Cervicogenic Headache Manipulative Treatment Success, MRI Imaging, TNF-α high levels.

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ABSTRACT:
Cervicogenic headache [CEH], a relatively common form of headache arises from the damaged structures around the neck. There is, however, a controversy about the role of whiplash injury in the generation of CEH. Furthermore, the efficacy of manipulative therapy in CEH is doubted. We present striking data on patients with CEH that developed following whiplash injury and the patients were treated successfully by manipulative therapy. TNF-alpha content in the plasma of the patients was observed to be strikingly large. TNF-alpha specifically interacts with the cell surface receptor molecules affecting the cell properties, adhesion, surface charges changes that govern permeability, gating currents and signalling, which should also be investigated and monitored for a meaningful correlation with the clinical state of the patient.

KEYWORDS: cervicogenic headache, whiplash injury, manipulative therapy, physical findings, zygapophyseal joint, TNF-alpha

ABBREVIATIONS cervicogenic headache: CEH, whiplash injury: WI, manipulative therapy: MT, zygapophyseal joint: ZJ, muscle post-isometric-relaxation: PIR.

INTRODUCTION

Cervicogenic headache [CEH], a relatively common form of headache arises from the damaged structures around the neck. These structures may include joints, ligaments, muscles, and cervical discs that have complex nerve endings.

There is a broad agreement about the diagnostic criteria of CEH described by Sjaastad (1) (2), but there is a controversy about the role of whiplash injury (WI) in the generation of cervicogenic headache (CEH) as well as its treatment by manipulative therapy (MT). Leone et al. (3) and Obelieniene et al. (4) doubt that CEH may start following WI. In contrast, Delfini et al., (5) Bono et al., (6), Radanov (7), Dumas et al., (8) Drottning et al. (9) have observed a number of CEH cases following WI, head and neck pain previous to car accidents were more frequent in CEH individuals than in those in the cohort without CEH. Jensen (10) reported pre-existing headache before the trauma in 39.9% of the patients, women being in the majority. Although MT is widely used for the complementary treatment of CEH, there are only a few studies on its efficacy in WI generated CEH cases (11).

At the Manual Medicine Outpatient Clinic of the National Institute for Rheumatology and Physiotherapy (NIRP) about 200 headache patients are treated each year, among them 1-2% started with WI and their number is increasing.

CASE REPORT

Patient No. 1

A 27-year-old female, dental assistant (born in 1976). She suffered the onset of a tension type headache at the age of 16, bilaterally in the temporal areas, attacks occurred 1-2 times a month. She attended our outpatient clinic first in 1997. At a thorough physical examination (see in (12) (13) (14)) the mobility of the upper ZJs were free, no sub-occipital muscle spasm was however found, but the peri-cranial muscles were sensitive to digital pressure, there were no limitation of the neck range of motion (ROM), neck movement was pain free, nevertheless the deep cervical flexor muscles were weakened. MT was performed, but without significant improvement and the patient discontinued MT. In December 1999 the patient was hit from behind while driving her car and suffered a WI. Following the accident a pain occurred in the cervical area, she received a cervical support for two weeks, and then a headache developed with a frequency of 3-4 days a week. A sharp and shooting pain could be induced bilaterally in the nuchal area (though it was more severe at the left side) by bending the neck backwards or by turning her head. ROM of the cervical spine was limited: left and right rotations were found 30 and 60 degrees respectively, extension 10 degrees, ante-flexion 50 degrees, whereas lateral flexions were 60-60 degrees. She received pain killer infusions, which temporarily improved her conditions. The MRI revealed a perpendicular disc protrusion at the C4/ C5 area, which slightly pressured the anterior cerebrospinal space and also a slight protrusion at the C5/C6 level (plate 1). From September 2001 she was treated at a pain clinic by repeated infusions, where she also received physiotherapy, nevertheless her condition did not improve. A neurosurgical examination recommended discectomy. The patient however returned for MT to our clinic rather than undergoing surgery. Headaches occurred 3 times a week and lasted 12 hours, with an intensity of 85 mm on a numeric pain scale (VAS, max. 100 mm). The special examination of the segmental/ ZJ mobility revealed that ante-flexion translation and the springing test in rotation of both C0/C1 cannot be carried out, the rotation to the right in the C1/C2 segment was reduced, while there a slight hypermobility could be felt in the C2/C3 segment, further on hypomobility and pain on pressure in the C4/C5 and C5/C6segments, but in the C6/C7 segment hypo-mobility without pressure pain. Pericranial muscles

