Low-dose oxytocin stops unexplained 'burning' pain in fibromyalgia: A case report

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Low-dose oxytocin stops unexplained ‘burning’ pain in fibromyalgia: a case report

M. Bouchon*

Corresponding author email*: mbouchon@ozemail.com.au

Abstract

Pain can take many forms, and finding an adequate treatment is sometimes difficult. In Fibromyalgia, the brain or nerves are usually seen as the culprit of hyperalgesia. The role of the 'hypothalamic osmostat' has been overlooked. We report here a pain effect relieved by the hormone oxytocin (OT) and better baseline dehydration.

Case presentation

A Caucasian 53 year-old menopausal female with fibromyalgia presented with unexplained 'burning’ pain, among others. Endocrine, nervous, and immune investigations revealed nothing that could explain it. Her medical history included a sensitive nervous system and an untreated lifelong low-grade dehydration. The triggering factor was traced back to a one-month course of bio-identical progesterone that had worsened the dehydration.
The hypothalamus is involved in various ways in symptoms of fibromyalgia and stress sensitivity, but also in the water balance regulated by the hypothalamic osmostat, so attention turned to the hormone oxytocin. OT is seldom used in therapeutic setting, except in obstetric care. Current research on oxytocin tends to focus on its central role in the brain, using large doses, and on its interaction with vasopressin, affecting reproductive and social behaviour.
A more basic role for oxytocin in the hypothalamic osmostat has become apparent through systemic effects in this patient. A two-week intranasal treatment with low-dose OT proved effective in resolving the burning pain, but also resulted in a general improvement, including of hydration. This report discusses sensitivity, similarity with critical conditions, dose-related and baffling 'inverted' effects.

The unexpected general improvement described here offers benefit for vital functions and other ‘basic’ needs, as well as the capacity for physical self-care and compliance with a treatment. The protocol used could be a new avenue to better match treatments to the needs of 'sensitive' patients.

Introduction

Fibromyalgia is a chronic, relapsing syndrome affecting more young or middle-aged females than males. Defined as a musculo-skeletal chronic pain syndrome (tender points, stiffness, widespread pain, fatigue), it is notoriously difficult to diagnose and its aetiology is still debated, often considered multi-factorial. Clinically, it is diffuse, overlapping with other syndromes, characterised by a broad set of neurological and stress-related symptoms, individually variable. It affects vital behaviours such as sleep, digestion, and fluid balance (e.g. associated neurally mediated hypotension, carpal tunnel syndrome, Raynaud's phenomenon, etc.). It is associated with other conditions and unexplained symptoms, such as the unbearable burning pain that is our focus here. This syndrome also affects cognition (e.g. sensory sensitivity, concentration, memory, finding names, performing complex tasks, general alertness), emotions (anxiety, depression), and general mood (feeling miserable, negative). It is accompanied by functional impairment of daily living activities, to various degrees, including social interaction, and includes an exhaustion-triggered systemic 'shut-down' or/and 'brain fog'. The literature does not provide a clear prognostic image of the syndrome's progression, but reports gradually worsening pain, fatigue and disrupted restorative sleep, diminishing work and physical exercise capacity, and increasing incidence of associated degenerative diseases (rheumatoid in particular). Treatment is also multi-faceted. Recently, fibromyalgia has been redefined as a central sensitivity syndrome (CSS) [1], a neuro-sensory disorder.

Oxytocin was originally considered a purely female hormone (labour, lactation). The use, from the nineteen fifties, of its chemical analogs for birth induction, in large intravenous doses, shed light on overdose side-effects such as water intoxication. It acts peripherally through the bloodstream on renal tissue response to increased plasma hyperosmolality, and affects other functions. [2, 3, 4, 5] It is now known to also have a central, adaptive and stress related role [6] as a neuro-hormone, with sexually dimorphic socio-behavioural impact [7, 8] involving AVP (see figure 1 and additional file 1: Oxytocin).

