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PRODUŽENA I NELEČENA HIPOTIREOZA KAO JEDAN OD MOGUĆIH UZROKA AKUTNE PSIHOTIČNE EPIZODE

Sažetak: Psihoza je skup simptoma koji dovode do poremećaja kontakta ili čak prekida kontakta sa stvarnošću. To može biti u vidu poremećaja, opažanja, emocija, mišljenja i ponašanja. Psihoze imaju mnoštvo različitih uzroka, a jedan od njih je i hipotireoza. Tiroksin je značajan za globalnu funkciju moždane aktivnosti, a holinergička aktivnost u frontalnom korteksu i hipokampusu značajno se povećava u njegovom prisustvu. Dijagnoza psihotične epizode postavlja se na osnovu auto- i hetero- anamneze, kao i psihijatrijskim pregledom. Prisutno je postojanje: pozitivnog sindroma, dezorganizacije i negativnog sindroma. Nakon postavljanja dijagnoze psihotičnog poremećaja u terapiju se uključuju antipsihotici, a po pristizanju nalaza koji verifikuju hipotireozu u terapiju se uključuje i tiroksin. Terapijski odgovor se postiže već nakon nekoliko dana do nedelja. Kod pacijenata sa akutnom psihozom, a posebno kod onih sa pozitivnom ličnom i porodičnom anamnezom na hipotireozu treba razmišljati u pravcu neprepoznatog endokrinološkog oboljenja.

Ključne reči: psihoza, psihotična epizoda, hipotireoza

Uvod

Psihoza je skup simptoma koji dovode do otuđenja pacijenta od realnosti (1). Ogleda se u poremećenom kontaktu ili čak prekidu kontakta sa stvarnošću koji se manifestuju kroz duboki poremećaj opažanja, emocija, mišljenja ili ponašanja (2). Psihoze imaju mnoštvo različitih uzroka. Gruba podela bi mogla da bude na neorganske (ili primarne), organske (ili sekundarne) i psihoze izazvane upotrebom psihoaktivnih supstanci (1). U neorganske bi spadale shizofrenija i bipolarni pore-

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mećaj, a u organske sva stanja koja dovode do homeostatskih poremećaja u mozgu, uključujući endokrinološke poremećaje. Hipotireoza ili hipotireoidizam predstavlja smanjeno lučenje hormona štitaste žlezde. Uzroci hipotireoze mogu biti urođeni (atireoza, hemiagenezija štitaste žlezde) ili stečeni. Najčešći uzrok hipotireoidizma predstavlja Hašimotov tireoiditis sa prevalencijom od 3% u opštoj populaciji (3). Psihotični simptomi, uključujući paranoidne ideje, vizuelne i auditivne halucinacije, ranije su smatrani čestim simptomima hipotireoze, dok se danas zna da se ovi simptomi javljaju u oko 5% pacijenata sa hipotireozom (4). Ovi simptomi se najčešće javljaju nakon pojave fizičkih simptoma, odnosno nekoliko meseci do nekoliko godina od početka hipotireoze.

Dijagnostika

Dijagnoza psihotične epizode postavlja se na osnovu auto- i hetero- anamneze, kao i psihijatrijskim pregledom. Psihičke tegobe najčešće prisutne kod pacijenata sa sumnjom na psihotičnu epizodu su postojanje:

I pozitivnog sindroma

- a) halucinacije – najčešće auditivne, vizuelne, taktilne i olfaktivne;
- b) sumanute ideje – persekucije (utisak da pacijenta neko prati, posmatra), uticaja (da je ponašanje pacijenta pod nečijom kontrolom) i odnosa (poruke iz okoline upućene samo pacijentu);

II dezorganizacije

- a) poremećaj govora kao najupadljiviji simptom, osiromašen govor, poremećaji misaonog toka, neologizmi, eholalila;
- b) dezorganizacija ponašanja u domenu motorike i socijalne interakcije, gde mogu biti prisutni simptomi od katatone ukočenosti, preko agitacije, sve do socijalnog distanciranja i zanemarivanja higijene;
- c) afektivna neusklađenost u smislu neadekvatne reakcije, ideo-afektivne disocijacije;

III negativnog sindroma

- a) alogija – poteškoće u komunikaciji kao posledica poremećaja mišljenja;
- b) anhedonija – osećaj emotivne praznine, poteškoće u pronalaženju zadovoljstva;
- c) abulija/hipobulija – potpuni ili delimični gubitak volje koji se manifestuje nedostatkom inicijative, pasivnošću, padom opšteg funkcionisanja;
- d) poremećaj pažnje (2).

