

# HİPERTANSİYON ve BÖBREK HASTALIKLARI

## ÇALIŞMA ve DERLEMELER

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ISBN  
978-605-258-793-5

Sayfa ve Kapak Tasarımı  
Akademisyen Dizgi Ünitesi

**Kitap Adı**  
Hipertansiyon ve Böbrek Hastalıkları  
Çalışma ve Derlemeler

**Yayıncı Sertifika No**  
25465

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**Baskı ve Cilt**  
Göktuğ Ofset

**Bisac Code**  
MED055000

**Yayın Koordinatörü**  
Yasin DİLMEN

**DOI**  
10.37609/akya.511

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Kitabın basımını ve okuyuculara ulaşımını sağlayan Türk Hipertansiyon ve Böbrek Hastalıkları Derneği Yönetim Kuruluna, kitabın oluşturulmasında emeği geçen yazar kadrosuna ve kitabın basım işini gerçekleştiren Akademisyen Kitabevi’ne teşekkür ediyoruz.

Saygılarımızla

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Literatürde hemodiyaliz ve periton diyalizi hastalarında osteoporoz sıklığını araştıran çok fazla yayın bulunmamaktadır. Evre 5D KBH'lılarda anti-osteoporotik tedaviler ile ilgili de yeteri kadar veri bulunmamaktadır.  $\beta$ B eskiden hipertansiyon tedavisi için major beş ilaç gurubundan biri olarak sayılırlarken günümüzde kullanım alanı daha çok koroner arter hastalığı ve eşlik eden hipertansiyon olarak kabul edilmektedir. Çalışmamızın retrospektif dizaynı osteoporoz ve  $\beta$ B ajanlar arasında bir neden-sonuç ilişkisi kurmamızı engellese de diyaliz hastalarında anti-hipertansif ilaç verileceği zaman  $\beta$ B'lerin kemik metabolizması üzerine de olumlu etkileri olabileceği akıldta tutulabilir.

Sonuç olarak çalışmamızda  $\beta$ B kullanan diyaliz hastalarında kullanmayanlara göre osteoporozun daha az görüldüğü tespit edilmiştir. Çalışmamızın retrospektif dizaynı, hasta sayısının az olması,  $\beta$ B kullanım süresinin ve dozlarının bilinmemesi ve  $\beta$ B ilaçlarının selektivitesinin değerlendirilmemiş olması kısıtlılıkları olarak sayılabilir. Ancak bu alana çok fazla yayın bulunmaması ve çalışmamızın diyaliz hastalarında  $\beta$ B kullanımı ile osteoporoz sıklığını araştıran ilk çalışma olması önem taşımaktadır.  $\beta$ B ilaçların diyaliz hastalarında kemik metabolizması üzerine etkilerini araştıran kapsamlı prospektif çalışmalara ihtiyaç vardır.

## KAYNAKLAR

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çalışmalar olsa da sonuçlar ülkeler arasında, hatta nakil merkezleri arasında da farklı sonuçlanabilmektedir. Donör olmayan kontrol grupları ile yapılan çalışmalarda da sonuçlar farklı çıkabilmektedir. Merkezimizde canlıdan nakillerin çoğunluğu akraba ilişkili olduğundan genetik faktörleri ve azalan böbrek kütlesini gözönünde bulundurarak donör güvenliğini adına daha büyük ölçekli çalışmalara halen ihtiyaç vardır.

