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Reseach Article

The Procaine-Base-Infusion: 20 Years of Experience of an Alternative Use with Several Therapeutical Effects

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Summary

Since its creation in 1905, Procaine (or Novocain) has been used in different ways, by several authors with various therapeutic aims. Within these authors, it is important to mention the names of vishnevsky, leriche, speransky, huneke and aslan. However, the highly-dosed infusion of Procaine-HCl with sodium bicarbonate as an additive was first published twenty years ago. This unique method later advanced into a routine therapy offered at many centers for pain treatment, rehabilitation and natural medicine clinics. Its specific pharmacologic benefits include: pain and inflammation inhibition, vasodilatation, anti-oxidation and to harmonize the nervous system. On one hand, the addition of sodium bicarbonate will balance the prevalent, albeit latent, pH-decrease in the periphery. On the other hand, the degradation products of Procaine (DEAE and PABA) have a systemic effect. Moreover, and for the welfare of the patients and to improve the method's success rate, it was shown that the classic procaine-base-infusion should only be administered with a prior acid-base-diagnostic.

Keywords: Inflammation; Infusion; Pain; Procaine, Rheumatism; Sodium bicarbonate

Introduction

The local anesthetic, Novocain (also referred to as procaine) was first synthesized in 1905 by Einhorn [1,2]. Since its creation, Procaine

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has not only been used with an anesthetic purpose, but with other therapeutic uses as well. In 1906, Vishnevsky described the anti-inflammatory effect of Novocain when it was applied [1]. In the next years, other authors including Leriche, Braun and Spiess reported various successful effects in treating several conditions such as trigeminal neuralgia, migraine, throat cancer, fractures, post-operative pain and a wide range of dystrophic disturbances [1-3].

In 1925, HUNEKE brothers were the first to administer procaine intravenously. Further, these German authors investigated several effects of procaine finding that it could be useful in the treatment of numerous pathologies via subcutaneous, intradermal, intramuscular and neural infiltrations. For this reason, they firstly titled this therapy as "therapeutic anesthesia". Later, they also reported not only changes in pathologies when it was applied segmentally, but also noticed immediate changes distant to the segment (the so-called "lighting reaction"). They later recommended this kind of therapy, referred today as neural therapy [1]. Nowadays, neural therapy is widely practiced by the medical community in Europe and Latin America, mainly [4-10]. In Russia, several authors were also investigating the therapeutic effects of Procaine. AD Speransky, a disciple of IP Pavlov, in 1936, published "Basis for a new theory of Medicine" in which he demonstrated the broad anti-dystrophic effect of procaine in numerous acute and chronic pathologies within which infectious diseases were included [3]. His observations were confirmed by AV Vishvensky and AA Vishvensky who explained procaine's mechanism of action as having an eutrophic effect on the organism which, in turn, is based on conditioned reflexes theory of IP Pavlov [2,11]. The term "throphism" refers to a physiological process of metabolism which keeps a normal physicochemical state of the internal medium in the organism and which is regulated by the sum of all innervation systems [4].

In Romania, Ana Aslan, a disciple of the neurologist Marinescu, investigated together with Pharon the effect of procaine intravenous injections according to Leriche's method and intramuscular injections. Later, she focused treatment on several geriatric disorders, using the concepts of Vishnevsky about procaine's eutrophic action. She reported with statistical data a wide therapeutic effect of procaine on nervous, cardiovascular, locomotor, cutaneous and gastrointestinal diseases in elderly people [2].

