Bölüm 15

Psikonöroimmünoloji Araştırmalarında PET Görüntüleme

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Özet

Pozitron-emisyon tomografisi (PET) görüntüleme fizyolojik bir olay veya beyindeki moleküler hedeflerin in vivo nicelendirilmesine olanak veren değerli bir araştırma aracıdır. PET görüntüleme, psikonöroimmünoloji araştırmalarında sık kullanılan çeşitli deneysel ve klinik model sistemlerle kombine edilebilir. Dolayısı ile hayvan ve insanlarda PET görüntülemenin kullanılabilmesi ile çoğu kez bir hayvan modelinden insan hastalığına çeviri yapılabilmektedir.

Anahtar sözcükler PET, FDG, PBR, TSPO, Yangı, Mikroglia, Endotoksin

1 Giriş

1.1 Pozitron-Emisyon Tomografisi Hakkında Temel Bilgiler

Nükleer görüntüleme deyimi ile fizyolojik bir olaya katılan veya o dokudaki moleküler bir hedefe spesifik olarak bağlanan radyoaktif bir farmasötiğin (radiyofarmasötik) zerkinden sonra doku veya bir organdaki radiyoaktiviteyi ölçen, in vivo görüntüleme modaliteleri betimlenir. İncelenen dokuda ölçülen radiyoaktivite hedefin yoğunluğunu veya fizyolojik olayın aktivitesini ölçmek için nicelendirilebilir. Radiyofarmasötikler eş anlamlı deyimler olarak radiyoligandlar veya radiyotraserler olarak da adlandırılır; bu ikinci deyimin anlamı PET çalışmalarında kullanılan radiyofarmasötiğin çok küçük kütle dozunda (mutad olarak 10 µg'dan daha az) kullanılmasıdır. Bu tür "iz = trace" miktarların ender olarak herhangi bir ölçülebilir farmakolojik etkisi söz konusudur zira radiotraser mevcut hedef moleküllerin sadece %1-5'ine bağlanmaktadır. Bu nedenle, radiotraserlerle yapılan ilk insan-çalışmalarında dayatılan düzenleyici önlemler farmakolojik dozlarda kullanılan yeni bileşiklerle yapılan ilk-insan çalışmalarındaki duruma göre daha yumuşaktır. Örneğin, tek bir türde yapılan tek-doz toksisite çalışmasında insanda yeni bir radiotraser kullanmasının onaylanması için tek bir örnek yeterlidir. Radiotraserler belli bir fizyolojik olayı (örn.,glükoz metabolizması, oksijen

5 Notlar

1. Endotoksin kullanılması insan deneklerde araştırma amacıyla hafif sistemik yangıyı indükte etmek için kullanılabilen birçok yöntemden bir tanesidir (yayın taraması için bakınız [5]). Sıklıkla kullanılan diğer immün uyartılar arasında *tifo aşısı* ve *interferon-alfa* (tedavi olarak kullanılabilen veya sağlıklı kişilerde kullanılabilir) bulunmaktadır. Bu son ikisinin insanda kullanılması FDA tarafından onaylanmış olup dolayısı ile yerel kurumsal inceleme kurulu tarafından onaylanması gerekmez.

2. Clinical Center Referans Endotoksin zerke mahsus dozaj formları Bureau of Biologics tarafından üretilmektedir. CCRE, Escherichia coli O:113'den hazırlanmış (U.S. Standard Reference Endotoxin) arıtılmış bir lipopolisakkarit olup iyi üretim pratiği rehberlerine göre şişelenmiştir. CCRE 5 mL'lik renksiz cam şişelerde verilmekte olup her şişe 10.000 endotoksin ünitesi (yaklaşık 1 mcg referans endotoksin), 10 mg laktoz ve 1 mg polietilen glikol 6000 içeren beyaz, liyofilize toz içerir. İnsanda kullanılan endotoksin dozunun sınırları bedenin kg ağırlığı başına 0,2-4 ng'dır. Ana amaç ufak tefek tepresyon semptomları içeren ılımlı bir sistemik yangı halini indükte etmek ise 1 ng/kg'dan daha küçük bir doz sağlık verilir [5].

3. ^{11}C'in kısa yarı-ömrü nedeniyle [^{11}C]PBR28'in kullanılacağı yerde sentez edilmesi zorunludur. Çok sayıda ^{18}F TSPO traseri bulunmakta olup bunların arasındaki [^{18}F]PBR06 [70], [^{11}C]PBR28'in yakın bir analoğu olup benzer performansa sahiptir. [^{18}F]PBR06 üretici tarafından sentezlenip PET noktasına postalanabilirse de ticari olarak bulunmamaktadır; bununla beraber [^{18}F]PBR06 sentezi yapabilen farklı noktalar arasında bir işbirliği sağlanması olasıdır.

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