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## TARTIŞMA

Çalışmamızın en önemli bulgusu; OPG seviyeleri bakımından hipertansif hastalar ile kontrol grubu ve dipper ile non-dipper grup arasında anlamlı bir fark bulunmaması ve OPG ile PWV arasında bir ilişki olmamasıdır. Literatürde OPG ve PWV arasındaki ilişkiyi araştıran çalışmalar bulunmakla birlikte bilgilerimize göre, OPG ile kan basıncı profili arasındaki ilişkiyi araştıran sadece bir çalışma vardır. Wang ve arkadaşlarının 106 hipertansif hasta ile 78 sağlıklı bireyden oluşan kontrol grubunda yaptıkları çalışmada; iki grup arasında karotiko-femoral PWV ve osteoprotegerin düzeyi arasında anlamlı fark bulunamamıştır. Aynı çalışmada osteoprotegerin düzeyinin 10'luk tabanda logaritmik dönüşüm yapılmış, log-OPG ile PWV arasında anlamlı farklılık olduğu görülmüştür. Kim ve arkadaşlarının 49 diyabetli ve 72 diyabeti olmayan hasta da yaptıkları çalışmada da, serum OPG düzeyi ile PWV arasında diyabetlilerde pozitif yönde bir ilişki bulmuşlardır. Yapılan çalışmaların birçoğunda hipertansiyon ile PWV arasında pozitif yönlü ilişki bulunmuştur. Wang ve ark'nın yaptığı çalışmada hipertansiyon ile c-f PWV arasında anlamlı ilişki bulunamamıştır. Bizim çalışmamızda hipertansiyon ile 24 saatlik ortalama PWV arasında pozitif yönde kuvvetli ilişki olduğu gösterilmiştir. Bu konuda daha fazla sayıda hasta içeren yeni çalışmalara ihtiyaç vardır. Sonuç olarak çalışmamızda; arteriyel sertlik ile yüksek kan basıncı arasında ilişki bulunurken, arteriyel sertlik ile kan basıncı profili arasında bir ilişki tesbit edilemedi. Ayrıca OPG ile kan basıncı ve kan basıncı profili arasında bir ilişki gözlenmedi. Bu konuda, daha fazla sayıda hasta içeren gruplarla yapılacak çalışmalara ihtiyaç olduğu kanaatindeyiz.

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pauci-immün glomerülonefrit, amiloidoz ve hafif zincir nefropati gibi paraprotein ilişkili hastalıklar ve ateroembolik böbrek hastalığı bulunur. Membranöz glomerülonefrit ve minimal değişiklik hastalığının sıklığı çoğunlukla 6. ila 7. dekatta artmaktadır. Nefrotik sendromun nedenleri arasında hem membranöz glomerülonefrit hem de minimal değişiklik hastalığı, yaşlılarda tedaviye iyi yanıt verir. Biz de çalışmamızda membranöz glomerülonefritin 65 yaş ve üstü hastalarda en sık primer glomerülonefrit olduğunu göstermiş olduk. Çalışmamızda yaşlı hastalarda kresentik glomerülonefrit ve paraprotein ile ilgili hastalıkların benzer yayınlara paralel olarak artmış sıklığını göstermiş olduk. Bu bulguları doğrulamak ve geliştirmek için daha geniş bir hasta popülasyonunda, karşılaştırmalı daha fazla araştırma gereklidir.

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anemi tedavisi ve yeterli diyaliz önemlidir. Sigarayı bırakmak, yürüyüş yapmak ve aerobik egzersiz yapmak gibi yaşam stilineki değişiklikler, depresyonu azaltarak ve vücut imajını geliştirerek cinsellik üzerine pozitif etki yapabilir. Çalışmalar incelendiğinde, HSDD'nin DM ve KBY hastası kadınlarda en sık gözlenen cinsel problem olduğu gösterilmiştir.

Sonuç olarak böbrek nakli HSDD'yi düzeltmektedir. Çalışmamız, böbrek replasman tedavisi veya kronik böbrek hastalığı tanısından sonra HD ve PreD gruplarının cinsel işlev bozukluğunda anlamlı bir artış olduğunu göstermiştir. Transplantasyonun, cinsel işlev bozukluğu üzerindeki gerçek etkisini anlamak için ileri çalışmalara ihtiyaç vardır.

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yüksek olmadığı görülmüştür. Bu noktalar da bize tedavinin erken uygulanması ile yanıt alınma şansının daha fazla olduğunu düşündürmektedir. Literatürde membranöz nefropatide ofatumumab kullanımına dair bir yayın bulunmamakla birlikte, MN'de Anti-CD20 tedavilerin başarısı bilinmektedir. Biz hastamızda alerjik reaksiyon nedeniyle rituksimab tedavisi kullanamamış olmamız nedeniyle ofatumumab tedavisi vermeyi planladık. Tedavi vermeden önce öngördüğümüz gibi hastada herhangi bir çapraz alerji gelişmemiş olsa da ne yazık ki tedavi açısından hastadan aldığımız sonuçlar olumlu değildir. Burda da tedavi başarısızlığını hastada gelişmiş olan GFR kaybı ve fibrozise bağlayabiliriz. Önceki dönemde B hücre supresyonunun MN hastalığındaki etkinliğini anlatan yayınlarda da tübülointerstisyel fibrozis gelişmiş hastalarda yanıtların zayıf olabileceği ve veya hiç olmayacağının belirtilmiş olması da bu düşüncemizi desteklemektedir.