The local anesthetic procaine is characterized by a sum of pharmaceutical features. With this in mind, Prof. Aslan, the founder of eponymous therapy, spoke of it as a vitamin-like action beside the anesthetic effects [1]. Contrary to all other anesthetic drugs, it causes vasodilatation of vessels and capillaries [1,12-17]. Therefore, and with this therapy, it is possible to reach and optimally influence very poorly circulated tissue [especially in case of inflammation and pain]. Further benefits of procaine are its good tractability and low-grade toxicity due to its short half-life and plasma degradation, the capillary impermeability effect, the inhibition of inflammation, anti-oxidative and fat-reducing action [18-25]. Krause has demonstrated that the anti-inflammatory effect of Procaine in rheumatic disease was especially high when combined with an alkali additive [7]. Beside the effect of blocking voltage-dependent sodium channels with the

result of a short-term anesthesia [26], additional actions of procaine on cell membranes and the matrix, as well as sympatholytic actions, were also highlighted [27-32]. In the field of oncology, the effect of procaine's reduction of radiotherapy side-effects or to improve the influence of chemotherapy is reported [33-38]. Furthermore, a wide epigenetic action of the procaine has been demonstrated. A growth-inhibition after incubation with human cancer cells due to the partial blockade of DNA-methylase in vitro was described in 2003 [39]. A diminishing effect of 5-methylcytosine into global genomic DNA and cell proliferation due to procaine was reported in a study of tumour suppressor genes [40]. In the same way, inhibition of DNA methylation in human hepatoma cells was found by Tada et al. [41]. In 2016, Sabit et al., showed that the use of procaine combined with carboplatin was the most effective treatment for diminishing the global level of DNA methylation in colon cancer cells [42]. Finally, procaine is used in the course of heart and coronary surgery as additive in cardioplegic solutions to block the axonal ion flow and to stabilize and conserve the membrane [43-47].

The first reference of combining procaine with alkaline salts appeared in 1930 [24]. With the aim of combining the well-known pure alkaline infusion and the pluripotent features of procaine, the first study was published as the so-called "neural infusion therapy" in 1997 [48,49]. After impressive positive results were demonstrated in chronic pain patients [50], the method gained popularity very fast in the German-speaking countries and was incorporated into textbooks of pain and neural therapy [51,52]. Glusa et al., were also able to confirm the vasodilation effect of procaine-base-mixture by using an animal model [53]. An increase of intra-cellular procaine concentration due to the addition of sodium bicarbonate and an accelerated initial effect were also observed in animal studies [54-56]. The continuous application of procaine-base via a medical pump demonstrated impressive results in many severe cases of pain and inflammation [57-59].

With the osteoarthritic model of rats the anti-rheumatic and joint-protective action of procaine-base after intra-articular injection was clearly superior compared to giving the drug Dexamethasone [60].

The primary aim by additionally adding the natural buffer-base sodium bicarbonate was its plasmatic degradation influence on procaine due to the action of serum esterase. All local anesthetics have the common characteristic of general build-up and ionization. These characteristics are essential for their action on the voltage-dependent sodium channels. The unloaded procaine molecule represents the transporting structure which is able to permeate. The loaded form, procaine-H+ (ionized form) binds the sodium channel receptor and thus blocks the propagation of an impulse. By changing the pH value of the solution and the terrain, the ionized and non-ionized forms of procaine can be influenced [61].

In figure 1 it can be observed that due to the pH value shift important features such as solubility and membrane penetration can be influenced. Therefore, by adding an alkaline additive the relationship between the form of transport and the form of action is changed. In the case of a low pH value (<6), only 0.1% of procaine was found in the lipid-soluble from [40]. Further, it is known that different sodium bicarbonate concentrations can influence the intracellular pH [62].

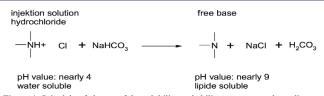


Figure 1: Principle of change of the solubility and ability to penetrate depending on the pH value.

Initially it was postulated that under an alkaline condition, that the conversion of Procaine to Para-Aminobenzoic Acid (PABA) and Diethylaminoethanol (DEAE) will be distinctly reduced. Contrary to this assumption, it is believed that after intravenously injecting procaine-base it is diluted in the blood of large vessels leading to a quick drop in pH, reaching normal physiological levels. In addition, the pulmonary circulation will cause a respiratory compensation of alkalosis. The actual retardation of procaine degradation can be explained as follows: The pH-dependent dissociation shift explained above will result in increased amounts of well-penetrating transport forms. This is generally typical for all local anesthetics and thus 3-40% of the liberated base is present depending on the pKa value of the anesthetic drug. Besides the distribution in a steady state, the speed of distribution is also important. The speed of distribution is the limiting factor meaning that the diffusion through the membrane is the rate determining step [63]. Accordingly, the distribution depends directly on the lipophilicity of the agent. By shifting the pH, the lipophilic features are changed. A higher amount of free base implies also a higher amount for permeation, which is immediately available to the surrounding tissue and cannot be metabolized so easily by the serum esterase [40].

