

EPÄTYYPILLINEN KILPIRAUHASSEN VAJAATOIMINTA

Käypä hoito – suositusehdotus

Funktionaalisen lääketieteen yhdistyksen (FLY) työryhmä

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Suosituksen tavoitteet

- Esitellä epätyypillisen kilpirauhasen vajaatoiminnan diagnostiikka sekä hoitoperiaatteet.

Kohderyhmä

- Kilpirauhaspotilaita työssään hoitavat terveydenhuollon ammattihenkilöt.

Määritelmä

- Epätyypilliseksi kilpirauhasen vajaatoiminnaksi voidaan katsoa tilanne, jossa on ristiriita potilaan oireiden ja tavanomaisten kilpirauhasen toimintaa mittaavien laboratoriotulosten välillä.
- Epätyypillistä kilpirauhasen vajaatoimintaa sairastavat potilaat kärsivät lukuisia kilpirauhasen vajaatoiminnan oireista, mutta seerumin tyreotropiini (S-TSH), vapaa tyroksiini (S-T4v) ja vapaa trijodityroniini (S-T3v) ovat viitealueella.
- Ristiriidan ymmärtämiseksi on tunnettava kudostason säätelyn keskeinen merkitys, joka on kuvattu kappaleessa ”Etiologia ja patogeneesi”.
- Suositusehdotuksemme esittää, että huonosti kilpirauhasfunktiota kudoksissa kuvaavien S-TSH:n ja S-T4v:n lisäksi pitäisi vaikeahoitoista kilpirauhasen vajaatoimintaa sairastavalta potilaalta mitata seerumin käänteis-T3 (S-rT3) ja vapaan T3:n ja käänteis-T3:n suhde, jotka näyttäisivät olevan parhaat kudostason tasapainon mittarit (1, 2, 3).

Esiintyvyys ja ennuste

- Suomessa kilpirauhasen vajaatoimintaa sairastaa lähes 270 000 ihmistä.
- Yleisesti arvioidaan, että valtaosa potilaista tulee oireettomiksi perinteisellä tyroksiini-monoterapialla (4).
- Tutkimusten mukaan kuitenkin 10 % tyrokseenilla hoidetuista potilaista ei saavuta tavoiteltavaa T3-hormonin pitoisuutta TSH:n ollessa viitealueella eikä 34-49 % pelkällä tyrokseenilla hoidetuista saavuta oireettomuutta (5, 6, 142).

Etiologia ja patogeneesi

- Kilpirauhasen erittämä tyroksiini (T₄) on pro- ja varastohormoni, jonka vaikutusta säädellään kudoksissa olevien dejodinaasientsyymien toimesta. Näiden entsyymien toiminta on puolestaan kytköksissä muuhun endokriinijärjestelmään, fysiologisiin tiloihin ja ravintotekijöihin.
- Vasta viime vuosina on alettu perusteellisimmin ymmärtämään kudoksissa olevien dejodinaasien toimintaa.
- Dejodinaaseja on kolmea tyyppiä: tyyppi I (D1) ja tyyppi II (D2) katalysoivat tyroksiinin muuttumista aktiiviseksi 3,5,3'-trijodityroniiniksi (T₃), kun taas tyyppi III dejodinaasi (D3) vähentää tyroksiinin muuttumista aktiiviseksi katalysoimalla sitä inaktiiviseksi 3,3'5'-trijodityroniiniksi nk. käänteiseksi T₃:ksi (rT₃).
- Dejodinaasi-entsyymit ovat ihmisen kehityksen eri vaiheissa ja fysiologisissa tiloissa juuri kudostason kilpirauhashormonien säätelyssä keskeisiä. Aivolisäkettä lukuun ottamatta kaikissa kudoksissa on sekä D1-että D2-entsyymiä (7).
- D1:n toimintaa estävät mm. fyysinen ja henkinen stressi (8-19), masennus (20-42), laihdutus (43-48), leptiiniresistenssi (49-90), insuliiniresistenssi, ylipaino, diabetes (91-99), autoimmuunitulehdukset (8, 100-114), krooninen väsymysoireyhtymä ja fibromyalgia (115-119) sekä toksiinialtistus (120-128). Näissä tilanteissa kudoksissa syntyy epätasapainoa aktiivisen T₃:n ja rT₃:n välille. Tämä muutos on mitattavissa myös perifeerisestä verestä.
- T₃:n toiminta estyy rT₃:n vaikutuksesta sen estäessä mm. D1-entsyymin toimintaa ja ja T₃:n sitoutumista reseptoreihin kudostasolla (7, 8).
- Kortikosteroidit estävät kroonisessa stressissä ja farmakologisilla pitoisuuksilla D1-entsyymiä ja stimuloivat D3-entsyymiä vähentäen täten T₄:n konversiota T₃:ksi ja lisäten sen muuntumista rT₃:ksi (9, 15-17).
- Fysiologinen kortikosteroidipitoisuus sen sijaan on edellytys D1-entsyymin toiminnalle ja D3-entsyymin estolle (15).
- Pienetkin rT₃-tason nousut kudoksissa ja seerumissa johtavat kilpirauhashormoni-reseptorien salpautumiseen ja kilpirauhasen vajaatoiminnan oireisiin, joita ei huomata pelkillä S-TSH tai S-T₄v - arvojen seurannalla (129-134).
- Tyroksiinihoito vain lisää oireita eikä sitä näin ollen tule käyttääkään silloin kun S-rT₃ on koholla (135-139).
- Dejodinaasi tyyppi II (D2) on hypofyysin dejodinaasi. Sen K_m on 1000-kertainen D1-entsyymiin verrattuna, mikä tekee siitä TSH:n erityistä säätelevänä tekijänä erityisen tehokkaan. Samasta syystä perifeerisen verenkierron T₃-arvot korreloivat sekä sen aktiivisuuteen että verenkierron tyreotropiiniin huonosti. Ongelmaa mutkistavat yksilölliset