Sonuç olarak, her ne kadar biz kendi hastalarımızda yüz güldürücü sonuçlar alamamış olsak da literatüre baktığımız zaman ofatumumab'ın tedaviye dirençli nefrotik sendromlarda olumlu sonuçlar verdiğini görmek mümkündür. Henüz GFR kaybının ve fibrozisin başlamamış olduğu geniş hasta gruplarında uygun dozda verildiğinde, prognozun son derece kötü olduğunu bildiğimiz bu hastalık grubunda alternatif bir tedavi olanağı olacağını halen düşünmekteyiz. Daha geniş hasta gruplarıyla yapılacak prospektif çalışmalar bu konuda daha detaylı bilgiler verecektir.

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yapılmıştır. BK virüs nefropatili 41 hastanın değerlendirildiği bir çalışmada kalsinörin inhibitör dozunun azaltılması sonucunda renal fonksiyonlarda belirgin iyileşme bildirilmiştir. BK virüs nefropatisinde, özellikle everolimus'un antiviral etkinliği nedeniyle etkili olabileceği bildirilmektedir. Polanco ve arkadaşları posttransplant ortalama 7.ayda BK virüs nefropatisi tespit edilen 9 hastada antimetaboliti kesmiş, takrolimustan everolimusa geçmiş ve takip sonunda tüm hastalarda BK virüs titrelerinde belirgin azalma ve kreatininde düşme, 5 hastada ortalama 26 ayda BK virüsün negatifleştiğini tespit etmişlerdir. Biz de kliniğimizde BK virüs tespit ettiğimiz hastalarda antimetabolit tedavisini keserek devam ettiğimiz farklı immünsupresif tedavi protokollerinin etkilerini değerlendirdik. Çalışmamızda takrolimus+everolimus+prednizolon grubu, everolimus+prednizolon grubu ve takrolimus+prednizolon grubu olmak üzere oluşturulan 3 grubun BK virüs titrelerinde belirgin azalma sağladığını fakat üç grup arasında titredeki bu azalma açısından istatistiksel anlamlı fark olmadığını ve tedaviye everolimusun eklenmesinin ek bir düzelme sağlamadığını tespit ettik.

İmmünsupresyonun azaltılmasıyla birlikte sıklıkla BK virüs titrelerinde azalma görülür fakat rejeksiyon riski de artar. BK virüs varlığında, histolojik olarak akut hücrel rejeksiyon ve BK virüs nefropatisinin ayırıcı tanısını yapmak zor olabilir. Hirsch ve arkadaşları BK replikasyonu olmayan alanlarda tübüler HLA-DR ekspresyonu, lenfositik infiltrat ve belirgin tübülit bulunmasının hücrel rejeksiyonu destekleyebileceğini bildirmişlerdir. Akut rejeksiyon varlığında öncelikle rejeksiyon tedavi edilir ve ardından BK virüs tedavisine devam edilir. Çalışmamızda ise hiçbir hastada akut rejeksiyon gelişmemiştir.

Sonuç olarak, BK virüs nefropatisi greft kaybının önemli bir sebebidir. BK virüsün posttransplant ilk aylardan itibaren takibinin yapılması ve pozitifliği saptandığında mikofenolik asit içeren immünsupresif tedavinin kesilmesi gerekir.

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Sonuç olarak, çalışmamızda tip 2 DM hastalarında sağlıklı bireylere göre düşük serum ÜT II düzeyleri gözlemlendi. ÜT II ile renal fonksiyon bozukluğu ve proteinüri arasında anlamlı ilişkinin olduğu bulundu. ÜT II ile SVH arasında anlamlı ilişkinin olmadığı gözlemlendi. Tip 2 DM hastalarında yüksek serum ÜT II düzeyleri olumsuz renal olayların gelişiminin değerlendirildiği bir belirteç olarak kullanılabilir. Buna rağmen Tip 2 DM hastalarında serum ÜT II ile olumsuz KV olaylar arasında ilişki yoktur. Bu konuda yapılan çalışmaların azlığı ve sonuçların farklılıkları nedeniyle daha çok DM hastası ile yapılan çok merkezli randomize kontrollü ileri çalışmalara ihtiyaç vardır.

