Serum nutrient deficiencies in the patient with complex temporomandibular joint problems

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This study evaluated serum nutrients in 23 patients who had previous Proplast/Teflon implants to their temporomandibular joints (TMJ) and continued to remain in chronic, severe, irresolvable pain despite subsequent surgical reconstruction. All of the patients were women, and their average age was 40.6 years (range, 28–55 years). Standard blood assays were performed for beta-carotene (vitamin A), folate, serum iron, ferritin, zinc, magnesium, and vitamins B1, B6, B12, and C. Each patient was deficient in at least one of these 10 elements, with an average of 3.3 elements. Some factors that may be responsible for the deficiency state include inadequate nutritional intake, malabsorption, utilization dysfunction, increased requirements, or drug interactions. In conclusion, the patient who has had multiple, complex TMJ operations with a history of TMJ Proplast/Teflon implants and poor treatment results may be suffering from an unrecognized malnutrition state, substantially adding to the patient's morbidity. Nutritional evaluations, dietary counseling, and appropriate medical management may improve the treatment outcomes for these patients.

INTRODUCTION

In the 1980s and early 1990s, Vitek Inc. (Houston, TX) placed products on the market for temporomandibular joint (TMJ) reconstructive procedures. These devices contained the material Proplast/Teflon (PT), a combination of polytetrafluoroethylene polymer matrix and either vitreous carbon, aluminum oxide, or hydroxyapatite particles suspended within the matrix. The company's premise was that the PT material would allow bone ingrowth to stabilize the implant in position on the fossa, and a superficial layer of Teflon would allow a smooth functional surface on which the mandibular condyle could articulate. This product was approved by the Food and Drug Administration (FDA) and used as an artificial articular disc replacement for the TMJ. A second product from Vitek released on the market without FDA approval was a total joint prosthesis to replace the natural TMJ joint; it contained large amounts of the PT material. The fossa component had an articulating surface of polyethylene backed with PT, and the mandibular component had a cobalt-chromium-molybdenum alloy condylar head and shaft (coated with PT) to attach to the mandible. Function and loading of the joints with these products resulted in fragmentation and microscopic particulization of the PT materials, creating a proliferative foreign body giant cell reaction that caused local destruction of the hard and soft tissues and migration to other parts of the body. The FDA finally recalled these products in 1992. However, thousands of patients were left to live with the adverse local and systemic consequences created by these materials. It was predicted that all of these Vitek products would fail.

Management of the untoward sequelae after failure of TMJ PT implants presents a significant challenge to the oral and maxillofacial surgeon. The FDA developed specific recommendations for patients with these implants still remaining, including patient notification and recall for clinical examination, magnetic resonance/computed tomography imaging of the TMJ and associated anatomic structures, and radiographic examination of the joint every 6 months for as long as the implant remains in situ (1, 2). Reconstruction in some patients who had had multiple, complex TMJ operations with a history of TMJ PT implants is challenging, and it is difficult to predict the surgical outcome. This patient population often presents to the clinician with complaints of severe pain, TMJ dysfunction, associated musculoskeletal deformity, and malocclusion.

PT implants can cause numerous complications, including fragmentation, foreign body giant cell reaction, particle migration, pain, lymphadenopathy, severe osteoarthritis, bone resorption, and perforation into the middle cranial fossa (3–9). The human body is unable to degrade these polymers, and severe local and systemic reactions can occur. Further, clinical observations suggest that some patients may develop nonspecific connective tissue/autoimmune diseases that may be promoted or exacerbated by the TMJ PT implant materials (3).