The pure procaine infusion was firstly described by Seifen et al., and was mostly used as a continuous treatment in cases of acute pancreatitis and for epidural anesthesia in infants, children and risk patients, which underlines the low toxicity of the substance [64-76]. O'Donnel et al., reported about the use of procaine infusion to block the cardiac nerves [77].

Presently, it's reported that long-term relaxing, anti-depressive and anxiolytic effects are often observed when IV applications or short-term infusions of Procaine are given [78,79]. It has been demonstrated that when procaine is administrated intravenously in humans, it increases blood flow to the anterior para-limbic zones and the amygdala cerebral, as well as improves hemodynamic effects of the heart [80,81]. Other areas of the limbic system have been studied after procaine administration in animal models, finding activity on many muscarinic cholinergic receptors of hippocampus. Several authors have reported procaine's activity on many biochemical systems such as dopamine, norepinephrine, serotonin, glutamate, among others. For these reasons, procaine is considered as useful for studying limbic system and emotions [82,83].

Recent studies have pointed out that procaine injection into the ventral tegmental area is able to temporarily suppress the fear conditioned avoidance response in rats and also acts on hippocampal theta rhythms which are related to arousal and attention [84]. Apparently, the metabolites of procaine are responsible for the additional pharmacologic actions. DEAE is able to act as an anti-inflammatory due to the inhibition of the fatty acid amide hydrolase which causes an increase in endo-cannabinoid levels [85,86]. The second metabolite

PABA operates as an antihistamine, capillary sealant and as a stabilizer for the membranes due to the ester binding with ceramide [87-89].

Methodology of Procaine-Base-Infusions

If there is no prior information concerning the tolerance of procaine before the infusion, we recommend a test application of one drop Procaine 1% into the conjunctiva. Normally, immediately redness (due to increased blood flow) can be observed, a numbness sensation, and perhaps, a very short burning sensation (due to HCl) may be reported by the patient. If the burning pain persists for some minutes, please abstain from parenteral infusion. It is important to highlight that only Procaine-HCl with a pharmaceutical permission for IV application and without any preservatives (e.g., parabens) should be used

We recommend to start with a dosage of 50-100 mg Procaine-HCl and 20 ml sodium hydrogen carbonate (8.4%) diluted in a 250 to 500 ml carrier solution. Meanwhile the isotonic sodium chloride solution, used routinely for many years can be exchanged by a similar electrolyte solution to prevent hypernatremia. The infusion takes place for approximately 45-60 minutes. By adding increments of 50 mg Procaine-HCl and 10 ml sodium bicarbonate (8.4%), the Procaine-Base infusion will be titrated until the desired therapeutic effect is reached. For a normal-weight person the maximal dosage of Procaine-HCl is 300 mg (Table 1a & 1b). In patients with cardiovascular risk factors, we recommend the use of a surveillance technique (EKG, oximetry) for dosages above 300 mg Procaine-HCl. It is advised to ensure an after-treatment observation period of 30 minutes. Furthermore, it is advised to avoid driving for about one hour after treatment. Because Procaine-Base-mixture stability, it should be used up within two hours because of Procaine's progressing degradation.