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Yüksek kardiyovasküler risk grubundaki hastalarda primer korumada etkili olduğu bilinen salisilatın, KBH hastalarında neden dramatik bir fark yaratmadığı anlaşılamamıştır. Hasta sayısının az olması ile ilgili bir durum söz konusu olabilir. Primer koruma çalışmalarında risk ne kadar yüksekse, salisilat etkisinin o kadar belirgin olduğu bilindiği halde KBH hastalarında etkinin net olmaması daha fazla sayıda prospektif, randomize kontrollü çalışma gereksinimini açıkça ortaya koymaktadır.

Sonuçta salisilat, aterosklerotik renal arter stenozunda kardiyovasküler koruma sağlaması ve renal progresyonu yavaşlatması açısından umut vaat ederken; yüksek riskli hasta gruplarında görülmesi beklenen dramatik etkiyi gösteremediği, az hasta sayılı, küçük çalışmalarda da kısmen hayal kırıklığı yarattığı görülmüştür. Renal aterosklerozun korunma ve tedavisinde salisilat etkisi ve dozu ile ilgili prospektif, randomize kontrollü çalışmalara ihtiyaç vardır.

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Kronik böbrek hastalığında (KBH) ÜA klerensinin azalmasına bağlı olarak hiperürisemi gözlenir. Hiperüriseminin, KBH gelişimi ve KBH progresyonu ile ilişkili olduğunu gösterir çok sayıda çalışma da bulunmaktadır. Bu nedenle KBH'da hiperürisemi neden-sonuç ilişkisi tartışmalı bir konudur. Ürat nefropatisinde, tıpkı Gut hastalığında olduğu gibi yüksek ÜA'nın interstisyum ve tübüllerde çökerek kristal ilişkili hasara yol açtığı düşünülür iken, takip eden yıllarda yapılan deneysel çalışmalarda, ÜA yüksek olan hastalarda kristal nefropatisindeki histopatolojik değişiklikler olmaksızın, birtakım patofizyolojik değişiklikler saptanmıştır. Böbrek dokusundaki patofizyolojik değişiklikler, Renin-anjiotensin sistemi (RAS) aktivasyonu, Nitrik oksit (NO) azalması, oksidatif hasar ve bunlarla ilişkili olarak gelişen periglomerüler arteriolopati, podosit hasarı, endotel-mezangial hücre transformasyonu, endotel disfonksiyonu olarak sayılabilir. Bu patofizyolojik değişiklikler sonucu fibrozis ve KBH geliştiği düşünülmektedir. Hiperüriseminin aynı zamanda hipertansiyon (HT) ile ilişkili olduğunu gösterir çok sayıda çalışma mevcuttur. Sonuçta hiperürisemi hem HT hem de KBH gelişimi ile ilişkili olup, kardiyovasküler (KV) risk faktörü olarak görülmeye başlanmıştır.

### Hiperürisemi ve insidan KBH gelişimi

Ürik asitin, insidan KBH ilişkisini değerlendirir çok sayıda çalışma vardır. Bunlardan birisi Iseki ve arkadaşları tarafından yapılmıştır. 6403 kişinin 2 yıllık verileri taranmış, kreatinin ve ÜA yüksekliği arasındaki ilişki değerlendirilmiştir. İki yılda 241 kişide kreatinin yüksekliği gelişmiş ve ÜA > 8 mg/dl olması, erkekte 2.91 kat, kadında 10.39 kat kreatinin artışı ile ilişkili bulunmuştur. 5808 kişinin verilerinin analiz edildiği Kardiyovasküler sağlık çalışmasında (CHS) ise ÜA yüksekliğinin insidan KBH ile ilişkili olmadığı, ancak KBH progresyonu ile ilişkili olduğu gösterilmiştir. 1988-2002 yılları arasında takipli 10.956 kişinin verilerinin analizinde, yüksek ÜA'nın düşük GFH ile ilişkili olduğu saptanmıştır. CHS ve ARIC çalışmalarının ortak analizinde ise ÜA'nın insidan KBH gelişimi için risk faktörü olduğu tespit edilmiştir. Japon erkek işçilerde yapılan bir çalışmada ise, ÜA > 7 mg/dl olduğunda, KBH gelişimi için risk faktörü olduğu gösterilmiştir. Sonuçta hiperürisemi ve KBH gelişimi arasındaki ilişkiyi gösterir fazla hasta sayılı çok sayıda retrospektif çalışma mevcuttur.