Po postavljanju sumnje na aktuelno prisutnu psihotičnu epizodu, a u toku hospitalizacije pacijenta pristupa se laboratorijskoj dijagnostici: određivanje kompletne krvne slike, biohemije, analiza urina uz toksikološke nalaze (kojima isključujemo zloupotrebu psihoaktivnih supstanci). Kod pacijenata sa pozitivnom ličnom anamnezom na hipotireozu (tireoiditisi, radiojod terapija), kod onih kod kojih se inspekcijom i palpacijom uočavaju promene na vratu (prisustvo strume, ožiljka od operacije) ili uvidom u medicinsku dokumentaciju (izveštaji endokrinologa o lečenju hipotireoze) određuje se nivo TSH, FT4, T4, T3. Ukoliko rezultati ukazuju na visok nivo TSH, uz snižene hormone štitaste žlezde, uz konsultaciju endokrinologa potrebno je uključiti/korigovati terapiju tiroksinom i pratiti potencijalno održavanje/povlačenje psihotičnih simptoma.

Posebno je važno biti oprezan i razmišljati o ovoj dijagnozi kod starije populacije jer se određeni somatski simptomi hipotireoze mogu prezentovati kao normalan proces starenja te da budu neprepoznati. Kod ovakvih osoba je u literaturi opisano da upravo simptomi psihoze nastupaju kao prvi, ne zato što je to zaista tako već zato što razvoj hipotireoze i brojni raniji simptomi nisu prepoznati ili su tumačeni kao proces starenja i očekivana posledica istog (5, 6).

Lečenje

Pacijenti sa akutnom psihotičnom epizodom se hospitalizuju na period od 4 do 6 nedelja, nakon čega se lečenje može nastaviti u slučaju postojanja potrebe u uslovima dnevne bolnice, a radi održavanja stabilnosti remisije. U toku hospitalizacije, paralelno sa ispitivanjem, pacijent se inicijalno tretira tiroksinom ili kombinacijom psihofarmaka (antipsihotika+tiroksin) i psiho/socioterapije.

Internistička terapija koja se primenjuje sa ciljem popravljavanja endokrinološkog disbalansa predstavlja osnovu lečenja, te vrlo brzo po započinjanju uzimanja tiroksina dolazi do kupiranja psihotičnih simptoma. Po pristizanju laboratorijskih rezultata u slučaju verifikovane hipotireoze (snižen FT4 uz povišen TSH) uz psihofarmake pacijentima se ordinira i tiroksin. Dnevna doza tiroksina se optimizuje prema telesnoj težini 1.6 mcg/kg/dan, uz merenje TSH nakon 4–8 nedelja (7). Poželjno je da nivo TSH bude do 2,5 mIU/L (8).

Čim se uoče simptomi psihoze potrebno je započeti lečenje antipsihoticima i pre dokazivanja endokrinološkog disbalansa. Kasnije se može nastaviti sa upotrebom kao dodatna terapija, pored tiroksina, sa ciljem bržeg postizanja remisije. Ipak, poslednji pregled literature, dovodi u pitanje da li postoji naučna osnova za ovakav pristup (mada ne isključuje mogućnost s obzirom na mali broj radova sa temom) (9). Do sada se preporučivao tretman niskim početnim dozama antipsihotika druge generacije (izuzev klopazina, koji ima izražene neželjene efekte zbog kojih se preporučuje kao poslednja linija).

