

Bölüm 9

GLUKOZ TAŞIYICILARI VE METFORMİN

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GİRİŞ

Glukoz, vücuttaki birçok doku için temel enerji kaynağı olmakla birlikte hücrel metabolizma için belirleyici bir rol üstlenmektedir. Glukoz homeostazının korunması, hücre içine alınması temel bir fizyolojik süreçtir. Glukoz, molekül ağırlığı 180 g/mol olan hidrofilik bir moleküldür. Hidrofilik özellikteki glukoz ve diğer monosakkaritler, lipofilik özellikteki olan hücre membranlarından geçemez. Bu yüzden hücrel membranlar boyunca glukoz ve diğer monosakkaritlerin taşınmasına eşlik edecek özel protein taşıyıcılar bulunmaktadır.

Glukoz taşıyıcıları, yapısal ve işlevsel olarak farklı iki türe ayrılır: kolaylaştırılmış glukoz taşıyıcıları (GLUT) kolaylaştırılmış difüzyonla çalışırken; sodyum bağımlı glukoz taşıyıcıları (SGLT), sodyum ile birleşerek konsantrasyon gradyanına karşı glukozu aktif olarak taşırlar.

Metformin, antidiyabetik bileşiklerin biguanid sınıfına aittir. Tip 2 diyabet tedavisinde birçok ilaçla kombinasyon halinde kullanılabilirdiğinden en çok tercih edilen antidiyabetik ilaçlardan birisidir. Metforminin antihiperlipidemik etkisinin yanı sıra pleiotropik etkileri de mevcuttur.

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SONUÇ

Glukoz taşıyıcıları, yapısal ve işlevsel olarak farklı iki türe ayrılır: GLUT'lar, kolaylaştırılmış difüzyonla çalışırken, sodyum-glukoz ko-transporterları (SGLT'ler), sodyum ile birleşerek konsantrasyon gradyanına karşı glukozu aktif olarak taşırlar. İnsanlarda tanımlanan 14 farklı GLUT bulunmaktadır. Tüm GLUT izoformlarının belirli fizyolojik rolleri vardır ve her biri farklı bir doku dağılımı ve substrat özgüllüğüne sahiptir. Sekans benzerliği ve substrat afinitesi özelliklerine göre bu GLUT'lar üç farklı gruba ayrılır. İnsanlarda, en az 6 farklı izoform içeren bir SGLT ailesi bulunur ve glukoz ile sodyum, hücrelere aynı anda taşınırken sodyum konsantrasyon gradyanından faydalanılır. GLUT'lar ve SGLT'ler, böbrek tübül hücrelerinde birlikte çalışır. SGLT'ler, ince bağırsak ve böbrek tübüllerinin yanı sıra luminal apikal zar boyunca çeşitli glukoz, amino asitler, vitaminler ve bazı iyonların taşınmasıyla ilgili geniş bir zar protein ailesini oluşturur. Genel işlevleri nedeniyle GLUT'lar ve SGLT'ler birçok hastalığın tedavisi için hedef haline gelmiştir. SGLT'ler, glukozu apikal zar üzerinden tübül hücrelere taşıırken, GLUT'lar, glukozu bazolateral zar üzerinden kan dolaşımına taşır. Son zamanlarda, renal glukoz reabsorpsiyonunu inhibe ederek glukozüriyi artıran yeni bir antidiyabetik etki kavramına dayanan SGLT2 inhibitörleri geliştirilmiştir. SGLT2 inhibitörleri, böbrekteki koruyucu etkileri ve kardiyovasküler ölümde azalma sağladığından dikkat çekici hale gelmiştir. SGLT1, ince bağırsakta glukoz emiliminden ve böbrekte filtre olan glukozun bir kısmının reabsorpsiyonundan sorumludur. Bugün glisemik kontrolün sürdürülmesi ve böbrek fonksiyon bozukluğunun iyileştirilmesini hedefleyen çalışmalar devam etmektedir. Metforminin antihiperglisemik etkisinin yanı sıra pleiotropik etkileri de mevcuttur. Bu etkileri sayesinde özellikle son zamanlarda kanser tedavilerinde kullanılması dikkat çekicidir.

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