

Mental Health, Emotional Stability, and Green–Psycho– Chemistry through Quality of Life Increased After Treatment for Non–Functioning Pituitary Macroadenomas: – A Systematic Approach

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Abstract: After treatment for a non- functioning pituitary adenoma (NFA) health-related quality of life (HR-QoL) improves considerably. However, the literature about the normalization of health-related quality of life after treatment is inconclusive. A concrete conceptualization of the health outcomes of patients with a non-functioning pituitary adenoma (NFA) can be helpful to understand the observed variety in HR-QoL outcomes and to improve clinical care and guidance of these patients. For this conceptualization, the Wilson and Cleary model were used. This model has a biopsychosocial character and has been validated in several patients' populations. In this present review, health outcomes of patients with a NFA were described at each stage of the model e.g., biological, physiological variables, psychological status, symptom status, functional status, general health perceptions and overall HR-QoL. Further improvement of quality of life should be supported by a pituitary specific care trajectory, including psychosocial care (e.g., self-management training), to beneficially affect characteristics of the patient and the healthcare environment, with the utmost goal to optimize HR-QoL in patients after treatment.

Although an increased quality of life (QoL) has been reported after long-term cure of functioning pituitary adenomas, the effect of successful treatment of non-functioning pituitary macroadenomas (NFMA) on quality of life has been fully addressed. Therefore, we evaluated of QoL parameters in patients successfully treated of NFMA.

Keywords: Mentalhealth, emotional stability, Green-Psycho-Chemistry, Non-functioning Pituitary macroadenomas.

I. Introduction

A non-functioning pituitary adenoma (NFA) is a benign growth in the pituitary gland that does not produce any excessive hormones into the blood and is not cancerous. Pituitary tumor (adenomas) that do not secrete active hormones are called clinically non- functioning pituitary adenomas. Most are large (macroadenomas), measuring more than one centimeter in size at the time of diagnosis. Intracranial lesions of pituitary adenomas, accounting for 6-10% of all symptomatic intracranial tumors. Pituitary adenomas are defined as abnormal

growth of tumors in pituitary glands (being adenomas, invasive adenomas, and carcinomas). Recent studies have shown that invasive adenomas may approximately affect 1 in 1000 people of the general population. The most frequent pituitary adenomas are microadenomas with an estimated incidence of 16.7%. Pituitary adenomas are also categorized as active-functioning adenomas; two-thirds of clinically diagnosed lesions are functional adenomas. Pituitary adenomas are also associated with psychiatric disorders including hostility, anxiety, apathy, depression, emotional instability, and irritability. Patients start experiencing symptoms when the large tumor compresses the optic nerves, leading to vision loss, or the loss of normal pituitary function. Endocrine-inactive pituitary adenomas comprise approximately 30% to 35% of pituitary tumors in most series and most common type of macroadenoma.

Non-functioning pituitary macroadenomas (NFMA) are most prevalent pituitary macroadenomas. The main symptoms are visual field defects and hypopituitarism, which are caused by mass effects of the tumor. Transsphenoidal surgery is considered the treatment of choice because medical therapy in general is ineffective to reduce tumor size. Visual field defects improve in more than 80% of all patients after surgery. In contrast, hypopituitarism does not improve in most patients after surgery for NFMA. To prevent tumor recurrence, selected patients may be treated by postoperative radiotherapy. Furthermore, patients also have improvement in sexual arousal and body shape after treatment and have a very prompt improvement in dimensions of socializing and tenseness.

Clinically Non-functioning pituitary Adenomas: Causes

1. Typically, the body produces hormones by taking a large molecule and cutting it at the right places to create a functioning-hormone. In some cases, something is wrong with this cutting process and a "functional" hormone is not made. The hormone might still travel into the bloodstream, but it is inactive and usually cannot be detected using standard blood tests.
2. In some cases, the hormones might be formed inside the cell, but there is something wrong with the transport process that is required to release it into the bloodstream.
3. In other cases, the tumor cells simply do not produce hormone.