Nacionalni vodič dobre kliničke prakse za dijagnostikovanje i lečenje shizofrenije u svom delu „terapija akutne faze” daje smernice i analizu antipsihotika urađenu na osnovu različitih međunarodnih vodiča, a u skladu sa registrovanim antipsihoticima u Srbiji, te može poslužiti kao vodič kliničarima pri odabiru leka kod akutne psihoze usled hipotireoze. Antipsihoticima druge generacije (atipični antipsihotici) daje se prednost u odnosu na one prve generacije (klasični antipsihotici) jer ne dovode do ekstrapiramidalnih neželjenih efekata (10). Sa druge strane, pri njihovoj upotrebi treba biti obazriv jer je i njihova upotreba praćena pojavom neželjenih efekata, pre svega u smislu razvoja metaboličkog sindroma. U Republici Srbiji aktuelno su registrovani sledeći antipsihotici druge generacije: klozapin, risperidon, olanzapin, sertindol, kvetiapin, ziprasidon, amisuprid i paliperidon.

Od klasičnih antipsihotika, koji se mogu koristiti kao alternative, u Republici Srbiji registrovani su sledeći: hlupromazin, flufenazin, haloperidol, levopromazin, sulpirid i ciklopentiksol (11). Bez obzira na izbor antipsihotika, uvek je potrebno napraviti balans u smislu primene minimalne efikasne doze kojom se smanjuje rizik od nastanka neželjenih efekata i praćenje potencijalne pojave istih.

Literaturni podaci o učestalosti psihotičnih epizoda nastalih kao posledica produžene i nelečene hipotireoze

Tiroksin je značajan za globalnu funkciju moždane aktivnosti, a holinergička aktivnost u frontalnom korteksu i hipokampusu značajno se povećava u njegovom prisustvu. Tireoidna disfunkcija najverovatnije dovodi do promena u holinergičkoj aktivnosti, globalnoj perfuziji i globalnom metabolizmu glukoze u CNS-u (12). Nedavni rezultati nalaza PET skenera kod osoba sa hipotireozom pokazali su da u nelečenom hipotireoidizmu dolazi do redukcije cerebralnog protoka krvi, kao i smanjenog metabolizma glukoze (13).

Najčešći uzrok hipotireoidizma u opštoj populaciji predstavlja Hašimotov tireoiditis sa prevalencijom od 3% u opštoj populaciji. Pik incidence je u petoj deceniji života, a javlja se 10–20 puta češće kod žena nego kod osoba muškog pola (3). Klinička slika hipotireoze obuhvata široki spektar simptoma od blagih, poput: suve kože, opstipacije, gubitka kose, gojenja ili depresije; ukoliko bolest napreduje i ne leči se jako dugo može doći do razvoja miksedema, akutne psihoze, akutne manije i miksedemske kome.

Uzročno-posledična veza između oboljenja štitaste žlezde i poremećaja funkcije centralnog nervnog sistema opisana je još krajem XIX veka (”Report on Myxoedema”, Clinical Society of London, 1888). Nakon ovog opisa u naučnoj literaturi počeli su da se objavljuju i psihijatrijski prikazi slučajeva pacijenata sa psihozama čiji je uzrok bila produžena neprepoznata-nelečena hipotireoza. Asher sa saradnicima je 1949. godine objavio rad u kome opisuje 14 pacijenata sa miksedemskom psihozom

i hipotireozom, od kojih se njih 9 oporavilo samo od primene supstitucione terapije tiroksinom (14). Halucinacije koje se javljaju u miksedemskoj psihozi se povlače uglavnom nedelju dana od početka terapije tiroksinom. U literaturi su opisane psihoze kod osoba sa hipertireozom, gde je hipertireoza bila uzrok akutne psihotične epizode, stoga treba biti obazriv kod davanja velikih doza tiroksina jer nagli skok tiroksina kod pacijenata koji su imali psihotične epizode možda može biti okidač za njihovo ponovno javljanje (15, 16).