Human leukocyte antigen studies

The possible relationship between certain arthropathies and an increased incidence of specific human leukocyte antigens (HLA) has been studied (3, 4). Namey et al (4) performed

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HLA typing on 37 patients (35 women and 2 men) with TMJ dysfunction and failed TMJ PT implants. It was hypothesized that an increased incidence of HLA markers is associated with a predisposition to connective tissue and autoimmune diseases. Most of the patients were experiencing chronic pain and dysfunction. In the patient sample, 11 of 37 (30%) had HLA-B locus antigens associated with psoriasis or psoriatic arthritis versus 22 (18%) of 125 control subjects. Other patients in the sample, 24 of 37 (65%), demonstrated antigens associated with other connective tissue or autoimmune disorders, including juvenile rheumatoid arthritis, sarcoidosis, ankylosing spondylitis, Reiter's syndrome, Sjögren's syndrome, scleroderma, Still's disease, and systemic lupus erythematosus. These observations suggest that predisposition to connective tissue and autoimmune diseases may predispose these patients to immune dysfunction and contribute to treatment failure. Medical histories of the 35 female patients in this study also included a history of hysterectomy (40%), removal of ovaries (31%), endometriosis or uterine fibroids (26%), fibrocystic breast disease (49%), low-grade fever (35%), and sensitivity to nonprecious metals (51%). The incidence of these findings is much higher than that in the healthy female population.

Immune system function after TMJ PT implantation

Wolford et al (10) evaluated the human immunologic response to TMJ PT implants in 12 patients. The total lymphocyte count was calculated and immune response assessed by immunophenotyping peripheral blood lymphocytes IA, CD2, CD3, CD4, CD8, CD4:CD8 ratio, CD20, CD56, and surface immunoglobulin-positive cells. The IA subset was below controls in 73% of patients, and the CD4:CD8 ratio was decreased significantly below the normal range. By contrast, the CD56 subset was elevated in 60% of patients. An in vitro lymphocyte activation assay was used with six patients to determine the presence of activated T cells. Lymphocytic activation was present in four of six patients. The activated T-cell response was greater in those patients experiencing more severe symptoms. The immunologic consequences of the activated T-cell response remain to be investigated. In four patients with TMJ PT implants who had a significant decrease in their immunodeficiency panel, removal of the PT implants with extensive joint debridement and reconstruction with a custom-made total joint prosthesis resulted in a significant improvement toward normal values in three of the four patients at 1 year after surgery.

Clinical observations suggest that some patients may have developed connective tissue diseases that have been promoted or exacerbated by TMJ implant materials. Some medical conditions that have been recorded in patients with TMJ implants that contain PT, Silastic, or polymethylmethacrylate implants include chronic fatigue syndrome, chronic pain, fibromyalgia, impaired cognition, short-term memory loss, lupus, psoriasis, psoriatic arthritis, sarcoidosis, polyarthritis, human adjuvant disease, scleroderma, Sjögren's syndrome, rheumatoid arthritis, visual disturbances, localized and distant muscular disease, neurologic dysfunction, chronic low-grade fever, generalized synovitis, and significant hormonal imbalances (10, 11). Undifferentiated or mixed connective tissue disease may be a common finding, or these patients may have an undefined polymeric disease. Problems associated with these conditions, especially chronic pain, physical limitations, and diminished mentation, often render these patients partially or totally disabled. Foreign body giant cell granulomas have been reported in the TMJ, masticatory muscles, parotid and submandibular glands, and regional lymph nodes, as well as on the roof of the orbit, within the orbit, in the lung, and in breast biopsy specimens (10, 11). The extent of systemic involvement with alloplastic materials remains unclear and requires further investigation.

TMJ reconstruction following failed TMJ PT implants

Henry and Wolford (1) previously reported on the treatment outcomes for TMJ reconstruction after PT implant failure and found that reconstruction of the TMJ in these patients was most predictable with a custom-made total joint prosthesis (TMJ Concepts Inc., Ventura, CA) compared with the use of various autogenous tissues. They found that reconstruction with the total joint prosthesis provided an 88% success rate for stability and function. In contrast, success rates with various autogenous tissues used for the same application were 13% to 31% for temporalis grafts, 8% for dermis grafts, 25% for conchal cartilage grafts, 12% for costochondral grafts, and 21% for sternoclavicular grafts. The level of pain reduction in patients after custom-made total joint prosthetic reconstruction was good in 46% of the patients, fair in 38%, and poor in 16% of the patients. Poor outcomes were related to no significant reduction in pain and/or jaw dysfunction. Wolford and Karras (12) reported that the use of fat grafts harvested from the abdomen and packed around the prostheses has significantly added to the success rate by decreasing the postsurgical recurrence of the foreign body giant cell reaction, as well as heterotopic bone formation around the prosthesis. Despite these advances in reconstruction techniques, a group of patients continues to experience chronic, irresolvable, severe pain and dysfunction after application of reconstruction methods that have seemed adequate for other PT patients with similar problems. This present study evaluated these patients for possible nutritional deficiency states that may contribute to their poor outcomes.