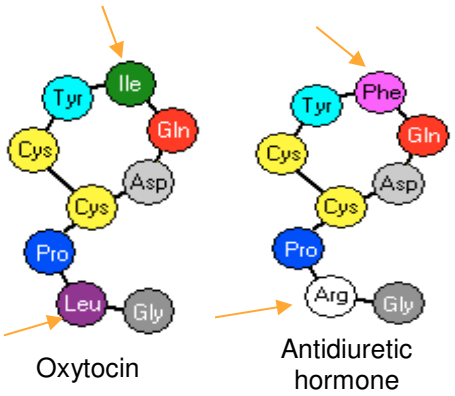

Figure 1. Oxytocin and arginine vasopressin (AVP or ADH) differ by two amino acids.

Case presentation

This 53 year-old Caucasian menopausal female (in Australia) has displayed most of the fibromyalgia characteristics described above for eleven years, and other progressive conditions. She presented an unexplained 'burning pain' in the left arm, shoulder, and neck, resistant to her usual treatments. The pain had been recurrent for about two years, in the sacroiliac area and spine, but more bearably, and not in the arm. The current spreading localisation originated from a left shoulder calcific tendonopathy involving supraspinatus (stiffness and painful restriction began in her twenties but attracted no treatment) and involved cervical dermatomes (spondylosis consequent to a laminectomy at C6-C7 eighteen years ago, compounded by low back pain since pregnancy and more recent thoracic kyphosis). This pain was worse at night, increased by hypopnea, ingestion of salt or sugar or dry processed carbohydrate foods, by physical exertion and postures restricting movement

(gardening or sitting at a computer for hours, bent). It was not improved by breathing exercises, or nutritional and amino-acid treatments that had partially relieved other pains.

Over the past 3 years, increasing pain and the deterioration in general health were accompanied by body fat gain, and progressive lean-mass weight loss attributed to cortisol driven catabolism. Endocrine evaluation was consistent with various low functions, most explained by ongoing stress and hormonal decline at menopause. No inflammatory markers could explain the burning pain. The patient has a history of treated precancerous conditions (and untreated multiple cherry haemangiomas from childhood, spreading). She was investigated further but no cancerous organic damage was found in gastrointestinal track, lungs or brain. Nerve conduction studies detected no demyelination or other neuropathy.
The acute presentation was traced back to a one-month course of bio-identical progesterone at low-dose (2mg/day) that had induced dehydration. This effect has been described in a few women, and deoxycorticosterone (DOC) implicated anecdotally [9]. The metabolism of progesterone into some hormonal metabolite, probably of a type that can act as both glucocorticoid and mineralcorticoid, suggested a relation to stress and the water metabolism. Because this involves antidiuretic hormone (ADH, or arginine vasopressin, AVP), the oxytocin hormone, which affects it, stood out as a possible treatment option (see discussion below).

This patient tends to display strong reactions to conventional treatments (medical drugs, and even herbal/'alternative'), often with counter-productive effects, so other approaches are necessary. Small doses are usually sufficient to obtain significant results with amino-acids. A reasonably safe approach was to choose a mild mode of peptide administration. A very low dose would avoid the recognised side-effects (hypotension, anaphylactic-type reactions, and water intoxication). The bio-identical OT has a different structure from that of the chemical analog drug named Syntocinon (or Pitocin) (figure 2), and therefore, effects are bound to display some differences. Using the bio-identical hormone promised less side-effect risk.

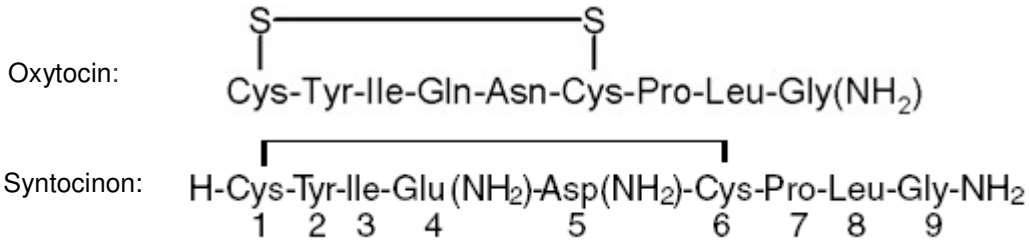

Figure 2. Different formulas for oxytocin and its chemical analog.