Pored psihotične simptomatologije, produžena i nelečena hipotireoza se može manifestovati i drugim psihijatrijskim poremećajima. Giunio-Zorkin i saradnici su opisali pacijenta sa manijom kao prvim simptomom izrazite hipotireoze (17). Hipotireoza je čest komorbiditet kod pacijenata sa bipolarnim poremećajem, a pacijenti koji boluju od terapijski rezistentnog bipolarnog poremećaja imaju veću incidencu hipotireoze nego opšta populacija (18). U prospektivnoj kohortnoj studiji, sprovedenoj u Danskoj, u kojoj su praćeni pacijenti sa hipotireozom rezultati su pokazali da pacijenti koji boluju od hipotireoze češće boluju i bivaju hospitalizovani na psihijatrijskim odeljenjima zbog depresije i bipolarnog poremećaja (19). Ueno i saradnici su potvrdili da se psihotični poremećaji mogu javiti pre fizičke manifestacije hipotireoze ili simptomi hipotireoze ne moraju biti izraženi kod psihotičnih pacijenata, posebno u starijoj populaciji gde se simptomi hipotireoze pripisuju procesu starenja (6).

Pregledom literature, uz svoj prikaz slučaja psihoze i hipotireoze, Sančez i saradnici su izveli zaključak da je period povlačenja simptoma psihoze iznosio: 4,4 dana kod pacijenata koji su bili samo na supstitucionoj terapiji tiroksinom; 6,25 dana kod pacijenata na terapiji tiroksinom i po proceni psihijatra kasnije dodatom terapijom antipsihotikom; 17,27 dana je trajao oporavak kod pacijenata kod kojih je inicijalno bio uključen istovremeno i tiroksin i antipsihotik (9). U sve tri grupe pacijenata muškarci su pokazali brži oporavak u odnosu na pacijente ženskog pola. Na osnovu ovih podataka mogao bi se izvesti zaključak da antipsihotici možda i nisu potrebni u lečenju psihoze izazvane hipotireozom (9). Ovakav zaključak bio bi pogrešan iz više razloga: 1) nije napravljena komparacija terapije, dužine oporavka u odnosu na starost pacijenata; 2) terapijski odgovor kako na tiroksin tako i na antipsihotike je sporiji u starijoj populaciji u odnosu na mlađu populaciju; 3) u prikazima slučajeva su možda izostali mogući udruženi faktori kod pojedinačnih slučajeva koji su uticali na ishod lečenja; 4) s obzirom na to da su autori koristili 27 do tada pronađenih prikaza slučajeva i sami navode kao limitaciju da je odluka o terapiji koja će biti uključena bila pod uticajem dodatnih faktora koji nisu zabeleženi (9). Stoga se mora biti oprezan sa definitivnim odgovorom. Trenutno stanje literature, nažalost, još uvek ne daje jasan odgovor na pitanje da li je potrebno uključiti antipsihotik zajedno sa tiroksinom. U dosad objavljenim radovima i prikazima slučajeva ne može se izvesti konsenzus ni o dužini trajanja antipsihotične terapije. Pristup u lečenju ovih pacijenata baziran je na osnovu kliničke slike, te se i inicijalno uključeni antipsihotični lekovi postepeno smanjuju.

Zaključak

S obzirom na to da se promene u ponašanju i psihičkom statusu mogu javiti kao znak hipotireoidizma, bez obzira na prisustvo drugih kliničkih znakova, jako je važno da kod pacijenata sa psihijatrijskim bolestima i manifestacijama, posebno onim akutnim, potražimo i razmišljamo i u pravcu endokrinološke pozadine oboljenja. Terapijski izbor kod pacijenata koji imaju akutnu psihozu, koja je nastala kao posledica hipotireoze ili u kombinaciji sa njom, zahteva lečenje tiroksinom, a često se primenjuje i kombinacija sa antipsihotikom iako je sud o opravdanosti takvog postupka i dalje otvoren. Nakon inicijalnog davanja tiroksina, a po dostizanju referentnih vrednosti FT4 i TSh pacijentima se daje doza održavanja uz kontrolu tiroidnog statusa kod endokrinologa. Antipsihotici koji su uvedeni u terapiju postepeno se smanjuju sa povlačenjem simptoma psihoze sve do njihovog konačnog isključivanja uz kontinuirani nadzor psihijatra.