No previous studies have examined the prevalence of nutritional deficiency states in patients who have had previous PT TMJ implants and remain in chronic, irresolvable pain with poor treatment outcomes. The aim of this study was to evaluate the general nutritional status in this patient population by screening for specific common nutritional deficiency factors.

MATERIALS AND METHODS

This study evaluated 23 female patients with multiply operated TMJs seen in the private practice of one of the authors (LMW). All patients were in severe, chronic pain and had a history of previous TMJ PT implant placement with multiple previous TMJ surgeries. The average age at the time of evaluation was 40.6 years (age range, 28–55 years). Standard serum assays were performed on each patient for the following nutritional elements: beta-carotene (vitamin A),

Table 1. Results of nutritional evaluation by serum assays (n = 23 patients)

Nutrient	Serum levels (% of patients)		
	Low	Normal	High
Iron	48%	46%	6%
Ferritin	70%	24%	6%
Beta-carotene	48%	52%	0%
Vitamin B1	52%	48%	0%
Vitamin B6	57%	37%	6%
Vitamin B12	35%	65%	0%
Folate	26%	74%	0%
Vitamin C	57%	43%	0%
Magnesium	22%	78%	0%
Zinc	26%	58%	16%

serum iron, ferritin, folate, magnesium, zinc, and vitamins B1, B6, B12, and C. The serum assays were performed during the chronic pain management of these patients or prior to a surgery, but not within 6 months after surgery. Fasting prior to blood acquisition was not requested. Laboratory results were categorized into one of the following three groups: low values (below normal range), normal values, and high values (above normal range). Clinical signs of nutrient deficiencies for patients were determined from medical reports, laboratory testing, and clinical evaluations.

RESULTS

A large incidence of malnutrition was encountered in the series of patients screened. *Tables 1* and *2* summarize the results of the 10 nutritional elements and clinical evaluation expressed as percentage values of the total number of patients. Each patient showed low values in an average of 3.3 elements (range, 1–6).

Iron, vitamin C, and vitamin B6 were the most common deficiencies seen. Depleted iron stores (evaluated by serum ferritin levels) were found in 70% (16/23) of the patients, while 48% (11/23) of the patients had low serum iron levels. A laboratory diagnosis of anemia was made on the basis of serum iron values obtained. Five of the 16 patients deficient in ferritin were thus not anemic based on measured serum iron levels. A high incidence of vitamin deficiencies was seen in patients for beta-carotene (48%, 11/23); vitamin B1 (52%, 12/23), vitamin B6 (57%, 13/23), vitamin B12 (35%, 8/23); folate (26%, 6/23); and vitamin C (57%, 13/23). Other deficiencies included zinc (26%, 6/23) and magnesium (22%, 5/23). The occurrence of excessively high values of the micronutrients tested was seen in an insignificant number of patients (≤6%), except zinc (16%).

Some other clinical and laboratory findings suggestive of deficiencies in this group of patients were as follows: glossitis, 48% (11/23); anemia, 48% (11/23); cheilosis, 26% (6/23); poor skin healing, 48% (11/23); and hair loss, 52% (12/23).

DISCUSSION

Table 2. Results of clinical evaluation (n = 23 patients)

Condition	Percentage of patients
Glossitis	48%
Anemia	48%
Cheilosis	26%
Poor healing	48%
Hair loss	52%

The wound healing process following trauma or surgery is a complex interaction of sequential events leading to repair of the injured site. It can broadly be divided into four phases: inflammation, proliferation, remodeling, and maturation (13). After any kind of trauma, the body enters into a catabolic state with increased metabolic and protein breakdown. Malnutrition is well known to significantly increase the rate of posttraumatic and postoperative complications (13). Malnutrition can also alter the host immune response, thereby affecting the person's healing capacity.

