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The Role of Boron Salts in the Treatment of Symptoms in Osteoartrosis: Presentation of 2 Cases

Jan M Keppel Hesselink[1]* and Alan L Russell[2]

[1]*Institute for Neuropathic Pain, Netherlands*

[2]*Brampton Pain Clinic, Canada*

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***Corresponding author:** Jan M Keppel Hesselink, MD, M Sc, PhD, Director Institute for Neuropathic Pain, Netherlands, Europe, Email: an@neuropathie.nu

Abstract

We will present 2 cases of patients suffering from osteoarthrosis, characterized by joint swelling and pain, treated with an organic boron salt, calcium fructoborate containing 6 mg of elemental Boron daily, resulting in a clinical significant decrease of pain and swelling. Boron salts have been implied to be essential for plants since the 20s of last century, and suggestions for such essential element status started to emerge for animals and humans since the 80s of last century, although the role of boron salts in a number of physiological functions have remained somewhat controversial and did not penetrate mainstream thinking.

However, since the last few years' new data emerged supporting the role of boron salts as an anti-inflammatory compound and thus these salts might play a role in chronic inflammatory disorders, such as arthritic disorder(s). Our 2-cases support such hypothesis: treatment with 6 mg of elemental Boron in the form of calcium fructoborate daily reduced pain and swelling of joints.

Introduction

Boron salts have been found to be essential for plants since around the 20s of last century [1-3]. Its function in animals was more difficult to evaluate, due to methodological problems supplying boron-salt free food, although a number of experiments pointing out boron salts might have an important physiological function in animals were published in since the 30s of last century [4,5]. However, some of these findings could not be reproduced, leading to the notion that boron salts most probably were not essential [6]. In the 50s boron was recognized as a trace element in human bones [7]. Soon, selected uptake of boron was described for certain human tumors, supporting the development of certain irradiation therapy modalities, a therapy also recently described as potentially valuable [8-10]. One first review on the role of boron in physiology of animals appeared in 1984 [11]. In that article Forrest H. Nielsen from the department of agriculture (North Dakota, USA) summarized the role of boron and described a series of early experiments with chicks where it seemed that boron deficiency negatively influenced bone metabolism. However, such results could not be reproduced in other studies in chicks [12]. Based on those early and immature and non-consistent experiments a sodium borate-magnesium carbonate supplement entered the market in the late 80s.

The putative relevance of boron salts in non-bone physiology of man was first described in the 80s of last century [13,14]. Based on epidemiological observations it was then suggested that low daily boron salt intake could be a risk factor for developing osteoarthritis [15]. A number of human pilot studies have been published, indicating that boron might have physiological roles in humans related to bone metabolism and in the field of endocrinology and immunity [16-18]. More recently the influences of boron salts on bone physiology have been substantiated [19].

Recent studies support boron's dose-dependent role as an anti-osteoporosis factor and a biological factor also influencing other related functions [20-26]. Animal studies suggest boron salts are easily absorbed. In rats fed a diet containing 68 mg boron/kg body weight/day (in the form of boric acid) for seven days, increased boron concentrations in blood were observed and bone boron levels continued to increase throughout the period of seven days, with the highest level of 47.4 mg/kg tissue, indicating greater boron accumulation in the bone compared to the other tissues. In humans, similar tissue distribution with bone accumulation was reported. Half-life of boron given to human volunteers as boric acid via either intravenous or oral resulted in comparable elimination at approximately 21 hours [27]. Kinetic data of organic boron salts seems however lacking to date.

Clinical Studies Evaluating Boron Salts

A clinical placebo-controlled pilot study (n=20) evaluating the efficacy and safety of one dose of boron salt (borax, sodium tetraborate decahydrate) was reported in 1990 by Travers, et al [28]. The authors reported that boron salts had been used in arthritis before 1975, but no data had been published. The dose selected was 6 mg of elementary boron per day taken orally as two tablets, each containing 25 mg sodium tetraborate decahydrate in an 8-week study. A 6-point patient-self scoring system was selected as primary endpoint, based on the following:

A. Completely cured (i.e. pain-free and no restriction of movement).

B. Much better but not completely cured.

C. Only slightly better.

D. No different.

E. Slightly worse.

F. Far worse.

A secondary endpoint selected was whether there was pain on passive movement. 20 patients were entered (17 males, 3 females), mean duration of arthritis was 6-3 years with in total 93 arthritic joints, pain on passive movement was present at the first visit in 56 (60%) of the affected joints, as was swelling, warmth or deformity. Restricted movement was present in 62 (67%) of all arthritic joints. In the two weeks prior to the first visit patients took an average of 1.3 palliatives dosages of analgesics per day. 5 patients dropped out of the trial before the endpoint analysis.