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PROLONGED AND UNTREATED HYPOTHYROIDISM AS ONE OF POSSIBLE CAUSES OF ACUTE PSYCHOTIC EPISODE

Abstract: Psychosis is a set of symptoms that lead to contact disorders or even cessation of contact with reality. It can be in the form of disorders of perception, emotions, thoughts, and behavior. Psychosis has many causes, and one of them is hypothyroidism. Thyroxin is important for the global function of brain activity, cholinergic activity in the frontal cortex and hippocampus increases significantly in its presence. The diagnosis of psychotic episodes is made on the basis of autoanamnesis and heteroanamnesis, as well as psychiatric examination. The presence of: positive syndrome, disorganization and negative syndrome. After the diagnosis of a psychotic disorder, antipsychotics are included in the therapy, and upon arrival, the findings that verify hypothyroidism, include thyroxin in the therapy. The therapeutic response is achieved after a few days or a week. In patients with an acute psychosis, and especially in those with a positive personal and family history of hypothyroidism, one should think in the direction of an unrecognized endocrine disease.

Key words: psychosis, psychotic episode, hypothyroidism

Introduction

Psychosis is a set of symptoms that lead to the patient's alienation from reality (1). It is reflected in disturbed contact or even cessation of contact with reality, which is manifested through a deep disturbance of perception, emotions, thoughts or behavior (2). Psychosis has many causes. The rough division could be into inorganic (or primary), organic (or secondary) and psychoses caused by the use of psychoactive substances (1). Inorganic would include schizophrenia and bipolar disorder, and or-

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ganic all conditions that lead to homeostatic disorders in the brain, including endocrine disorders. Hypothyroidism is a decreased secretion of thyroid hormones. Causes of hypothyroidism can be congenital (atherosis, thyroid hemiagenesis) or acquired. The most common cause of hypothyroidism is Hashimoto's thyroiditis with a prevalence of 3% in the general population (3). Psychotic symptoms including paranoid ideas, visual and auditory hallucinations were previously considered common symptoms of hypothyroidism, while today it is known that these symptoms occur in about 5% of patients with hypothyroidism (4). These symptoms usually appear after the appearance of physical symptoms, i.e. a few months to several years from the beginning of hypothyroidism.

Diagnosis

The diagnosis of a psychotic episode is made on the basis of autoanamnesis and heteroanamnesis, as well as a psychiatric examination. Mental disorders most commonly present in patients with suspected psychotic episode are presence of:

I positive syndrome

- a) hallucinations – most often auditory, visual, tactile and olfactory.
- b) lunatic ideas – persecution (the impression that someone is following, observing the patient), influence (that the patient's behavior is under someone's control) and relationships (messages from the environment sent only to the patient).

II disorganization

- a) speech disorder as the most conspicuous symptom, impoverished speech, thought flow disorders, neologisms, echolalia.
- b) disorganization of behavior in the domain of motor skills and social interaction where symptoms can be present from catatonic stiffness, through agitation all the way to social distancing and neglect of hygiene.
- c) affective mismatch in terms of inadequate reaction, ideo-affective dissociation.

III negative syndrome

- a) alogia – difficulties in communication as a consequence of thinking disorders.
- b) anhedonia – a feeling of emotional emptiness, difficulty finding pleasure.
- c) abulia / hypobulia – complete or partial loss of will which is manifested by lack of initiative, passivity, decreased general functioning.
- d) attention deficit disorder (2).