were not sensitive to pressure applied during palpation, whereas sub-occipital deep muscles and upper trapezius were in spasm and tender to palpation. The head/neck of the patient was in an increased forward bending position, the strength of the deep cervical flexor muscles decreased (their flexion endurance was reduced to 8 seconds). Laboratory analysis demonstrated extremely high TNF-alpha values (Table 1.). According to the above findings the patient met the diagnostic criteria for CEH. As no neurological deficit was demonstrated in the upper arm, discectomy was delayed and MT started, twice a week for the first two weeks, and then once a week for another two weeks. The hypo-mobile segments (C0/C1, C1/C2, C6/C7) were mobilised, weakened muscles were isometrically strengthened, muscle spasm was treated by muscle post-isometric-relaxation (PIR). After four weeks MT, both active and passive range of motion returned to normal, suboccipital muscle spasm disappeared; movements in the hypo-mobile segments became free, whereas abnormal tenderness in the segments C4/5/6 resolved, cervical flexion endurance was increased to 22 seconds. The patient continues physical exercises, 10 minutes a day, to strengthen her cervical muscles. Patient was symptom free until January 2002, when following a sledge accident her headache returned. MT was again successfully used; subtle cervical pain can be however provoked by physical overburdening.

Patient No. 2

A 62-year-old female, computer technician (born in 1941), was a competitive rowing athlete at her youth; she still rows as a leisure. She suffered pain onset at the age of 20, when she had 2-3 attacks in a month, pain started in the morning, at the back of her head, and spread bilaterally to the temporal areas. The patient describes her pain as sharp, shooting, and intense. The pain was triggered by moving her neck; she had to use pain killers. In 1996 she was treated for CEH by MT (4 times during 2 weeks), hypo-mobility in the ZJs: bilateral C0/C1, left C1/C2 and bilateral C6/C7 was resolved and

she became symptom free. In July, 1997 she suffered a WI, commotion and fracture of her leg during a car accident, and her headache reoccurred. A sharp pain started bilaterally at the occipital area almost each morning (though it was more severe on the left side), she received pain killer infusions and electrotherapy, which somewhat improved her condition, nevertheless, she had to take pain killers twice a day. In August 1999 she suffered an injury after an awkward neck positioning during rowing, following which the cervical movements became restricted and her pain worsened. She were treated at a pain clinic and she also received electrotherapy, both of which were however unsuccessful. An MRI scan revealed that a para-median disc hernia between the C4/C5 vertebras intruded into the right ventral cerebrospinal space (plate 2) Laboratory analysis demonstrated extremely high TNF-alpha values (Table 1.). Following a neurosurgical examination a discectomy was recommended to be performed within two weeks. Then she returned to our department for a MT. The frequency of the attacks was six times a week, with an average duration of 31 hours a week; the intensity was 78 measured on VAS (max. 100 mm). Left rotation was found to be 20, right rotation 45, flexion 30, extension 0 degrees. The special physical examination revealed ZJ hypomobility bilaterally in the C0/C1, in the left C1/C2, in the C5/C6 and C6/C7, whereas hyper-mobility was found in the C2/C3 bilateral ZJs, furthermore there were spasms in the left suboccipital and also in the bilateral upper trapezius muscles. The patient's flexion endurance was reduced to 12 seconds. Since there was no neurological deficit at the upper extremities, surgery was postponed and MT started twice a week for 2 weeks; it consisted of the mobilisation of the C0/C1, C1/C2, C 5/C6 and C 6/C7 ZJs, furthermore, the isometric strengthening of muscles for stabilizing the C2/C3 segment, and PIR is used to resolve the spasm of the suboccipital extensor muscles and the upper trapezius muscles. After two weeks of the MT the patient became symptom free, nevertheless, she continues her strengthening exercises for 10 minutes every day. Cervical pain may be triggered by physical overburdening, but it does not require pain killer medication.