Treatment Protocol

• *Preparation*: a commercial chemist prepared a solution of the bio-identical hormone OT at 40iu/ml dilution in an alcoholic base, in intranasal spray form.
• *Rate of administration*: This is the dosage used for lactation, recommending several intakes in both nostrils per day. This could be further reduced by using an 'as-needed' approach. The patient was able to determine a daily dosage that was effective for the pain: 2 sprays per day (1 nostril only each time, morning and night). This represents approximately 1.5μg/kg/day — a much smaller dose (by an order of tens to hundreds) than those habitually used in human research and animal studies (1mg/kg/day for rodents). These are also often administered by injection, and generally use chemical analogs.
• *Timing*: The doses were administered primarily in response to the burning pain and to nocturia that awoke her 2 to 4 times between 2:30 am and 4:30 am, and in early evening, to stop facial and heel pain and open breathing passages. Once, an extra dose was added. The prescribed maximum of 6 sprays per 24 hours was never reached. The trial treatment lasted for 2 periods of 6 days, chosen because the research literature mentions 5 to 8 days for repeated administration, and with a 2-day interval, to assess post-administration effects and possible dependence.

• *Results:* This treatment protocol was effective in stopping the burning pain in two weeks. It also reduced a number of other pains and symptoms, and produced an unexpected generalised improvement.

Discussion

The solutions mentioned to counter progesterone-induced dehydration are contradictory, and none resolved the pain (this patient's very low doses represent a clinical limitation). Natural pprogesterone was discontinued, but the pain did not abate. A diarrhoea-inducing pre-endoscopy drug treatment also triggered an acute bout of the burning. The patient reported that pain intensity correlated with the degree of dehydration, and with other pains: in kidneys, spleen, heel joints, bones of the face, and spine. Other symptoms of dehydration included mild oedema (face, extremities, and abdomen), often triggered by sugar, dry processed carbohydrates, or salt, and other symptoms such as blurred vision, difficulty swallowing, altered urination, wildly fluctuating thirst stimulus, and 'bruised' tender sensation upon touch without visible bruising. The neural studies confirmed neural sensitivity (a lifelong, highly strung condition without known cause, characterised by mild autonomic dysfunction, clonic spasms, and cognitive symptoms), and reported a mild carpal tunnel swelling.

Sensitivity and water metabolism (dehydration and swelling) were the most salient elements.

The recent redefinition of fibromyalgia offered a new perspective. As a central sensitivity syndrome (CSS), fibromyalgia involves high sensory sensitivity and dysautonomia, low thresholds for nociception and pain tolerance but, more relevantly here, also a sensitisation and central deregulation of 'the stress response system' that can lead, in some patients, to an auto-reinforcing neuroendocrine cascade.

A group of common characteristics suggested an avenue to explore: Effects related to pain thresholds and sensory sensitivity (sometimes formulated in Internet documents as a 'rheostat turned up too high'); connection to developmental, environmental, and social variables; sexually dimorphic responses to stress; their initiation, sensitisation, and central regulation; the involvement of the autonomic nervous system in vigilance and arousal; the activation of the hypothalamus-pituitary-[thyroid]-adrenal axis (HPA or HPTA axis) and of other neuro-endocrine axes, and alterations in corticotropin-releasing hormone (CRH) neuron response (CRH is secreted by the paraventricular nucleus of the hypothalamus) — are all elements common to fibromyalgia and to descriptions of the actions and effects of the hormone/ neuro-hormone oxytocin (OT). The OT/ADH system in the hypothalamic osmostat is also called 'stress system', and was the focus of treatment.

The detailed effects of the treatment, as observed and recorded by the patient, are presented in tabular form, and varied with time and dose (discussed later):

-a short-term cascade effect (table 1 below)
-a cumulative effect with repeated dose (table 2 below)
-a long-term effect: stress-governed and remnant effect after 2 weeks of treatment (table 3 below).

The follow-up office visit for assessment demonstrated successful reduction of the 'burning'. Moreover, some other pains reduced as well (facial, heels, kidney, spleen, spine, and from stretch stiffness). The blood pressure had risen beneficially to 95/60, a figure it had not reached since 2002. Core temperature had risen back to 36.6°C, which other treatments (including thyroid hormones T3/T4) had not achieved. There was a general improvement, small but broad: in menopausal symptoms, in hydration and other vital functioning, especially breathing and sleep, and in the capacity for physical self-care (compliance with the nutritional schedule, getting sufficient exercise and sunshine, eating properly…), which the patient had come to find taxing. There was no undesirable side effect to low-dose OT, even months later. The positive effects of OT treatment lasted for about two further weeks after the trial treatment, and then began to wane, confirming a definite role of OT in the 'sensitive' and declining state of this patient.