Clinically Non-functioning pituitary Adenomas: Symptoms

1. When large pituitary adenomas (macroadenomas) grow upward into the brain cavity, the tumor can elevate and compress the optic chiasm.
2. A loss of outer peripheral vision, called a bitemporal hemianopsia.
3. When severe, a patient can only see what is directly in front of them; many patients do not become aware of their visual loss until it is quite severe.
4. Loss of visual acuity (blurry vision), especially if the macroadenoma grows forward and compresses an optic nerve.
5. Inability to perceive colors as brightly as usual.

II. Pituitary Failure or Hypopituitarism:

Increased compression of the normal gland can cause hormone insufficiency, called hypopituitarism. The symptoms depend upon which hormone is involved.

1. Reduction of sex hormones, luteinizing hormone (LH) and follicle-stimulating hormone (FSH).
 - In men, this can lead to a low testosterone level, causing decreased sexual drive and impotence.

- In some cases, there can be loss of body and facial hair.
 - In women, this can lead to infertility.
2. Large pituitary tumors can slightly elevate blood prolactin levels. Doctors think this occurs because of compression of the pituitary stalk, the connection between the brain and the pituitary gland. It is called the “stalk effect.”
 - In premenopausal women, this can lead to reduction or loss of menstrual periods and breast milk production (galactorrhea).
 - Prolactin levels are only slightly elevated, as opposed to prolactinomas in which the prolactin level is usually very high.
 3. More severe hypopituitarism can lead to hypothyroidism or abnormally low cortisol levels, which may be life threatening. Symptoms of severe hypopituitarism include:
 - Loss of appetite.
 - Weight loss or weight gain.
 - Fatigue.
 - Decreased energy.
 - Decreased mental function.
 - Dizziness.
 4. Changes in hormonal function can cause electrolyte imbalance in the blood, typically low sodium levels (hyponatremia). Symptoms could include:
 - Fatigue.
 - Seizures.

III. Clinically Nonfunctioning Pituitary Adenomas: Diagnosis

Imaging scans are not method doctors use to diagnose clinically nonfunctioning pituitary adenomas. We will also order hormone tests to evaluate the levels of pituitary hormones, confirming that there is no evidence of hormones production by the tumor.

Your doctor will conduct a thorough physical examination and ask you about your symptoms and medical history. He or she will order tests as necessary, including:

- Magnetic resonance imaging (MRI) scan.
- Hormone test.
- Vision test.

1. MRI imaging:

MRI imaging allows us to detect whether there are tumor present. Your doctor will use a special MRI pituitary protocol to best visualize the tumor. There are other tumors that produce symptoms like that of a pituitary adenoma. Your doctor will want to rule out these other tumors before confirming a diagnosis. Tumors that mimic the symptoms of a pituitary adenomas includes:

- Craniopharyngioma
- Rathke’s cleft cyst
- Meningioma
- Arachnoid
- Granulomatous diseases
- Glioma of the suprasellar region
- Metastatic tumor
- Chordoma

2. Hormones Testing

If your symptoms suggest pituitary failure (hypopituitarism), your doctor may order a complete evaluation of the endocrine system. Based on results of these blood tests, you may undergo additional hormonal studies.

3. Visual Testing

If you are experiencing vision problems, your doctor will be recommended that an experienced ophthalmologist evaluate you. The evaluation should include:

- Acuity testing of each eye
- Formal visual field testing

This will determine if you have a loss of peripheral vision.

IV. Surgery for Clinically Nonfunctioning Pituitary Adenomas:

For most patients with nonfunctional adenomas, surgically removing the adenoma is the most effective treatment.

Whether this will lead to long-term cure depends on the extent of surgical removal, which is related to:

- Tumor size.
- If the tumor invaded the cavernous sinus (the compartments on either side of the pituitary Sella).
- If the tumor expanded into the brain cavity.
- The experience and expertise of the operating surgeon.