DISCUSSION

The patients suffered from headaches before WI, nevertheless, following the accidents the main CEH criteria became relevant, which suggests that WI may trigger CEH. Their physical findings were very specific for WI, as to our experience. These are, hypomobility (according to the terminology of some schools of manual medicine: blockage (12)) of the upper cervical ZJs, hypermobility of the ZJs in the midcervical party, and again blockages of the ZJs in the lower segments. The hypomobility and pressure pain in the C4/5/6 segments proved to be the consequences of disc herniation, which we avoided to manipulate. Our therapeutic goals were to solve the blockages in the craniocervical segments and the C 6/7 ZJs by mobilisation/manipulation, and to treat the severe muscular disbalance characterised by the weakened deep flexors by strengthening and the spasm of the extensors by PIR. By solving the ZJ blockages and by the stabilisation of hypermobile segments we succeeded to reduce the compression force effecting on the disc herniation. We believe that physical findings found in CEH cases, are basic to the fact that the pain originated from different anatomical sites, as it was earlier suggested (15). Aprill demonstrated how occipital headaches stemming from the lateral atlanto-axial (C1-2) joint can be diagnosed (16), this can also be established according to the methods of manual medicine (17). It should be emphasized that segmental hypo- and hyper-mobility of the ZJs were simultaneously present (though in different segments), and mobilisation (or manipulation) was performed only in the hypo-mobile segments, but not where disc hernia could be demonstrated. The physical findings which are highly characteristic for CEH in our case the spasm of the deep suboccipital muscles, the abnormal tenderness of the periarticular ZJ tissues and the hypomobility of ZJs, since these are resolved within minutes following successful MT. The correction of head/neck posture, the stabilisation by exercises are basics in the perspectives of therapeutic results.

Martelletti (18) speculating that the pathophysiology in CEH probably results from various local pain-producing factors such as intervertebral dysfunction, investigated interleukin-1 beta (IL-1 beta)

and Tumour Necrosis Factor alpha (TNF-alpha). These compounds, in turn, would exert their multifunctional biological effects by promoting and increasing the molecular events of cellular inflammation [see also (19)]. Martelletti (18) found that the cytokine pattern of CEH patients is similar to cluster headache, 'biased towards an inflammatory status'. Higher levels of both IL-1 beta and TNF-alpha were detected in the sera of CEH patients than the levels in patients with migraine without aura and in healthy subjects. We also observed strikingly large amounts of TNF-alpha in the presented CEH patients (see Table 1.) and believe that these would interact with the cell surface receptor molecules altering cell properties and function (19-23). Several laboratories now believe that in subcutaneous inflamed tissue there is local stimulation of immune cells by various cytokines or by corticotropin-releasing factor (CRF).

Interactions between immune cells and peripheral sensory nerves, lymphocytes and other immunocytes resident in inflamed tissue contain opioid peptides (24) (25) (26) (27). These peptides are thought to be secreted and activate opioid receptors (OPRs) on peripheral terminals of sensory neurons. This decreases the excitability of those neurons and the release of proinflammatory neuropeptides (i.e., substance P [8]) and results in the inhibition of pain (for review **see ref. 9 in JNM July 06-4**). Such endogenously released compounds underlie These phenomena are based on

Martelletti (18) noted that there were also differences between the spontaneous and mechanically worsened pain phases of CEH. Nitric oxide (NO) synthase was also activated in cervicogenic headache, but no change in NO metabolites levels was observed after NO donor administration. This behaviour was clearly different from that observed in migraine and tension headache patients. Martelletti (18) concluded that the high degree of cytokine and NO production in CEH might depend on different pathophysiological mechanisms at work in CEH than in other forms of headache.

In conclusion, the diagnostic and therapeutical tools of the manual medicine – in addition to the recently widely used local injection blockades – are very useful in the localization and treatment of the anatomical disorders that trigger CEH (see in Fredriksen et al. (15)). Furthermore, we believe that the

role of the endogenously released compounds (Interleukins, TNF-alpha, even opioid peptides) that specifically interact with the cell surface receptor molecules affect the cell properties, adhesion, surface charges changes that govern permeability, gating currents and signalling (28) should also be investigated (21). These can be quantified with sensitive physicochemical techniques that measure electron charges (e.c.s) to within 0.5m/100 μm^2 of the cell surface area (29) and related changes in current as small 1-10nA (22;23). Such quantitative studies should help to establish a sound rational basis for meaningful correlation between injury (childhood pre-existing conditions and immediate precipitating occurrence requiring medical intervention), trauma, inflammation and quantitative biochemical parameters.