Her many but low-grade fluid-related symptoms are confusingly reminiscent of several uncommon osmosis-related conditions. Striking similarities exist, for example, with diabetes *insipidus*, syndrome of inappropriate antidiuretic hormone secretion (SIADH), osmotic stress demyelination, and reset osmostat syndrome [10]. The manifestations are low-grade, however, not connected to the high-degree critical states of medical emergency (e.g. reset osmostat mostly occurs in critically ill patients). The first two conditions mentioned are also contradictory — or symmetric. The symptoms are located differently, in *variable* sets that never fully match any recognisable disease definition. Why?

Several forms of 'stress system' have been invoked to explain counter-productive effects such as systemic cellular dysfunctions, or long-term cortisol damage to the hippocampus. Since the main three sub-systems are not directly causing this patient's most troublesome pains, and since symptoms in fibromyalgia may often be qualified of 'subclinical' (no objective findings), could the central sensitivity of fibromyalgia implicate directly the hypothalamus and its 'OT/ADH stress system', in at least some particularly sensitive patients? It makes sense to suppose that this patient's mild dehydration and oedema might be early signs of a subclinical osmotic strain related to initiating and stopping the stress state. The dose- and time-dependence effects and patient observations, during this low-dose OT regimen, warrant some comments, related to the literature and theoretical considerations. (See additional file 2: Reflections)

Conclusion

The daily intranasal administration of oxytocin, at the unusually low dose of 1.5μg/kg/day (in 2 intakes) over 2 weeks, successfully reduced the 'burning' pain in this fibromyalgia patient, but also improved unexpectedly a broader array of pains, symptoms, and vital mechanisms, without apparent undesirable side-effects, even months later.

Maintaining these benefits for a highly sensitive patient, however, might involve a longer-term treatment (1) with an 'as needed' (not necessarily daily) administration for flexibility (OT spray is not constraining, although the aggressive alcohol content is a problem), and (2) under conditions of limited stimulation (especially sensory and by foods).

More knowledge of oxytocin is needed in clinical family practice, about its *basic physiological* effects on water metabolism, hypothalamic osmostat and vital functions, about those of *low-dose* OT treatment and *endogenous* OT production, about osmolytes in foods/drinks and how these affect the yet unexplained drift ('with age', from birth) of the *baseline* hydration level, a basic but little studied need of health.

Their systemic role in inducing but also in stopping states of central, nervous or stress sensitivity (and possibly immune reactivity), needs to be investigated with a different framework. This could provide the physician with new means to reduce progressions and help maintain the health of fibromyalgia and other such patients within the limitations of what a 'sensitive' system can manage without damage, under the normal biosocial pressures and 'allostatic load' of chronic environmental challenges.

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Additional files:

Additional file 1
Title: *Oxytocin in the hypothalamic osmostat stress system*
File name: Added File 1 – Oxytocin (.pdf format)

Additional file 2
Title: *Reflections, patient's perspective, and theoretical considerations*
File name: Added File 2 – Reflections (.pdf format)

Tables:

Table 1: Short-term cascade effects of low-dose OT treatment (patient perspective)
Table 2: Cumulative effects of low-dose OT treatment (patient perspective)
Table 3: Long-term effect of low-dose OT treatment: stress-governed and remnant effect after 2 weeks (patient perspective)

Consent
Written informed consent was obtained from the patient for publication of this case report.

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Competing interests
The author declares that she has no competing interests.