If the surgeon was able to remove the entire tumor, the cure rate is 70 percent to 80 percent. Overall surgery improves:

- Vision in 75 to 90 percent of patients.
- Headache in 80 to 90 percent of patients.
- Suppressed pituitary function in 10 to 30 percent of patients.

If the pituitary adenomas require surgery, typically the best procedure is through a nasal approach. Our neurosurgeons who specialize in pituitary tumor surgery are experts in the minimally invasive endoscopic endonasal techniques. This procedure removes the tumor while minimizing complications, hospital time and discomfort. This advance technique requires specialized training and equipment. Very large tumors that extend into the brain cavity may require opening the skull (craniotomy) to access the tumor. Our surgeon are also experts in the minimally invasive “key-hole” craniotomy, utilizing a small incision hidden in the eyebrow. If after your surgery, some tumor cells remained or regrew, you may be a candidate for radiation therapy or a repeat surgery.

V. Medical therapy:

Medical therapy is available for most hypersecretory tumors. Most prolactin-secreting adenomas are effectively treated with dopamine agonists (bromocriptine and cabergoline). Cabergoline is generally preferred due to a better side-effect profile, and between 80-90% of patients can achieve hormonal control. Surgical intervention is ordinarily reserved for those who are intolerant of medical therapy due to side effects (e.g., nausea, headache, impulsive and compulsive behavior), whose prolactin levels remain elevated, or whose tumors continue to grow despite maximal medical treatment.

VI. Radiation therapy:

Doctors may recommend radiation therapy as a second-line therapy for endocrine-inactive tumors. Focused-beam radiation, named stereotactic radiosurgery, can be effective in controlling tumor growth. In some cases, radiation therapy may cause a loss of pituitary function, but less frequently than external beam radiation. Radiotherapy is most often employed in conjunction with medical or surgical therapy. Fractionated external beam radiation therapy can reduce excessive hormone production and can reduce the incidence of tumor recurrence. Radiation therapy has been used in patients who are deemed to be poor surgical candidates and has also been used as adjunctive therapy in patients with residual or recurrent active tumor.

Mental health, Emotional stability, and Green-psycho-chemistry associated with NFMA after Surgery:

Mental health:

Patients with pituitary diseases present with many psychiatric symptoms such as body image disturbances, depression, and adjustment disorder. In pituitary adenomas, one of the most common psychiatric manifestations is the presence of depressive systems significant enough to warrant diagnosis of a major depressive disorder.

Pituitary patients may recognize that the first signals of something being wrong with their system and body is when they find their sexual health and mental health deteriorating. For example, Cushing's Disease is a complex endocrine condition that results from abnormally high level of cortisol. This is characterized by such symptoms as truncal obesity, diabetes, hypertension, muscle weakness, and emotional lability. Major depression is noted as a prominent feature as well. Since women are affected five times more often than men and are often misdiagnosed as obese or depressed (Stewart, D, 2004). They may first find themselves in the therapist office searching for help. Causing, himself, acknowledged that 'psychic traumas may play an important role in the pathogenesis of pituitary disease (Causing, 1913). Acromegaly is also a serious and often undiagnosed and unrecognized condition that may be characterized psychologically with changes in personality and increased irritability, anxiety, and agitation. An increase in anger, with outbursts at the slightest provocation is possible. Acromegaly is a chronic and debilitating condition that usually results from a growth hormone (GH) secreting pituitary tumor (Furman & Ezzat, 1998).

Another disorder, thyroid hormone deficiency (hypothyroidism) is marked by such mental and emotional symptoms as mood changes, decreased cognitive abilities and mental slowness, decreased libido, hair loss, loss of energy, menstrual irregularities, erectile difficulties, and possibly infertility.