Conclusion:

The present investigations are encouraging in demonstrating the success of manual therapy to treat a patient, who had been awaiting neurosurgery for discus hernia that could not be treated conventionally, let alone cured by any other means. The risks of surgery were avoided. Such successes are rare and the few published, have been quotes. This paper emphasises that by careful physical examination and manual therapy, such cases can be selected from other headache cases and treated successfully.

The efficacy, safety, and the exact mechanism of action of the manual therapy, furthermore the role of constitutional factors and the endogenously released compounds in CEH must, however, be evaluated systematically in randomized clinical trials. It is hoped that many colleagues would be inclined to agree that such studies are likely to be not only of theoretical interest but also of practical clinical value. One has got every reason to be optimistic.

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Reference List

1. Sjaastad O, Saunte C, Hovdahl H, Breivik H, Gronbaek E. "Cervicogenic" headache. An hypothesis. Cephalalgia 1983;3(4):249-56.

2. Sjaastad O, Fredriksen TA, Pfaffenrath V. Cervicogenic headache: diagnostic criteria. The Cervicogenic Headache International Study Group. Headache 1998;38(6):442-5.

3. Leone M, D'Amico D, Grazzi L, Attanasio A, Bussone G. Cervicogenic headache: a critical review of the current diagnostic criteria. Pain 1998;78(1):1-5.

4. Obelieniene D, Bovim G, Schrader H, Surkiene D, Mickeviaiene D, Miseviaiene I et al. Headache after whiplash: a historical cohort study outside the medico- legal context. Cephalalgia 1998;18(8):559-64.

5. Delfini R, Salvati M, Passacantilli E, Pacciani E. Symptomatic cervicogenic headache. Clin Exp.Rheumatol. 2000;18(2 Suppl 19):S29-S32.

6. Bono G, Antonaci F, Ghirmai S, D'Angelo F, Berger M, Nappi G. Whiplash injuries: clinical picture and diagnostic work-up. Clin Exp.Rheumatol. 2000;18(2 Suppl 19):S23-S28.

7. Radanov BP, Di Stefano G, Augustiny KF. Symptomatic approach to posttraumatic headache and its possible implications for treatment. Eur.Spine J 2001;10(5):403-7.

8. Dumas JP, Arsenault AB, Boudreau G, Magnoux E, Lepage Y, Bellavance A et al. Physical impairments in cervicogenic headache: traumatic vs. nontraumatic onset. Cephalalgia 2001;21(9):884-93.

9. Drottning M, Staff PH, Sjaastad O. Cervicogenic headache (CEH) after whiplash injury. Cephalalgia 2002;22(3):165-71.

10. Jensen OK, Nielsen FF. The influence of sex and pre-traumatic headache on the incidence and severity of headache after head injury. Cephalalgia 1990;10(6):285-93.

11. Jensen OK, Nielsen FF, Vosmar L. An open study comparing manual therapy with the use of cold packs in the treatment of post-traumatic headache. Cephalalgia 1990;10(5):241-50.

12. Lewit K. **Manipulative Therapy in Rehabilitation of the Locomotor System**. 2ed. London: 1991.

13. Janda V. Muscles and motor control in cervicogenic disorders: Assessment and management. In: Grant R, editor. **Physical Therapy of the Cervical and Thoracic Spine** . 2 ed. **New York**: **Churchill Livingstone**; 1994.

14. Grimshaw DN. Cervicogenic headache: manual and manipulative therapies. Curr.Pain Headache Rep. 2001;5(4):369-75.

15. Fredriksen TA, Sjaastad O. Cervicogenic headache: current concepts of pathogenesis related to anatomical structure. Clin Exp.Rheumatol. 2000;18(2 Suppl 19):S16-S18.

16. Aprill C, Axinn MJ, Bogduk N. Occipital headaches stemming from the lateral atlanto-axial (C1-2) joint. Cephalalgia 2002;22(1):15-22.

17. Biondi DM. Cervicogenic headache: mechanisms, evaluation, and treatment strategies. J Am.Osteopath.Assoc. 2000;100(9 Suppl):S7-14.

18. Martelletti P. Proinflammatory pathways in cervicogenic headache. Clin.Exp.Rheumatol. 2000;18(2. Suppl. 19):S33-S38.

19. Mehrishi JN, Bauer J. Electrophoresis of cells and the biological relevance of surface charge. Electrophoresis 2002;23(13):1984-94.