From the remaining 15 patients, six patients claimed to have improved while nine patients indicated no improvement or worsening, in favor for boron ($p<0.05$). There was a significantly greater improvement in the condition of all joints on boron than on placebo ($p<0.01$) and significantly less pain on passive movement on boron ($p<0.01$). There were no side effects reported.

In a small case collection in 10 patients, calcium fructoborate was tested for 2 weeks (108 mg twice a day containing a total of 6 mg of elemental Boron) on subjects diagnosed with minor osteoarthritis conditions of the knees based on the CT scan. Calcium fructoborate was well tolerated by all study subjects with no reports of adverse effect and resulted in several positive outcomes. After 2 weeks, WOMAC and McGill indexes were reduced by an average 29% and 14% respectively compared to baseline [29].

A small pilot study evaluated the effects of 6 mg of boron per day, administered as sodium tetraborate decahydrate, in a double-blind fashion in 20 patients, diagnosed as severe osteoarthritis. Of the 10 patients on boron, five improved and one of the 10 patients on the placebo improved. In completers, completed the trial, 71% improved while using boron and only 10% of patients in boron. There were no side-effects [30]. Due to the fact that boron salts in pain and arthritis are not patent protected, no further relevant studies have been conducted yet. That is why we presented these 2 case descriptions, in order to start building more clinical experience using boron salts in pain and arthritis. These cases are selected from a cohort of 80 patients, all treated by boron salts, and both cases were quite characteristic.

Case Presentations

Case study one

A 61-year-old Pakistani woman was referred with considerable diffuse joint pains much worse in her knees. Pain in both knees for three years, gradual onset, progressive symptoms were resistant to the standard treatment of anti-inflammatory, Acetaminophen, and mild opioids. The pain limited her exercise of walking and gradually her weight increased aggravating the pain in her knees. X-rays confirmed extensive osteoarthritis, worse in her knees. Left knee was boggy with swelling over medial aspect, no locking, marked crepitus with movement painful. Her body pain tolerance was normal using pain probe. However, her pain score on the NRS at rest was 3/10 and 7/10 walking. A blood screen was normal with no evidence of diffuse hematological etiology. It was noted that she was not on any vitamins. Examination revealed she was overweight at 215 pounds. Her blood pressure was 140/90 mm Hg sitting and was well controlled on Tiazac (Diltiazem Hcl). A general skeletal examination demonstrated Heberden's nodes and pain on movement of her interphalangeal joints.

Age and her blood pressure contraindicated NSAID's which had failed in the past. She was started on glucosamine hydrochloride, manufactured from grain, 500 mg three times per day. After six months, there was little positive change. To this regimen, we added Boron in the form of calcium fructoborate, a chemical copy of the natural form, at a dose of 6 mg of Boron per day. To pre-empt the onset of constipation, as per our routine, she was started on prunes, a natural source of Boron.

Within six months she was walking well without pain, the swelling around her knees had decreased. She had no side effects from the medication, except very slight constipation which responded to her escalating her dosage of prunes. It was rewarding to note that with her walking there was a significant reduction in her weight from 215 pounds to 200 pounds. After a lengthy discussion on the fact that Boron was natural and not a drug we agreed that she should stay on this treatment regime. She seemed happier and brighter due to the reduction of pain.

Case study two

A 61-year-old woman was seen initially at age 51 with extensive osteoarthritis and cervical stenosis with significant root irritation causing pain both arms radiating to her fingers. For a number of years, she had been diagnosed with classical fibromyalgia and tender points and trigger points. Her pain was

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poorly controlled with a combination of acetaminophen and oxycodone 5 mg in the form of Percocet®. She was unable to work and only able to do minimal housework. The pain in her hands, together with morning stiffness, was minor compared to cervical C4-5 root pain.

Two years after having been seen she underwent cervical laminectomy, with fusion and metal fixation. She made a slow but steady recovery after this extensive surgery. The alternative to not having the surgery was increasing cord compression and possible paralysis. Gradually over the course of 2-3 years, her hands increased in localized pain due to confirmed increasing osteoarthritis. This caused her great discomfort as the use of one's hands is so important. The pain was aggravated by the cold associated with stiffness affecting even dressing, doing buttons etc. Pain score on NRS at rest was 2-3 and during activity 6-7.

In the past, she had tried various analgesics, and anti-inflammatories with minimal effect. An extensive course of glucosamine hydrochloride, 750 mg three times per days was ineffective and expensive as she was on a limited budget due to disability.