### Hiperürisemi ve KBH progresyonu

Hiperüriseminin KBH progresyonu ile ilişkisini inceleyen çalışmalara baktığımızda, çoğunluğunun retrospektif çalışmalar olmasına rağmen, hasta sayısının ve takip süresinin fazla olduğunu görmekteyiz. Bu çalışmalardan birisi Hsu ve arkadaşları tarafından yapılmıştır. 25 yıllık retrospektif analizde araştırmacılar, 177.570 hasta verisini analiz etmişler ve klasik risk faktörlerine ilave olarak ÜA yüksekliğinin KBH progresyonu ile ilişkili olduğunu göstermişlerdir. 16.630 hastanın 10 yıllık takip verilerinin retrospektif analiz edildiği Iseki ve arkadaşlarının yapmış olduğu çalışmada, hiperüriseminin GFH azalması için güçlü belirleyici olduğu gösterilmiştir. Amerika Birleşik Devletlerinde yapılan bir çalışmada ise 3885 evre 2-4 KBH hastasının 7.9 yıllık takip verileri analiz edilmiş ve ÜA yüksekliğinin GFR  $\geq 45$  ml/dk olan hastalarda

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cevabı için daha fazla randomize ve prospektif çalışma sonuçlarına ihtiyacımız vardır. Ancak oldukça heterojen, inflamatuvar aktivitesi çok yüksek, artmış kardiyovasküler mortalite riskine sahip olan bu hasta grubunda glisemik hedefler belirlenirken bu faktörler de göz önünde bulundurulmalıdır. Kılavuzların daha çok önermekte olduğu HbA1c'nin anemi ve ESA kullanımı ile ilgili olan kısıtlı yönleri daima akılda tutulmalıdır. Glikozile albumin ölçüm yöntemlerinin daha da standardize edilmesi, bu indeksin kullanımını yaygınlaştıracaktır. Glikozile albuminin de hipalbumemisi olan ve diyaliz ile fazla protein kaybı olan hastalar ile ilgili kısıtlayıcı yönleri vardır. Herşeyden önemlisi; glisemik hedef koyduğumuz hastada neyi kazanmayı hedeflediğimizin farkında olmaktır. Hangi glisemik indeksi kullanıyorsak, yöntemin kısıtlılıklarına ve avantajlarına iyi hâkim olmak zorundayız.

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Sertralin, Droksidopa, Adenozin antagonistleri; kafein, aminofilin ve Adenozin 1 blokörü; FK352 gibi ilaçlar çeşitli çalışmalarda denenmiş ve İDH'yı azalttıkları gösterilmiştir. Bu ilaçların İDH'da kullanımı için ileri çalışmalara ihtiyaç vardır.

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Haziran 2016'ya dek yapılmış diyabetik hipertansif hastalarla yürütülmüş olan randomize kontrollü çalışmaların 13'ünün değerlendirildiği geniş bir analize göre; ACE inhibitörleri bu grup hastalarda tüm nedenlere bağlı mortaliteyi, kardiyovasküler nedenli mortaliteyi, major kardiyovasküler olay sıklığını azaltmaktadır; ARB'lerin ise myokard enfarktüsü dışında gösterilmiş önemli bir faydalanımı mevcut değildir.

2013 yılında yayımlanmış olan NEPHRON-D çalışmasında; diyabetik nefropatili hastalarda lisinoprille birlikte losartan kullanımının, kardiyovasküler açıdan anlamlı bir kazanım yaratmamasına rağmen, artmış yan etki sıklığı ile birlikte olduğunun anlaşılması ile klinik pratiğimizde daha az kullanım şansı bulan ADE inhibitörü ile birlikte ARB kullanımına dair de yeni literatür verileri mevcuttur; Ocak 1990 ile Ocak 2018 yılları arasında yapılmış olan toplam 42 randomize kontrollü çalışma değerlendirildiğinde görülen o ki; diyabetik böbrek hastalığı olanlarda dual blokajla kan basıncında ve proteinüride belirgin azalma sağlanmasına rağmen, tüm nedenlere ve kardiyovasküler nedenlere bağlı mortalite oranı azalmamakta; hiperpotasemi ve hipotansiyon riski ise artış göstermektedir.