After the suspicion of a currently present psychotic episode, and during the hospitalization of the patient, laboratory diagnostics is performed: determination of

complete blood count, biochemistry, urinalysis with toxicological findings (which exclude the abuse of psychoactive substances). In patients with a positive personal history of hypothyroidism (thyroiditis, radioiodine therapy), in those in whom inspection and palpation show changes in the neck (presence of goiter, scar from surgery) or inspection of medical records (endocrinologist reports on the treatment of hypothyroidism) it is necessary to determine the level of TSH, FT4, T4, T3. If the results indicate a high level of TSH with reduced thyroid hormones in consultation with an endocrinologist, it is necessary to include / correct thyroxine therapy and monitor the potential maintenance / withdrawal of psychotic symptoms.

It is especially important to be careful and think about this diagnosis in the elderly population because certain somatic symptoms of hypothyroidism can be presented as a normal aging process and be unrecognized. In such persons, it has been described in the literature that the symptoms of psychosis appear first, not because it is really so, but because the development of hypothyroidism and numerous previous symptoms are not recognized or interpreted as an aging process and the expected consequence (5,6).

Treatment

Patients with an acute psychotic episode are hospitalized for a period of 4 to 6 weeks, after which, in case of need, treatment can be continued in the conditions of a daily hospital with the aim of maintaining the stability of remission. During hospitalization, in parallel with the examination, the patients are initially treated with thyroxin or a combination of psychopharmaceutical (antipsychotics + thyroxin) and psycho/sociotherapy.

Internal medicine therapy used to correct endocrine imbalance represents the basis of treatment, and very soon after starting to take thyroxin, relief occurs psychotic symptoms.

Upon arrival of laboratory results in case of verified hypothyroidism (decreased FT4 with elevated TSH) in addition to psychopharmaceutical, patients are also prescribed thyroxin. Daily dose of thyroxin is optimized according to body weight 1.6 mcg /kg/day, with TSH measurement after 4-8 weeks (7). Preferably, the TSH level is up to 2.5 mIU /L (8).

As soon as the symptoms of psychosis are noticed, it is necessary to start treatment with antipsychotics even before proving endocrine disbalance. Additionally antipsychotics can be used as an adjunct therapy thyroxin, with the aim of achieving remission faster. However, the last review of the literature calls into question whether there is a scientific reason for such an approach (although it does not exclude the possibility given the small number of papers with topic) (9). So far, treatment with low initial doses is recommended second-generation antipsychotics (except clozapin, which has severe side effects that cause is recommended as the last line).

National guide for good clinical practice for the diagnosis and treatment of schizophrenia in its work "Acute phase therapy" provides guidance and analysis of antipsychotics based on different international guides, and in accordance with registered antipsychotics in Serbia, so it can serve as a guide for clinicians in choosing a drug for acute psychosis due to hypothyroidism. Antipsychotics of the second generation (atypical antipsychotics) is given priority over those of the first generation (classical antipsychotics) because they do not lead to extrapyramidal side effects (10). On the other hand, their use should be cautious, because their use is accompanied by the appearance of side effects, primarily in terms of the development of metabolic syndrome. Currently registered antipsychotics of the second-generation in the Republic of Serbia are: clozapine, risperidone, olanzapine, sertindole, quetiapine, ziprasidone, amylsupride and paliperidone.

Of the classic antipsychotics, which can be used as alternatives, registered in the Republic of Serbia are as follows: chlorpromazine, fluphenazine, haloperidol, levopromazine, sulpiride and cyclopentixol (11). Regardless of the choice of antipsychotics, it is always necessary to find balance in terms of the application of the minimum effective doses that reduce the risk of side effects and monitor potential occurrence of the same.

Literature data of the frequency of psychotic episodes resulting from prolonged and untreated hypothyroidism

Thyroxin is important for the global function of brain activity, and cholinergic activity in frontal cortex and hippocampus significantly increases in its presence. Thyroid dysfunction most likely leads to changes in cholinergic activity, global perfusion and global glucose metabolism in the CNS (12). Recent results of PET scanner of people with hypothyroidism have shown that there is a reduction in untreated hypothyroidism cerebral blood flow as well as decreased glucose metabolism (13).