Beta-carotene from green, leafy vegetables is ingested and converted to vitamin A (retinol) in vivo. Vitamin A is required for epithelial integrity and helps in lysosomal stability and glycoprotein synthesis. Vitamin B1 (thiamine) is involved in neurotransmitter synthesis and energy production, while vitamin B6 (pyridoxine) is essential for the synthesis of many proteins, including neurotransmitters. Vitamins B6 (cyanocobalamin) and folate are needed for DNA synthesis, which is essential for cell replication and repair. A deficiency of folate can cause central nervous system irritability, glossitis, diarrhea, depression, weight loss, and anemia. Vitamin C (ascorbic acid) is important for collagen synthesis and repair of body tissues. It is also known to decrease postexercise stiffness and reduce capillary fragility (14). Many dietary minerals, including iron, calcium, and magnesium, are also considered important factors in bodily functions, especially muscle function, and zinc is essential for cell mitosis and proliferation (13). Iron is needed for synthesis of hemoglobin, which provides oxygen transport to the tissues. Oxygen is necessary in all four phases of wound healing (13). Supplemental nutritional support, including zinc and certain vitamins, has been shown to increase the wound healing capacity of patients with diabetes mellitus (13).

Deficiency of vitamin A causes night blindness, xerophthalmia, keratomalacia, perifollicular hyperkeratosis of the skin, and increased susceptibility to infection (15). Deficiency of vitamin B1 can cause beriberi. Early deficiency symptoms include fatigue, irritation, poor memory, sleep disturbances, anorexia, abdominal discomfort, and constipation. Dry beriberi commonly presents with peripheral neuropathic changes, and wet beriberi includes cardiovascular changes. Wernicke's encephalopathy and Korsakoff syndrome are forms of cerebral beriberi (15). Deficiency of vitamin B6 can cause glossitis, seborrheic dermatitis, lymphopenia, and peripheral neuropathy (15). Vitamin B12 deficiency can cause peripheral neuropathic changes and megaloblastic (pernicious) anemia. Severe deficiency states of vitamin C (scurvy) can lead to lassitude, fatigue, irritability, vague arthralgias, and myalgias in the initial stages, followed by swollen and bleeding gums, the appearance

of splinter hemorrhages, and petechiae (15). Vitamin B12 deficiency is rare in the general population but was present in 35% of our patients.

Deficiency of iron causes microcytic, hypochromic anemia with symptoms like koilonychia, dysphasia, and tiredness (15). Zinc deficiency affects cell-mediated immunity and wound healing, with poor growth and appetite (15). Severe hypomagnesemia can cause personality changes, anorexia, tetany, vomiting, and lethargy (15). It also causes hypocalcemia and hypokalemia, which further affect muscle function.

Nutritional inadequacies are considered crucial perpetuating factors in myofascial pain and dysfunction and commonly occur with sources of mechanical stress (14, 16–18). Vitamins and minerals are considered micronutrients. They are usually consumed in small amounts (<1 g/day) and are usually absorbed unchanged (15). While vitamins A, D, E, and K are fat soluble, vitamins B group and C are water soluble. It has been established that low normal levels of vitamins B1, B6, B12, and/or folic acid are considered suboptimal and are frequently responsible when only transitory relief is obtained by specific myofascial treatment of involved muscles (14). Abnormally low values constantly aggravate myofascial trigger points and can cause chronic pain (14). Five nutritional elements assayed in this study that have been previously reported to be important in pain syndromes are vitamins B1, B6, B12, folic acid, and vitamin C. Other vitamins and micronutrients are also considered significant but have not yet been investigated in detail (14).