Procaine dosage 1 %	sodiumhydrogencarbonate dosage 8.4 %	Sodium chloride 0.9 %	Total volume
100 mg = 10 ml	20 ml	500 ml	530 ml
200 mg = 20 ml	40 ml	500 ml	560 ml
300 mg = 30 ml	60 ml	500 ml	590 ml
400 mg = 40 ml	80 ml	500 ml	620 ml
500 mg = 50 ml	100 ml	500 ml	650 ml

Table 1a: Table of dosage in case of using Procaine 1 %

Procaine dosage 1 %	sodiumhydrogencarbonate dosage 8.4 %	Sodium chloride 0.9 %	Total volume
100 mg = 5 ml	20 ml	500 ml	525 ml
200 mg = 10 ml	40 ml	500 ml	550 ml
300 mg = 15 ml	60 ml	500 ml	575 ml
400 mg = 20 ml	80 ml	500 ml	600 ml
500 mg = 25 ml	100 ml	500 ml	625 ml

Table 1b: Table of dosage in case of using Procaine 2 %.

Without any prior acid-base diagnostic, the procaine-base infusion should not be administered more than three times per week with a minimum of one day break between treatment days. A series of 6 to 10 infusions depending on the medical condition have been approved.

The classic blood parameters for inflammation such as blood sedimentation rate and C-Reactive Protein (CRP) should improve after a series of procaine-base infusions. Frequently, and after four to six infusions, patients report a much better mood and improved overall condition. If there is a positive reaction to the treatment (so-called "responders", in approx. 80 % of patients) it is advised especially in chronic diseases, to continue with a long-term therapy using the helpful dosage for longer intervals, e.g., one to two times a monthly [34-36].

General Experiences with Procaine-Base-Infusion

The hypersensitivity to Procaine (also called "para-group allergy") reported in old textbooks with an increased allergy rate has not been confirmed yet [90,91]. A published meta-analysis monitoring vital data during procaine-base infusions in 5.698 patients, which included a complete documentation of blood pressure, oximetry and pulse rate before, during and after the infusion, showed no statistically significant differences between the main groups [92]. The mean values, standard deviations and ranges of assessed vital parameters are shown in table 2. Even in high-dosed ranges of procaine, the stability of values was remarkably high. Most treatment ranges registered used medium concentrations of procaine (100-300 mg) and sodium hydrogen carbonate (8,4 %, 20-60 ml) which are considered as standard daily practice. Just a slight tendency of increased average blood pressure was found with a high dosage of procaine (over 500 mg) and especially sodium bicarbonate (8,4 %, over 100 ml). Furthermore, it is of interest that the measured blood pressure had no significant difference after 15 and 30 minutes of the start of the infusion (Table 2).

After over 400.000 applications of procaine therapy infusions according to the described regime in our clinic and outpatient department, we have not observed one case with long-term or severe side effects. No case was registered with a serious allergic emergency situation, which underlines the observations of Becke concerning the huge therapeutic safety of procaine [58]. Sometimes patients report of heart palpitation (6%) and profuse sweating (5%). According to our experience, patients who are using nitro compounds, calcium antagonists and beta-blockers, seem to have a higher disposition to these side effects. Apparently in such cases the reflective and over-segmental disinhibiting effect of the anesthesia dominates over the negative-ionotropic and negative-rhythmotropic potential of procaine. As expected, in approximately 6% of patients a short-time reduction in blood-pressure and vasovagal syncope situations can occur during the application. All these symptoms disappear within a few minutes, especially after reducing the infusion speed [34,63].

Some patients report sleep disorders (5%) and a general hyperactive feeling up to one day after finishing the infusion, which does not reduce the physical working capacity. Approximately 4.5% of treated persons complained of temporary headaches and slight vertigo. Especially during the first couple of infusions such reactions can occur in scope of a so-called "first reaction" (Hering's effect) according to the holistic thinking in neural therapy and homeopathy [1,93].

Indications and Contraindications of Procaine-Base-Infusions

The multiple therapeutic effects of procaine in combination with an alkaline additive are responsible for the enormous palette of medical indications (Table 3a). Especially acute and chronic pain, inflammatory and autoimmune diseases, vegetative imbalances, in addition to the complementary cancer treatments are of primary importance.

The few contra-indications should receive attention in practice which is summarized in table 3b.