The most common cause of hypothyroidism in the general population is Hashimoto's thyroiditis with prevalence of 3% in the general population. The peak incidence is in the fifth decade of life, and occurs 10-20 times more often in women than in males (3). The clinical presentation of hypothyroidism encompasses a wide range of mild symptoms such as: dry skin, constipation, hair loss, weight gain or depression; if the disease progresses and it is not treated for a very long time, it can cause myxedema, acute psychosis, acute mania and myxedema coma.

A causal link between thyroid disease and dysfunction of central nervous system was described in the late nineteenth century ("Report on Myxoedema", Clinical Society of London, 1888). After this description, clinicians began to publish case reports of patients with psychosis which was caused by prolonged unrecognized-untreated hypothyroidism. In 1949, Asher et al. published a paper describing 14 patients with

myxedema psychosis and hypothyroidism, of which 9 recovered only from application thyroxin replacement therapy (14). The hallucinations that occur in myxedema psychosis usually withdraw within a week after starting with thyroxin therapy. Psychosis has been described in the literature in persons with hyperthyroidism, but also it was described that hyperthyroidism was the cause of an acute psychotic episode, so clinicians should be careful when administering high doses of thyroxin because that sudden peak in thyroxin level in patients who had psychotic episodes may be trigger psychotic recurrence (15, 16).

In addition to psychotic symptoms, prolonged and untreated hypothyroidism can also be manifested other psychiatric disorders. Giunio-Zorkin and co-workers described a patient with mania as the first symptom of severe hypothyroidism (17). Hypothyroidism is a common comorbidity in patients with bipolar disorder, and patients with therapeutically resistant bipolar disorders have a higher incidence of hypothyroidism than the general population (18). In prospective cohort study conducted in Denmark in which patients with hypothyroidism were monitored, the results showed that patients with hypothyroidism are more likely to get sick and hospitalized at psychiatric clinics due to depression and bipolar disorder (19). Ueno and al. confirmed that psychotic disorders may occur before the physical manifestation of hypothyroidism or symptoms of hypothyroidism may not be pronounced in psychotic patients especially in the elderly population where the symptoms of hypothyroidism are attributed to the aging process (6).

Sancez et al. analyzed 27 cases from literature and they showed that period of reduction of psychosis can vary: from 4,4 days in patients who were on single thyroxin therapy; 6,25 days in patients who were treated with initially thyroxin and few days after with antipsychotic if there was need for it; 17.27 days was recovery in patients who was treated initially with antipsychotic and thyroxin (9). In all three groups of patients faster recovery was seen in mail than in female patients. This data suggests that antipsychotic drugs are not necessary in patients with acute psychosis that was caused by prolonged untreated hypothyroidism (9). This presumption would be wrong because of several reasons: 1) comparison between length of therapy and years of patient wasn't made; 2) response to therapy can vary and usually it is prolonged in elderly population than in younger people; 3) in all case reports there might be confounding factors that may impact on response to therapy; 4) authors pointed that one of limitation of their study is that they have analyzed 27 case reports in which decision on therapy could be under confounding factors that were not recognized and noticed (9). At this moment literature on this topic does not give clearly answer to question is antipsychotic necessary along with thyroxin. From analyzed case reports we can not find consensus about length of antipsychotic therapy. In every patient with this pathology who are initially treated with antipsychotic drugs those drugs should be gradually exclude.

Conclusion

Since changes in behavior and mental status can occur as a sign of untreated and prolonged hypothyroidism, regardless of the presence of its other clinical signs, it is very important that in patients with psychiatric diseases and manifestations, especially with acute ones, we must seek for its endocrine background. Therapeutic choice in patients with acute psychosis that occur as result from hypothyroidism or in combination with it, requires thyroxin treatment, and combination with antipsychotic is often needed, although the justification for such therapy is still not recommendation. After administration of thyroxin, and after reaching the reference values of FT4 and TSH, patients are transferred to a lower dose-maintenance therapy which is enough to control thyroid status in reference levels, by an endocrinologist. Initially administrated antipsychotics into the therapy are gradually reduced when we see withdrawal of the psychosis symptoms, and their final exclusion may be made with the continuous supervision of a psychiatrist.

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