Mental health professionals have believed for years in the importance of a holistic approach, one that looks at the mind, emotions, spirit, and body. Professionals are needed as essential members of a well-formed treatment team. Research on families and health suggests that marriage and family therapist do have an important role in the treatment of physical illness (Campbell, 2003). Medical family therapy, or family systems medicine (Block, 1984) provides us in the mental health field with skills to work within, and with the medical field (McDaniel et al., 1992). Family therapist and other psychological professionals need to become more familiar with pituitary and hormonal disorder to identify potential symptoms, refers to qualified physicians, and assists patients and

families in relationship difficulties that often accompany such disorders more quickly. Family therapy can be an important component in the early identification and subsequent treatment of pituitary and hormone disorder.

VII. Emotional stability:

Several studies have shown that acromegaly after pituitary adenomas is associated with psychological impairments, mostly emotional: depression, anger, anxiety, fatigue. Worse emotional states have negative impact on quality of life. Pituitary tumors and other disorders of the neuroendocrine system can certainly bring about change: physical, mental, emotional, and behavioral. And such changes often disrupt and change family connections and relationships. It is important to understand the illness and its potential impact on all aspects of life. It is vital for patients, their doctors, family, and others to communicate about expectations for physical as well as mental health recovery. Getting a proper diagnosis and medical treatment is important but pituitary disorders involves a lot more. Patients and their family are also often surprised at the mental and emotional changes that occur for a while even following medical and surgical treatment. The ups and downs of hormonal shifts until thing become stabilized can be disastrous without proper expectations and the support close family members. The family must be considered part of the treatment team, perhaps the most important since they will hopefully be there for a lifetime that follows. The process of healing can be lengthy and certainly scary but a skilled treatment team it doesn't have to be a lonely path.

Green-Psycho-Chemistry:

Green-psycho-chemistry (Green exercise, meditation, yoga, and use of natural products) serotonin replenishing effect works to create a utopian chemical environment of the production of new brain cells, making you a happier and healthier person overall. Green-psycho-chemistry and some natural are influencing the human body at the motivator level. Approximately 86 billion brain cells, most act are influenced by serotonin, known as the happy neurotransmitter, serotonin is key to helping relay signals from one part of the brain to another. This crucial chemical has a profound impact on our mood, contributing greatly to our overall state of well-being. Green-psycho-chemistry is called for its ability to make (help) relax and de-stress the mind and body. When we are stressed, our bodies produce cortisol, and adrenaline is abundance. However, over the long term, the chemical cocktail presents when under chronic stress is not normal, and can tear your body down, destroying healthy muscle and bone, blocking the creation of good hormones, eventually leading to anxiety, depression, increased blood pressure, brain fog, insomnia, inflammation, the test goes on and on. Clearly, we can say, too much of this stress hormone is really bad news for overall physical health as well as mental health. Research (at UC Davis in 2013) discovered a very powerful connection between mindfulness and stress hormones like cortisol, with remarkable results seen within only a few short weeks. Today's, meditation, green-psycho-chemistry, and green exercise are seen as effective remedy to deal with stresses of daily life, to address the conflict in our mind and in society too.

Pituitary macroadenoma: Coping with Treatment.

We will learn more about coping with the physical, emotional, social, and financial effects of a pituitary adenomas and its treatment. Every treatment can cause side-effect or changes to your body and how you feel. For many reasons, people do not experience the same side-effects even when they are given the same treatment for the same type of tumor. This can make it hard to predict how you will feel during treatment.

As you prepare to start treatment, it is normal to fear treatment-related side-effects. It may help to know that your health care team will work to prevent and relieve side-effects. Doctor's call this part of treatment "palliative care" or "supportive care". It is an important part of your treatment plan, regardless of your age or the stage of disease.

Coping with physical side-effects

Common physical side-effects from each treatment option for a pituitary macroadenoma are described within the type of treatment section. Changes to your physical health depend on several factors, including the tumor's size, the length and dose of treatment, and your general health.