In 2011 she was started on boron in the form of calcium fructoborate in a dose of 6 mg of elemental Boron per day. After six months, she started to notice improvement with the pain reduced significantly, NRS pain score for activity went from a 6 to 2 and cold sensitivity was also reduced.

Pain in her other arthritic joints particularly her neck was also reduced. Swelling in her hands which was causing increasing problems resolved to very occasional swelling. From time to time she would stop her boron due to cost and commented "If I go without Boron for over a month I do notice the symptoms returning but not as drastically as before". Her mood is much better due to pain relief and she is able to work part time! The Heberden nodes over the distal interphalangeal joints have shrunk. We have noticed this in patients using boron.

Discussion

In a variety of recent experiments boron salts have certain anti-inflammatory or perhaps pro-resolving effects [31-36]. These mechanisms of action may help to understand why the treatment with boron salt (we used calcium fructoborate) in our patients resulted in the meaningful changes in the reduction of pain and swelling. The active ingredient is Boron 3 mg or 6 mg. It comes in various salt forms - citrate, fructoborate etc. So, it is the Boron content that defines the dose. Each has a different molecular weight; thus, we use the amount of Boron in the molecule to spell out dose.

It seems that treating arthritis with 6 mg of boron in the form of calcium fructoborate daily is able to reduce pain and swelling, suggestive of anti-inflammatory activity and confirmed by changes in inflammatory markers. The two cases that we present of arthritis treated with calcium fructoborate orally are selected from an open case collection of approximately 80 cases. They demonstrate the effectiveness of boron in treating the pain of arthrosis to a level of good control and taken long term it prevents exacerbations of pain.

The long-term use of calcium fructoborate over a 5-year period of observation demonstrated no significant side effects except constipation in 4-5% of cases which responded well to dried prunes. The latter is not only a simple laxative but contains a high concentration of boron salts [37]. Reviewed against the standard treatment of osteoarthrosis with NSAIDs, boron salts may show a number if benefits over NSAIDs which are not without significant adverse effects [38]. At one time, it was thought that some NSAIDs would be banned from sale.

NSAIDs do decrease the inflammatory process and have been used in long term maintenance again with a somewhat risky profile in the older patient and those with GI problems. In the case of Indomethacin there may be a concern of the arthritis becoming worse. Long term use is expensive and this is increased by the use of gastric protective agents. Calcium fructoborate is inexpensive, long term continuation is without significant side effects and as we will discuss later has the potential for benefits in other conditions. Within the normal dose range of 3-12 mg per day, ideally 6 mg, the side effect profile is no different from natural fruit ingestion.

The 'father of Boron', Dr. Rex E. Newnham, in 1965 stumbled upon the action of Boron while working as a plant physiologist in Australia. He noted in areas where certain crops were failing that the soil was short of Boron. Adding Boron to the fertilizer resolved the crop failures. By chance he noticed that in these areas his arthrosis which had been troubling him for years was worse.

It seemed logical to him to try taking small amounts of Boron and he was quite impressed that his Arthritis improved. He shared this knowledge with his colleagues and friends and again there was marked improvement in their Arthritis. A small study in Australia on osteoarthrosis showed positive results but was too small to establish boron [28]. Newnham then turned his attention to countries like Jamaica or Mauritius where arthrosis is extensive and demonstrated that this was most likely due low amounts of Boron in the soil. The reverse is seen in countries like Israel where high levels of Boron in the soil correlate to one of the lowest incidence of Arthritis in the world with a mixed genetic population.

The boron deficiency idea is reinforced in the study by Professor Meyers that demonstrated that the Xhosa tribal people (a Bantu ethnic group of Southern Africa), had approximately 2% arthritis while living in their normal habitat but when people moved to towns their arthritis level jumped to 20% due to the reduced boron intake in their food being farmed rather than grown naturally [39].

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What we find particularly interesting is the studies from the Middle East that demonstrated that patients with rheumatoid arthritis have a 50% lower serum Boron than controls [40]. There are many studies that have been carried out throughout the world in the past 30 years – one striking fact is that they all show a decrease in inflammatory markers whether it be atopic eczema or Rheumatoid Arthritis [18,41].

One great advantage of boron salts is it is extremely cheap and many people overlook the fact that taking a NSAID with a proton pump inhibitor is much more expensive. Sadly enough, agents without patent are never used to their full potential. This can be said of boron salts, niacinamide, glucosamine, turmeric, palmitoylethanolamide and many others. We hope our case description will rekindle interest in this mineral.