Procaine-HCl+	100 mg +	200 mg +	300 mg +	400 mg +	500 mg +	over 500 mg
Na-HCO3 8.4 %	20 ml	40 ml	60 ml	80 ml	100 ml	+ 100 ml
analysed						
data (n)	215	2241	3031	88	105	18
PULS rate per	74.8 ± 13.1	74.2 ± 12.4	74.5 ± 12.0	74.4 ± 13.1	75.8 ± 11.7	73.1 ± 12.6
Minute (Min.)	[44 - 121]	[55 - 145]	[48 - 164]	[48 - 123]	[59 - 105]	[55 - 95]
after 15 Min.						
02-saturation	95.3 ± 4.6	95.4 ± 4.9	95.7 ± 5.9	95.1 ± 4.5	95.3 ± 5.8	95.3 ± 2.2
(%)	[80 - 100]	[79 - 100]	[77 - 100]	[81 - 100]	[88 - 99]	[85 - 98]
after 15 Min.						
RR systolic	145.6 ± 21.5	145.3 ± 21.0	145.7 ± 21.8	144.6 ± 20.5	139.2 ± 24.1	151.0 ± 14.1
after 15 Min.	[90 - 220]	[84 - 214]	[74 - 221]	[89 - 198]	[83 - 210]	[115 - 190]
RR diastolic	83.0 ± 10.9	83.9 ± 11.5	84.5 ± 11.1	86.4 ± 12.0	81.7 ± 15.3	87.6 ± 13.0
after 15 Min.	[45 - 146]	[47 - 137]	[44 - 135]	[54 - 133]	[53 - 116]	[70 - 107]
RR systolic	139.8 ± 19.7	140.1 ± 19.2	139.2 ± 19.1	134.5 ± 22.2	127.0 ± 22.1	140.6 ± 19.1
after 30 Min.	[68 - 210]	[80 - 205]	[80 - 210]	[97 - 206]	[86 - 208]	[105 - 198]
RR diastolic	80.4 ± 11.9	80.7 ± 11.2	80.9 ± 11.9	81.1 ± 12.8	81.7 ± 12.1	82.9 ± 11.8
after 30 Min.	[48 - 122]	[47 - 140]	[44 - 155]	[45 - 122]	[55 - 127]	[76 - 116]

Table 2: Mean [M], simple Standard Deviation [± SD], Minimum and Maximum [from - to] protocolled surveillance data during infusion with different dosages of procaine and sodium bicarbonate in isotonic sodium chloride basic solution [n=5698], taken from Oettmeier and Reuter, 2000 [63].

Acute situations	Radicular syndrome, pseudo-radicular syndrome, acute infection, early stage of algodystrophy, sudden deafness, inflammations, migraine, activated osteoarthrosis, postoperative pain treatment
Chronic pain	multiple arthralgia, chronic radicular-/pseudo-radicular syndrome, algodystrophy, all kinds of neuralgia, facet pain syndrome
Chronic inflammations	Lupus erythematosus, rheumatoid arthritis, psoriatic arthritis, scleroderma, neurodermatitis, multiple sclerosis, Crohn's disease, ulcerative colitis, polymyalgia rheumatica
Others	periphery circulatory disorders, constipation, dysmenorrhea Clinical and para-clinical hints for tissue acidosis, osteoporosis, Complementary cancer therapy, pre- and post-operative

Table 3a: Main indications of procaine-base-therapy.

Patient	Hypersensitivity towards Procaine, Neurosis or Psychosis with unclear compliance See also expert information at Procaine and Na-bicarbonate producers
Therapist and Staff	Lack of knowledge in handling local anesthetics, inadequate educated staff, Under-resourced rooms and lack of adequate emergency equipment

Table 3b: Contra-indications of procaine-base therapy.