ADE inhibitörü ve ARB kullanımı ile kardiyovasküler anlamda tam olarak istenildiği ölçüde kazanım elde edilememesinden; ilaç kullanımı ile gözlemlenen ve değişik yayınlarda sıklığı farklı oranlarda verilen aldosteron kaçış fenomeninin de rolü olabileceğini düşünmek akıllıca olacaktır. Bilindiği üzere mineralokortikoid reseptörler beyin, kan damarları, kalp ve böbrek üzerinde olumsuz etkilerden (endotelial disfonksiyon, fibrozis, inflamasyon, vazokonstriksiyon, proteinüri gibi) sorumlu tutulmaktadır. Günümüze değin klinik pratikte sıklıkla faydalandığımız spironolakton; mineralokortikoid reseptör (MR) selektivitesi düşük, bu nedenle de yan etki potansi yüksek bir ilaç olarak kullanımını kısıtlandırmaktadır. İkinci jenerasyon MR antagonisti olan eplerenon ile reseptör selektivitesi daha olumlu hale gelmiş ise de, 3. jenerasyon MR antagonisti olan finerenon ile reseptör selektivitesinin en üst düzeyde olduğu bilinmekte olup önümüzdeki tarihlerde sonlanması beklenen ve diyabetik nefropatili hastalarda yürütülen FİDELİO-DKD ve FİGARO-DKD çalışmaları ile bu konudaki bilgilerimizin daha da netleşmesi mümkün olabilecektir.

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- **Danurobisin:** siklosporin danurobisinin kan düzeyini artırır.
- **Topotekan:** siklosporin topotekan kan düzeyini artırır.
- **Etoposid:** siklosporin etoposid kan düzeyini artırır. Etoposid dozu %50 azaltılmalı

Sonuç olarak, kemoterapötik ajanlar kanser hastasının hayatta kalmasını sağlar. Bu durum nefrotoksisite prevalansının da artmasına neden olmaktadır. Kemoterapi, nefrotoksisitesinin önlenmesi hasta sağ kalımına önemli katkıda bulunur. Kemoterapi verilecek hastalarda değiştirilebilir risk faktörleri mevcut ise klinisyenler tarafından önleyici tedbirler alınmalıdır. Klinisyenler, kemoterapötik ilaçların nefrotoksisitesine, klinik ve laboratuvar belirtilerine aşina olmalıdırlar. Onko-Nefroloji, onkologlar ve nefrologlar arasında yakın bir çalışma ilişkisi gerektiren hızla genişletilmesi gereken bir alandır.

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## Sonuç

Kronik böbrek hastalığında vitamin D eksikliği, RAS aktivasyonu ve insülin direnci üzerinden renal yetmezlik patogenezinde artan oksidatif stres, immün bozukluk, hiperparatiroidi ile aterogenezi daha da tetikleyerek kardiyovasküler hastalık progresyonuna neden olur. Bu nedenle, vitamin D eksikliği kronik böbrek hastalığı ve hemodiyaliz grubunda düzeltilmelidir. Peki hangi preparatla ve nasıl? Yapılan çalışmaların çok heterojen olması dezavantaj olsa da verilen inaktif D vitamini tedavisinin güvenilir, yan etki profilinin iyi olduğu söylenebilir. Çalışmalarda diyaliz hastalarında Vitamin D eksikliği mortalite ile ilişkili olup tedavinin kardiyovasküler risk etkileri tutarsızdır. İnaktif D vitaminin etkileri hemodiyaliz grubunda belirsiz olup randomize kontrollü çalışmalara ihtiyacımız vardır. Diyaliz hastalarında vitamin D eksikliğinde direkt aktif D vitamininin TEMD'in önerdiği şekilde verilmesi dinamik kemik hastalığı riskini artırabilir.

Sonuç olarak diyalizde hedef PTH düzeyi 2009-2017 KDIGO kronik böbrek hastalığı kemik mineral hastalığı kılavuzuna göre 2-9 kat aralığı olup, bu aralıkta tutmak için hastaya aktif D vitamini verilir. Eğer D vitamini düzeyi 30 ng/ml'nin altında ise kolekalsiferol verilmelidir. 1-alfa hidroksilaz sadece böbrekte değil başka dokularda da bulunmaktadır. Bu nedenle tam etkinlik oluşamayabileceği, özellikle kardiyovasküler korumada yetersiz kalılabileceği unutulmamalıdır. Yapılan çalışmalarda tedavinin önemli bir yan etkisi gösterilmeyip, güvenlidir.

Son söz olarak; diyaliz hastalarında eğer serum 25(OH)D; 30 mg/dl altında ise Vitamin D tedavisi genel popülasyon gibi yapılmalıdır, tedavide yan etki yoktur, güvenli, ancak etkinlik, özellikle kardiyovasküler etkinlik yetersiz ve belirsizdir.

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