Common clinical signs and symptoms that are suggestive of nutritional deficiencies fall into four categories: 1) *neurologic:* muscle cramps, twitching, irritability, dysesthesias, loss of taste/smell, depression; 2) *gastrointestinal:* anorexia, abdominal cramps, diarrhea, nausea; 3) *dermatologic:* dry skin, hair loss; and 4) *general:* fatigue, weakness, listlessness. As many of these findings are nonspecific, they may overlap with other deficiencies and illnesses that may coexist. Our limited nutritional assessment suggests that other nutritional deficiencies may also be present. Additional research in this area is needed.

Nutritional deficiencies can occur in 30% to 40% of the normal population. Multiply operated patients with failed TMJ PT implants and with chronic, severe pain are prime candidates for developing nutritional problems. Several etiological factors may contribute to this malnutrition state: 1) inadequate nutritional intake secondary to masticatory difficulties, pain, or depression; 2) malabsorption due to gastrointestinal dysfunction or disease (i.e., Crohn's disease, celiac disease, irritable bowel syndrome); 3) nutrient utilization dysfunction (e.g., liver disease); 4) increased nutritional requirements (i.e., thyrotoxicosis, pregnancy, lactation); and/or 5) interaction with other drugs (e.g., vitamin B6 is deactivated by drugs like penicillamine, isoniazid, hydralazine).

Each of the 23 patients studied had at least one deficiency, and up to six, in the 10 micronutrients studied. The average number of deficiencies was 3.3 per patient. A comparison group of rheumatoid arthritis patients with no history of exposure to the PT materials or TMJ surgeries showed a deficiency of only 1.1 micronutrient per patient (19). This group comparison may indicate that the PT material, number of TMJ operations, and associated pain may increase the occurrence of deficiencies in the nutrients studied.

Although the sample size of our study is small, the results show that significant deficiency states of micronutrients do occur in those patients who have been exposed to TMJ PT implants but continue to have severe, chronic pain and poor clinical outcomes (e.g., poor jaw function, difficulty eating, facial imbalance). Development of systemic autoimmune-like diseases has been documented because of reactions to the PT materials. The role that PT plays in the development of malnutrition, if any, is unknown. It may be that patients predisposed to malnutrition states may be at greater risk of developing malnutrition after exposure to TMJ PT implants due to multifactorial reasons that are not yet clearly understood. Malnutrition may possibly play a role in other TMJ conditions, but these groups have not been studied. Likewise, malnutrition may possibly play a role in other medical conditions or diseases where patients suffer from severe, chronic, irresolvable pain. Malnutrition conditions can lead to further deterioration of the patient's medical health, thereby promoting pain, systemic infections, and disease, interfering with the body's reparative mechanisms, and thus preventing optimal and successful surgical treatment of these patients. Such patients often require high-dose analgesic therapy for adequate pain control. It is possible that malabsorption syndromes and drug interactions cause a decreased uptake of oral drugs administered, which leads to higher dosage requirements, thereby increasing the likelihood of adverse effects and narcotic dependency. The results of this study suggest that nutritional assessment may be helpful in treating patients who have had multiple, complex TMJ operations and experience severe, chronic, irresolvable pain. Appropriate dietary counseling and supplemental nutritional treatment may be beneficial to improve treatment outcomes.

CONCLUSIONS

Reconstruction of complex TMJs is challenging. The systemic effects of PT, Silastic, and other polymeric materials that undergo fragmentation and formation of particulate debris in the TMJ are not clearly understood (11). The importance of nutrition in clinical medicine is being increasingly acknowledged, primarily due to recognition of the fact that malnutrition frequently occurs in prolonged illness and accompanies acute injury and complicated surgical procedures (15). Malnutrition may be a cofactor interfering with the healing process and causing or augmenting pain and/or depression in these patients.

The findings of this study also suggest that many other unknown deficiencies, which were not evaluated, may coexist. Based on our preliminary findings, it is suggested that patients with complicated TMJ problems and previous exposure to PT implants who continue to be in severe, chronic, irresolvable pain may also be suffering from an unrecognized state of malnutrition that may add to the morbidity. Nutritional evaluations, dietary counseling, and appropriate medical management may be beneficial to these patients. Identification and correction of

the malnutrition problem in its early stages may decrease one of the adverse contributing factors for poor clinical outcomes in these complex patients.

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