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References

1. Sommer, Anna L, Lipman CB(1926) Evidence on the indispensable nature of zinc and boron for higher green plants. Plant physiology 1(3): 231-249.
2. Johnston, Earl S, Dore WH(1929) The influence of boron on the chemical composition and growth of the tomato plant. Plant physiology 4(1): 31-62.
3. Sommer AL, Helen S(1928) Effects of the absence of boron and of some other essential elements on the cell and tissue structure of the root tips of Pisum sativum. Plant physiology 3(3): 237-260.
4. Skinner JT, McHargue JS(1945) Response of rats to boron supplements when fed rations low in potassium. American Journal of Physiology 143(3): 385-390.
5. Hove E, Elvehjem CA, Hart EB(1939) Boron in animal nutrition. American Journal of Physiology 127(4): 689-701.
6. Follis R H(1947) The effect of adding iron to a potassium-deficient diet in the rat. Am J Phvsiol 150: 520-22.
7. Alexander GV, Nusbaum RE, Macdonald NS(1951) The boron and lithium content of human bones. J Biol Chem 192(2): 489-496.
8. Anghileri LJ, Miller ES(1971) Studies on the long-term selective uptake of boron by tumors other than brain tumors: its possible use in neutron-capture cancer therapy. Strahlentherapie 141(4): 404-408.
9. Futamura G, Kawabata S, Siba H, Kuroiwa T, Suzuki M, et al.(2014) A case of radiation-induced osteosarcoma treated effectively by boron neutron capture therapy. Radiat Oncol 4(9): 237.
10. Farías RO, Bortolussi S, Menéndez PR, González SJ(2014) Exploring Boron Neutron Capture Therapy for non-small cell lung cancer. Phys Med. 30(8): 888-897.
11. Nielsen FH(1984) Ultratrace elements in nutrition. Annu Rev Nutr 4: 21-41.
12. Elliot MA, Edwards HM(1992) Studies to determine whether an interaction exists among boron, calcium, and cholecalciferol on the skeletal development of broiler chickens. PoultSci 71(4): 677-690.
13. Nielsen FH, Hunt CD, Mullen LM, Hunt JR(1987) Effect of dietary boron on mineral, estrogen, and testosterone metabolism in postmenopausal women. FASEB J 1(5): 394-397.
14. Naghii MR, Samman S(1993) The role of boron in nutrition and metabolism. Prog Food Nutr Sci 17(4): 331-349.
15. Newnham RE(1991) Agricultural practices affect arthritis. Nutr Health 7(2): 89-100.
16. Nielsen FH(1994) "Biochemical and physiologic consequences of boron deprivation in humans." Environmental health perspectives 102(7): 59-63.
17. Nielsen FH, Hunt CD, Mullen LM, Hunt JR(1987) Effect of dietary boron on mineral, estrogen, and testosterone metabolism in postmenopausal women. FASEB J 1(5): 394-397.
18. Rogoveanu OC, Mogoşanu GD, Bejenaru C, Bejenaru LE, Croitoru O, et al.(2015) Effects of Calcium Fructoborate on Levels of C-Reactive Protein, Total Cholesterol, Low-Density Lipoprotein, Triglycerides, IL-1β, IL-6, and MCP-1: a Double-blind, Placebo-controlled Clinical Study. Biol Trace Elem Res 163(1-2): 124-131.
19. Hakki SS, SiddikMalkoc, Dundar N, Kayis SA, Hakki EE, et al.(2015) Dietary boron does not affect tooth strength, micro-hardness, and density, but affects tooth mineral composition and alveolar bone mineral density in rabbits fed a high-energy diet. J Trace Elem Med Biol 29:208-215.
20. Gümüşderelioğlu M, Tunçay EÖ, Kaynak G, Demirtaş TT, Aydın ST, et al. (2015) Encapsulated boron as an osteoinductive agent for bone scaffolds. J Trace Elem Med Biol 31: 120-128.
21. Shuai C, Han Z, Feng P, Gao C, Xiao T, et al. (2015) Akermanite scaffolds reinforced with boron nitride nanosheets in bone tissue engineering. J Mater Sci Mater Med 26(5):188.
22. Li X, Wang X, Jiang X, Yamaguchi M, Ito A (2016) Boron nitride nanotube-enhanced osteogenic differentiation of mesenchymal stem cells. J Biomed Mater Res B Appl Biomater 104(2): 323-329.
23. Chen X, Zhao Y, Geng S, Miron RJ, Zhang Q (2015) In vivo experimental study on bone regeneration in critical bone defects using PIB nanogels/boron-containing mesoporous bioactive glass composite scaffold. Int J Nanomedicine 22(10): 839-846.
24. Apdik H, Doğan A, Demirci S, Aydın S, Şahin F (2015) Dose-dependent Effect of Boric Acid on Myogenic Differentiation of Human Adipose-derived Stem Cells (hADSCs). Biol Trace Elem Res 165(2): 123-130.
25. Danti S, Ciofani G, Moscato S, D"Alessandro D, Ciabatti E, et al. (2013) Boron nitride nanotubes and primary human osteoblasts: in vitro compatibility and biological interactions under low frequency ultrasound stimulation. Nanotechnology 24(46): 465102.
26. Taşlı PN, Doğan A, Demirci S, Şahin F (2013) Boron enhances odontogenic and osteogenic differentiation of human tooth germ stem cells(hTGSCs) in vitro. Biol Trace Elem Res 153(1-3): 419-427.
27. Zhao Q, Jason U, Michael D (1999) "Replacing the default values of 10 with data-derived values: a comparison of two different data-derived uncertainty factors for boron." Human and Ecological Risk Assessment: An International Journal 5(5): 973-983.
28. Travers R, Rennie GR, Newnham RE (1990) Boron and Arthritis: the Results of a Double-blind Pilot Study. Journal of Nutritional Medicine 1(2): 127-132.
29. Reyes-Izquierdo T, Nemzer B, Gonzalez AE, Zhou Q, Argumedo R, et al. (2012) Short-term intake of Calcium Fructoborate improves WOMAC and McGill scores and beneficially modulates biomarkers associated with knee Osteoarthritis: a pilot clinical double-blinded placebo-controlled study. Am J Biomed Sci 4(2): 111-122.
30. Pietrzkowski Z, Phelan MJ, Keller R, Shu C, Argumedo R, et al. (2014) Short-term efficacy of calcium fructoborate on subjects with knee discomfort: a comparative, double-blind, placebo-controlled clinical study. ClinInterv Aging 5(9): 895-899.

