrü, kemik remodeling türü, hayvanın tepe kemik kütle yaşı ve deneysel manipülasyona uyarlabilirliğinin yanı sıra ekonomik, etik, yasal konuların da dikkate alınması gerekir.

Anahtar Kelimeler: Osteoporoz, kemik mineral yoğunluğu, deneysel hayvan modelleri

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