20. Mehrishi JN, Mills IH. Opiate receptors on lymphocytes and platelets in man. Clin.Immunol.Immunpath. 1983;27:240-9.

21. Mehrishi JN. The usefulness of the electrokinetic method for quantitative studies on cell membrane-drug interactions in psychiatry and neuroendocrine disorders. In: Schütt W, Klinkmann H, editors. **Cell Electrophoresis 84** . **Berlin**: **Walter de Gruyter**; 1985. p. 97-112.

22. Svetliic V, Ivoevic N, Kova S, Zutic V. Charge displacement by adhesion and spreading of a cell. Bioelectrochemistry 2001;53(1):79-86.

23. Svetlicic V, Hozic A. Probing Cell Surface Charge by Scanning Electrode Potential. Electrophoresis 2002;23(13):2080-6.

24. Cabot PJ, Carter L, Schafer M, Stein C. Methionine-enkephalin-and Dynorphin A-release from immune cells and control of inflammatory pain. Pain 2001;93(3):207-12.

25. Cabot PJ. Immune-derived opioids and peripheral antinociception. . Clin Exp Pharmacol Physiol. 2001;28(3):230-2.

26. Machelska H, Cabot PJ, Mousa SA, Zhang Q, Stein C. Pain control in inflammation governed by selectins. Nat Med. 1998;4(12):1425-8.

27. Cabot PJ, Carter L, Gaiddon C, Zhang Q, Schafer M, Loeffler JP et al. Immune cell-derived beta-endorphin. Production, release, and control of inflammatory pain in rats. J Clin Invest. 1997;100(1):142-8.

28. Mehrishi JN. Fc receptors of lymphoid cell membranes. In: Hemmings WA, editor. **Protein Transmission through Living Membranes. Elsevier-North-Holland**; 1979. p. 83-117.

29. Mehrishi JN. Molecular aspects of the mammalian cell surface. In: Butler JAV, Noble D, editors. **Prog. Biophys. Mol. Biol. Oxford**: **Pergamon Press** ; 1972. p. 1-70.

Legend of plates:

Plate 1.: Magnetic resonance imaging (MRI) scan of the cervical spine of Patient 1, showing that the discus is prolapsed at C 4/ C 5 and also a slight protrusion at the C5/C6 level.

Plate 2.: Magnetic resonance imaging MRI scan of the cervical spine of Patient2, showing that discus is prolapsed at C 4/ C 5, the para-median disc hernia intruded into the right ventral cerebrospinal space