Table 1: Short-term 'cascade' effects of low-dose OT treatment (patient perspective)	
Timing from administration	**Effects noticed (on symptoms, sensations, behaviours)** Those noticed at first administration were reproduced on other days)
Within 10 seconds:	*Noticed at first administration:* pain stopped in scar tissue around spinal bone spurs at C5-C8 level
	Cumulative observations over 2-week treatment: reduced 'sticky' sound at the top of the spine
Within 3 minutes:	*Noticed at first administration:* reduced spinal ligaments stiffness pain in occipital-atlas, at thoracic level, and in front of spine, and moving to other tendons: inside rib cage and at hips-legs juncture
	Cumulative observations over 2-week treatment: kidney and spleen pain stopped; reduced bruise-like pain; tinnitus-like whistle reduced; evening face bones pain and heel pain stopped, also in the elbow
After 10-15 minutes:	*Noticed at first administration:* mucus loosened in sphenoid sinuses; much reduced 'burning pain' in left head-to-arm connection (usually, when pain is not 'burning', it is the ligaments/tendons that hurt)
	Cumulative observations over 2-week treatment: reduced stiffness and pain from straining to stretch; mucosa moistened and mucus loosened, 'dry' headache stopped. Breathing better: less swollen breathing passages (lungs, throat; nostrils no longer blocked or coated with dried mucus, sphenoid sinuses no longer swollen/blocked); rib cage muscle more tonic and active, actually lifting again (no longer expanding into belly because of weak muscles); left-right nostrils breathing evened out (not just one open with the other one blocked, as most of the time)
After 20-30 minutes to day-long:	*Noticed at first administration:* urge to urinate (but normal amount and clear) and mucus produced in sphenoid sinuses and lungs (triggering one cough)
	Cumulative observations aver 2-week treatment: catabolic proteinuria pain stopped; bowel motion(unstrained peristalsis and stool softened: counter-constipation) -if moving to move body fluids and activate breath: nose remains moist -if sedentary (e.g. at computer): sphenoid sinus becomes encumbered by thick mucus newly produced -reduced hot flushes and relaxed agitation/tension (both are induced by sugar and processed glucid foods, by chocolate as well as by not eating enough)

Table 2: Cumulative effects of low-dose OT treatment (patient perspective)	
Timing from administration	**Effects noticed (on symptoms, sensations, behaviours)** (Those noticed at first administration were reproduced on other days)
Within 10 seconds:	repeated yawning, and stretching of body and jaw, uncontrollable;
Within 3 minutes:	eyelids no longer sting (as in tired child); eyes watering: stopped dry itching; stretch pain response reduced in spine (bending the neck forward)
Within 8-10 minutes:	spontaneous 'yoga' - mechanical repetitive movements of the neck bent backwards, which loosens fibrous/calcified tendons/ligaments lower down (located about T1-T5, inside the vertebral column); also mobilised the sacro-illiac area mechanically. Other stretching movements mobilised and re-'placed' several vertebral discs or tendons (cracking sound).
After 15-20 minutes to day-long:	-somewhat reduced pain in 'fighting gravity' to lift the left arm (seat of the burning pain), which had not been possible in over a month: easier to get dressed, do driving manoeuvres, lift objects -the spinal ligaments surprisingly loosened enough to stop the 'front spring' that had created an uncontrollable bend of the spine forward, preventing from lying flat on the back, and causing increased automatic slouching -reduced 'alarm/alert', but change in the cognitive mode to the annoying style of chronic discursive thought that the single OT low-dose stops -after time spent taking notes, the relaxed-active state (with lesser hypopnea) allowed to go back to sleep

Table 3: Long-term effects of low-dose OT treatment: stress-governed and remnant effect 2 weeks after treatment (patient perspective)
improved core body temperature: finally risen by half a degree, back up to 36.6°C after several years; improved peripheral warmth distribution especially about the abdomen; less reaction to external temperature changes
menopausal hot flushes and spinal cold disappeared
reduced problems with thirst and urination (quantity, colour, cortisol-related catabolism and proteinuria)
improved appetite (actually feeling 'hungry', a sensation lost ten years ago; not forget to eat; desire for more nourishing than 'energy food'; but stopped craving for sugar and other 'energy foods' (dry processed carbohydrates, dark chocolate, red meat, brie cheese) – as long as stress challenges remain low
stopped clonic jerks, restless legs, and micro-muscular tension (perceptible only upon retiring at night as a body-wide vibration) much reduced nail biting tension(reappeared, from childhood, at menopause)
reduced dream agitation and no more waking up for burning pain
reduced hair loss & breaking, and breaking nails (not so brittle)
easier breathing, better sleep, less straining to keep up posture, easier physical self-care (going to bed earlier, exercise, and 'eating properly')and treatment compliance
reduced swelling & itching (involved in the aetiology of VIN3); reduced reactions to insect bites