- Talk with your health care team regularly about how you are feeling.
- It is important to let them know about any new side-effect or changes in existing side-effect. If they know how you are feeling, they can find ways to relieve or manage your side-effects to help you feel more comfortable and potentially keep any side effects from worsening.
- You may find it helpful to keep track of your side-effects so it easier to explain any changes with your health care team. Tracking side-effect is not a new development. When a new drug is developed and first tested in a clinical trial, the researchers record the side-effects of the new treatment.
- Sometimes, physical side-effects can last after treatment ends. Doctors call these long-term side effects. They call side-effect that occur months or years after treatment late effects.

Coping with emotional and social effects:

You can have emotional and social effects as well as physical effects after a diagnosis. They may include dealing with difficult emotions, such as sadness, anxiety, anger, or managing your stress level. Sometimes, people find it difficult to express how they feel to their loved ones. Some have found that talking to an oncology social worker, counselor, or member of the clergy can help them develop more effective ways of coping and talking about tumor.

Sometimes patients with a pituitary adenoma have cognitive changes or experience depression. Talk with your health care team if you experience any of these changes. You can also find coping strategies for emotional and social effects in a separate section. This section includes many resources for finding support and information to meet your needs.

Coping with financial effects:

Treatment can be expensive. It is often a big source of stress and anxiety for patients and their families. In addition to treatment costs, many people find they have extra, unplanned expenses related to their care. For some people, the high cost of medical care stops them from following or completing their treatment plan. This can put their health risk and may lead to higher costs in the future. Patients and their families are encouraged to talk about financial concerns with the member of their health care team. That is managing financial consideration.

VIII. Discussion:

Health-related quality of life is a concept that refers to individual wellbeing. It is based on how a particular individual feels, respond and functions in daily life. Subjects will value their quality of life, taking into account their expectations, standard and goals, as well as emotional, physical, and social aspects in their lives, which may be effects of their lives, which may be affected if a disease is present. Mental health and psychological function measures have been described to be impaired in prolactinoma patients. In men, decreased libido, erectile dysfunction and poor seminal fluid quality are frequent consequences in prolactin hypersecretion. In women, hyperprolactinemia causes amenorrhea, galactorrhea, vaginal dryness, dyspareunia, and decreased libido, which can lead to infertility. These reproductive impairments have a great influence on patients' quality of life, especially in women. To treat these reproductive impairments is important because they can impact on patient's quality of life even after correction of hyperprolactinemia.

IX. Conclusion:

Surgery, radiotherapy, and pharmacotherapy constitute the present therapeutic armamentarium of the management of pituitary macroadenoma. Surgery, which includes trans frontal craniotomy and transsphenoidal surgery, allows removal of the macroadenomas or reduction of the tumoral mass and is considered the first -line therapy for non-functional macroadenomas and acromegaly. Several studies have reported recovery of visual function after transsphenoidal surgery.

The present study for the first time revealed that transsphenoidal surgery for pituitary macroadenomas can improve not only visual dysfunction but also deteriorated VR-QoL (visual- related quality of life). Thus far, the improvement in VR-QoL after surgical interventions for macular hole, epiretinal membrane, and age-related macular degeneration has been evaluated. Compared with that reported in these previous studies, the VR-QoL in the patient in this study improved to a greater degree after transsphenoidal surgery for pituitary adenomas. Because most pituitary adenomas are benign and rarely infiltrate the optic nerve or chiasm, transsphenoidal surgery usually enables the removal of the pituitary adenomas without wounding the optical nerve or chiasm. Therefore, visual dysfunction of pituitary macroadenomas, which is caused, not by infiltration by the mass effects, may be easily improved by transsphenoidal surgery.

Knowledge of tumor pathophysiology and biology is rapidly increasing, and pharmacotherapy of tumors is evolving. Targeting specific receptors and genes implicated in tumor pathogenesis and determining predictors of response using radiological, psychological, pathological, and clinical characteristics will lead to more personalized medicine. It is our hope that care of patients with pituitary adenomas will continue to advance over time, achieving both biochemical and tumor response, but also significant improvement in quality of life and comorbidities.

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