Appendix

Table 1. Laboratory analysis data of the patients

		(Case 1)		(Case 2.)	range
Internal medicine routine:					
Albumin:		63.2		62.2	39-50 g/L
Erythrocyte Sedimentation Rate (ESR)		11		8	2-20 mm/h
Glucose		5.8		5.2	3.6-6.1 mmol/L
Triglycerides (TG)		1.2		1.4	0.4-2 mmol/L
Cholesterol, Total		4.9		4.5	3.2-5.2 mmol/L
HDL-Cholesterol (HDLC)		1.1		1.8	0.91-2.33 nmol/L
Protein Total		n.d		n.d	63-82 g/L
Urea Nitrogen	*	7.3	*	6.8	2.5-6.1 mmol/L
Creatinine		110		101	44-124 μmol/L
Bilirubin Total		16.2		14.6	3-22 μmol/L
Aspartate Aminotransferase (SGOT)		27		16	8-39 U/L
Alanine Aminotransferase (ALT,GPT)		35		33	9-52 U/L
γGlutamyltransferase (GGT)		31		36	8-78 U/L
Phosphatase, Alkaline		98		86	38-126 U/L
Uric Acid		368		348	149-446 μmol/L
Sodium (Na)		142		139	135-147 mmol/L
Potassium (K)		4,8		4.2	3.6-5 mmol/L
Calcium, Total (Ca)		2.2		2.3	2.1-2.55 mmol/L
Phosphorus, Inorganic (P)		1.3		1.4	0.81-1.45 nmol/L
Haematology and Coagulation:					
Leukocyte Count (WBC Count)		6.8		7.66	4-11 Cells x 10^9/L
Lymphocytes		1.72		2.23	1-4 Cells x 10^9/L
Monocytes		0.27		0.37	0.2-1.1 Cells x 10^9/L
Granulocytes		2.07		3.6	2-7.7 Cells x 10^9/L
Lymphocytes		3.9		39.2	20-45%
Monocytes		6.5		8.2	1-10%
Granulocytes		54.2		62.0	45-70%
Erythrocyte Count (RBC Count)		4.78		4.9	3.9-5.5 Cells x 10^6/μL
Hemoglobin (Hb)		15.0		15.3	12-17.5 g/dL
Hematocrit (HTC)		44.6		43.8	36-54%
Mean Corpuscular Volume (MCV)		88		92.1	82-98 fL
Mean Corpuscular Hemoglobin (MCH)		3.1		34.4	27-33 pg/cell
Mean Corpuscular Hemoglobin Concentration (MCHC)		32.8		34.1	32-36 gHb/dL
RDW		14		13.5	12-15%
Platelet Count (Thrombocyte Count)		188		184	150-400 10^3/μL
Prothrombine Consumption (PCT)		n.d.		0.22	0.12-0.4%
MPV		10		10.1	7-11 fL
PDW		10.7		10.6	10-18%
Immunology:					
Serum TNF-alpha: (during painful phase)	*	63	*	72 increased	0-5 pgr/ml
Serum TNF-alpha: (during painless phase)	*	28	*	35 increased	
ANF 1:40 and 1:100		negative	*	nucleolaris	
Cytoplasma antibody		negative		negative	
anti-centromere antibody		negative		negative	
cytoskeleton antibody		negative		negative	
PCNA antibody		negative		negative	
C reactive protein		3		3	0-5 mg/L
C3		1.52		1.67	0.80-1.80g/L
C4		0.10		0.33	0.20-0.50g/L
Immune complexes		270		180	110-200mg/L

Anti-DNA antibody	3	5	0-10 U/ml
Cardiolipin IgG	negative	negative	
Cardiolipin antibody	negative	negative	

Urine analysis:

Glucose, Qualitative	Negative	negative	
Bilirubin	Negative	negative	
Ketone bodies, Qualitative	Traces	negative	
Specific Gravity	1.020	1.023	
pH	6 µmol/L	5.6	
Protein	Negative	negative	
Urobilinogen	0.2 EU/d	0.2	
NIT	Negative	negative	
BLO	Negative	negative	
LEU	Negative	negative	
Triiodothyronine (T_3)	2.30 nmol/L	2.5	1.45-3.48 nmol/L
Thyroxine (T_4), Total	107 nmol/L	102	71-181 nmol/L

Summary of treatments

Patient # 1. Female (age 27).

1999. December: the patient suffered whiplash injury and received the following treatment: for 2 weeks collar support, then 10 times daily, she received infusions of Lidocaine 1% 10 ml, novaminophenazum 1000 mg, Solu Medrol 20 mg, followed by daily doses 2x1 tbl. Quarelin (novaminophenazum natr. 400 mg, coffeinum 60 mg, drotaverinium chlor. 40 mg.

2001 September: the patient received again the same infusions 10 times, daily, followed by daily doses 2x1 tbl. Algopyrin (Metamizol sodium 500 mg).

2001 October : the patient was given manipulative therapy, PIR, two times/week for 2 weeks, than once a week for two weeks. Thereafter, no medication was needed.

Patient # 2. Female (age 62).

1997. July: the patient suffered whiplash injury with left tibia fracture and received the following treatment: 3 weeks of collar support and operation because of left tibia fracture. Thereafter, the patient needed daily 2x1 tbl. Algopyrin (Metamizol sodium 500 mg).

1999 August: the patient unfortunately suffered a repeated neck injury, and received 10 times a day infusions of Lidocaine 1% 10 ml, novaminophenazum 1000 mg, Solu Medrol 20 mg., followed by daily 2x1 tbl. Quarelin (novaminophenazum natr. 400 mg, coffeinum 60 mg, drotaverinium chlor. 40 mg).

2000 July: the patient was given manipulative treatment PIR, twice a week for 2 weeks and then once a week for two weeks. Thereafter, no medication was needed.

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Successful Manipulative Treatment of Cervicogenic Headache Following Whiplash Injury

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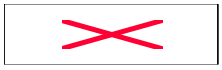

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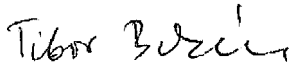

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