Bölüm
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DİSLİPİDEMİ YÖNETİMİ

Fatih LEVENT[1]

Dislipidemi tanımı; arteryel hastalıklarda lipid ve lipoproteinlerin transport yolundaki bozukluklar için kullanılır. Çoğu dislipidemi nadiren semptom verir. Ancak laboratuvar olarak tespiti ve tedavisi kardiyovasküler hastalıkların azalmasında önemli yer tutar.(1)

LİPOPROTEİN TRANSPORT SİSTEMİ

Lipid Biyokimyası

Biyolojik lipidler; t-yağ asitleri, monogliseridler, digliseridler trgliseridler, fosfolipidler, sfingolipidler steroller yağda çözünen vitaminler (A,D,E,K vitaminleri) gibi çok çeşitli formlarda bulunabilirler. Lipidlerin major görevleri; hücre membranında bulunma, enerji depolama ve hücre içi sinyal iletimidir. Lipidler suda çözülmediği için (hidrofobik) kanda taşınmaları amfipatik (iç kısmı hidrofobik dış kısmı hdrofilik) yapıda olan apolipoprotein denen moleküller sayesinde olur. Kanda dolaşan lipidler başlıca kolesterol ve kolesterol esterleri gliserofosfolipid,sfingolipid ve trigliseridlerdir.

Triglidseridler 3 yağ asidine bağlı 3 karbonlu gliserolden oluşur çok hidrofobik olmaları nedeniyle apolipoproteinlerin merkezinde taşınır. Yıkımları lipaz enzimi ile olur(1)

Lipoproteinler Apoliporoteinler

Lipoproteinler; fosfolipİdler, kolesterol ve apolipoproteinlerden meydana gelen hidrofilik bir katman ve kolesterol ester ve trigliseridlerden oluşan bir çekirdekten oluşur. Lipoproteinler ultrasantrifüjle dansiterlerine göre ayrılır. Şilomikron, şilomikron kalıntısı, çok düşük dansiteli lipoproteinler (VLDL) ,trigliseridden zengin olması nedeniyle dansitesi 1006g/ ml nin altındadır. Dansitesi daha yoğun olanlar ;düşük dansiteli lipoprotein (LDL) ,yüksek dansiteli lipoprotein (HDL) ve lipoprotein a dır..

Apolipoproteinlerin 3 ana görevi vardır. Lipoproteinlerin yapısını oluşturmak, enzimlerin koaktivatörü ve inhibitörü olmak ve spesifik reseptörlere bağlanmak.

LDL reseptörünün keşfi, kolesterol metabolizmasının anlaşılmasında bir köşe taşı olmuştur. LDL reseptörleri; kolesterolün hücreye girişini ve hücreden atılımını kontrol eder. Makrofajlarda özellikle okside lipoproteinlere bağlanan çöpçü(scavenger) reseptörler bulunur. Bu reseptörler okside LDL nin hücre içine alınmasından sorumludur. Okside LDL ile dolan makrofajlar köpük hücresine (foam cell) dönüşür. Bunlar damarlardaki yağlı çizgilenmeden sorumludur.(1)

Lipoprotein Metabolizması ve Transport

Lipoprotein transportu iki önemli rol oynar: 1) trigliseridin barsaklardan ve karaciğerden kullanılmak üzere yağ veya kas dokusuna aktarımı 2) kolesterolün perifer dokulara ve karaciğere membran sentezi , steroid hormon üretimi, safra asidi sentezi gibi görevlerde kullanılmak üzere iletilmesi.(1)

[1] Kardiyoloji Uzman Hekimi Fatih LEVENT Özel Tınaztepe Torbalı hastanesi

selme, myopati , kolelithiazis en çok bilinen yan etkileridir. Statinlerle kombine edildiğinde(özellikle gemfibrozil) myopati riski 5.5 kat artar. (55) Homosistein ve kreatinin yüksekliği ve pankreatit diğer yan etkileridir(56,57). Kreatinin yüksekliği renal fonksiyon bozukluğu ile ilişkili değildir. İlaç kesilince düzelir.

N-3 Yağ Asitleri

N-3 (ya da omega -3) yağ asitleri ([eicosapentaenoic asit (EPA) and docosahexaenoic asit (DHA)), farmakolojik dozlarda(2-4gr/gün) trigliserid düşürücü tedavi olarak kullanılır. Doz bağımlı olarak trigliserid düzeyinde %45 azalma izlenir.(70)

REDUCE -IT çalışmasında trigliseridi yüksek ve kardiyovasküler risk faktörü olan hastalarda farmakolojik dozda n-3 yağ asidi kullanıldığında (2x2 gr) , major kardiyovasküler olaylarda anlamlı azalma sağlanmıştır.(59)

En çok görülen yan etki gastrointestinal bozukluktur.Antitrombotik etkisi nedeniyle antiagregan kullanan hastalarda kanama açısından dikkatli olunmalıdır.(10)

Bunlar dışında nikotinik asit ve Kolesterol ester transfer protein inhibitörleri; faydalarının görülmemesi ve zararlı yan etkileri nedeniyle günümüzde kullanılması önerilmeyen ilaçlardır.(10)

SONUÇ

Dislipidemiler özellikle kardiyovasküler hastalıklar başta olmak üzere bir çok önemli sağlık sorunu için önemli bir risk faktörü olmaya devam etmektedir. Önlenebilir bir risk faktörü olması nedeniyle erken tespiti ve tedavisi büyük önem taşır. Günümüzde yaşam tarzı değişiklikleri, ilaç ve aferez gibi uygulamalarla tedavisi büyük oranda mümkün hale gelmiştir. Gelecekte çalışmaları yapılan ve onay bekleyen yeni ilaçlarla (mipopersen, lomitapid) tedavi seçenekleri ve etkinliğinin artması beklenmektedir. (60,61)

Anahtar Kelimeler: Dislipidemi; Ezetimib; Fibrat; HDL; HMG CoA; Lipoprotein; LDL; PCSK9; Statin; SCORE; Şilomikron; Trigliserid.

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