seikat mm. D2-entsyymiä koodaavan geenin polymorfismi, joista tavallisin variaatio hidastaa TSH-stimulaation tuottamaa T3-vapatumista (140).

- Käytännössä syntyy tilanteita, jossa rT3:n nousu aiheuttaa kliinisesti hypotyreoosioireet, joihin ei aivolisäkkeen tyreotropiinieritys reagoi. Tutkijat ovat nimenneet tilan `euthyroid sick syndroomaksi`, joka teorian mukaan korjaantuu ajan myötä itsekseen (3, 141).

Hoito:

- Kliinisesti on havaittu, että epätyypillistä kilpirauhasen vajaatoiminnasta eli euthyroid sick syndrooman` kaltaisista kilpirauhasen vajaatoiminnan oireista pitkään kärsineillä potilailla saadaan hyvä hoitovaste T3-substituutiohoidolla (kauppanimet Liothyronin, Thybon, Cytomel).
- Terapeuttisen ja pysyvän vasteen saamiseksi tulee kohonnut käänteis-T3 saada laskemaan riittävästi.
- Liian suurien T3-annosten käyttö saattaa kuitenkin altistaa hypertyreoosiriskille.
- Yhdysvalloista löytyy klinikoiden julkaisemia monografioita ja kirjoja sekä Institute for Functional Medicine –järjestön järjestämiä kurseja, joilla näitä hoitoprotokollia on perusteellisesti käyty läpi (143-145).
- Hoitokokeilu T3-valmisteella on perusteltu rajallisen ajan oireisilla potilailla, joiden S-T3v on matala ja/tai S-rT3 korkea. Hoitokokeilu edellyttää lääkärin tarkkaa seurantaa ja potilaalta kykyä soveltaa annettuja ohjeita oman tilanteensa mukaan.

Lopuksi

- Käänteis-T3-määrittämiä on tehty myös suomalaisissa kliinisissä laboratorioissa vielä 2000-luvun alussa, mutta lääkäreiden kiinnostuksen puutteen vuoksi niitä ei ole enää saatavana Suomessa, vaan analyysi on lähetettävä muualle EU:n (146) tai USA:n laboratorioihin (147).

Vastuun rajaus

- Tämä Käypä hoito –suositusehdotus on epätyypillisen kilpirauhasen vajaatoiminnan diagnostiikkaan ja hoitoon perehtyneiden asiantuntijoiden laatima. Tämä ei korvaa lääkärin tai muun terveydenhuollon ammattilaisen omaa arviota yksittäisen potilaan parhaasta mahdollisesta diagnostiikasta ja hoidosta.

Tiedonhakukäytäntö

Tämä Käypä hoito –suositusehdotus on laadittu asiasta olemassa olevan tieteellisen näytön sekä hoitokokemusten perusteella.

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