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31. Scorei ID, Scorei RI (2013) Calcium fructoborate helps control inflammation associated with diminished bone health. Biol Trace Elem Res 155(3): 315-321.

32. Demirci S, Doğan A, Aydın S, Dülger EÇ, Şahin F (2016) Boron promotes streptozotocin-induced diabetic wound healing: roles in cell proliferation and migration, growth factor expression, and inflammation. Mol Cell Biochem 417(1-2): 119-133.

33. Tepedelen BE, Soya E, Korkmaz M (2016) Boric Acid Reduces the Formation of DNA Double Strand Breaks and Accelerates Wound Healing Process. Biol Trace Elem Res 174(2): 309-318.

34. Jarnagin K, Chanda S, Coronado D, Ciaravino V, Zane LT, et al. (2016) Crisaborole Topical Ointment, 2%: A Nonsteroidal, Topical, Anti-Inflammatory Phosphodiesterase 4 Inhibitor in Clinical Development for the Treatment of Atopic Dermatitis. J Drugs Dermatol 15(4): 390-396.

35. Routray I, Ali S (2016) Boron Induces Lymphocyte Proliferation and Modulates the Priming Effects of Lipopolysaccharide on Macrophages. PLoS One 11(3): e0150607.

36. Demirci S, Doğan A, Karakuş E, Halıcı Z, Topçu A, et al. (2015) Boron and Poloxamer(F68 and F127) Containing Hydrogel Formulation for Burn Wound Healing. Biol Trace Elem Res 168(1): 169-180.

37. Nielsen, Forrest H (1992) Facts and fallacies about Boron. Nutrition Today 27(3): 6-12.

38. Fine M (2013) Quantifying the impact of NSAID-associated adverse events. Am J Manag Care 19(16):S267-S272.

39. Meyers OL, Daynes G, Beighton P (1977) Rheumatoid arthritis in a tribal Xhosa population in the Transkei, Southern Africa Rheumatoid arthritis in a tribal Xhosa population in the Transkei, Southern Africa. Annals Rheum Dis 36(1): 62-65.

40. Al-Rawi ZS, Gorial FI, Al-shammary WA, Muhsin F, Al-Naaimi AS, et al. (2013) Serum boron concentration in rheumatoid arthritis: correlation with disease activity, functional class, and rheumatoid factor. J E Integr Med 3(1): 9-15.

41. Mogoşanu GD, Biţă A, Bejenaru LE, Bejenaru C, Croitoru O, et al. (2016) Calcium Fructoborate for Bone and Cardiovascular Health. Biol Trace Elem Res 172(2): 277-281.

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