Current Status: Procaine-Base-Infusion Adapted to the Acid-Base-Balance

The author Saha reported that after a total of seven procaine-base-infusions with daily increasing dosages up to a maximum of 300 mg procaine-HCl and 120 ml 8,4% sodium bicarbonate, 3 out of 13 patients showed clinical symptoms of metabolic alkalosis [94]. Before and after these series of infusions the Base Excess (BE) measured via arterial blood gas analysis was determined and in all cases amounted to over plus two, which indicates a verified metabolic alkalosis. It is important to emphasize that according to the above-described procedure of procaine-base-infusion, a daily application of such a high dose of sodium bicarbonate is unacceptable. This kind of daily treatment only applies to patients with an adequate acid-base

homeostasis. Simply, the body intrinsic buffer system should not be overloaded.

However, patients having a metabolic alkalosis with a reduced compensatory ability in acid-base balance are increasing. Quite often, this is found in cases of over-proteinization, advanced stages of cancer, liver weakness and putrefaction dysbiosis of the large intestine. Furthermore, the use of antacids, alkaline powders, loop diuretics and excessive sodium intake enhances the shift in the acid-base-balance towards alkalosis [95,96]. For the practical analysis of the acid-base balance we prefer the venous blood titration system BUFFY® over the arterial Blood Gas Analysis (aBGA) because it is hematocrit-adapted and calibrated to 37°Celsius [97-100]. The test gives very good information about the buffer capacity of whole blood and plasma and

indicates exactly the amount of base needed [101,102]. Metabolic alkalosis can also occur in hyponatremia, hypokalemia and in increased ammonia levels (in EDTA plasma).

In cases of inflammation, cardiac and renal dysfunctions, rheumatic and pain-related diseases, a metabolic acidosis are mostly likely detected [103]. These patients have an increased need of a buffer base and should receive sodium bicarbonate ranging from 60 - 120 ml (8.4% solution) in addition to procaine.

In contrast to cases of metabolic alkalosis, see figure 2 below, there is only a small or no need of additional base treatment. In this case, we only administer infusions of procaine-HCl together with a carrier solution. In addition, we suggest to give 3-5 ampules of L (+)-lactic acid. Alternatively, the newly developed ProcCluster® compound as a ready to use fast infusion (0.1-0.3%) is recommended [104].

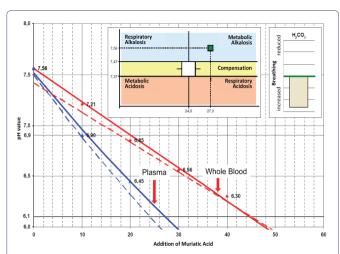


Figure 2: Findings of metabolic alkalosis (Buffy test system, venous blood and plasma-titration).

Another possibility of a safe procaine-base therapy is the use of a moderate alkaline base solution (1.68%), which is used in the Paracelsus Clinic Lustmühle. In this case, the dosage of procaine-HCl is increased stepwise.

In figure 3 the pH-values of different concentrations of procaine-HCl, different alkaline mixtures and some of the most important local anesthetics are compared.

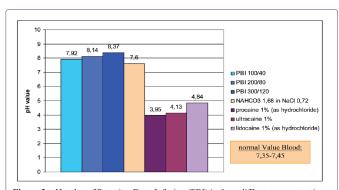


Figure 3: pH-value of Procaine-Base-Infusion (PBI) in three different concentrations, base mixture (1.68%) and some local anesthetics.

Examples from Treated Patients

The following case reports underline the various methods and diagnoses:

Case 1

Psoriatic arthritis: patient R.N, 60 years old, suffering from psoriatic arthritis since ten years, additional symptoms are chronic fatigue, depression, hypertension, sleep apnea.

State before procaine treatment (11th November 2016): Diffuse muscle cramps and pain permanently between VAS 6-7 despite complex medication (Sirdalud®, Relaxane®, Ibuprofen, Prednisolon 12.5 mg, Novaminsulfon (2x500 mg), Otezla® 60 mg), awkward gait with two crutches, intensive pain and reduction of movement left shoulder, hip and metacarpophalangeal joints both sides, CRP 41 mg/l, aBGA: pH: 7.43, BE: 2.1 mmol/l.

Therapeutic procedure: first series (10x) procaine-base-infusion twice a week (titration till 400 mg procaine), due to much better general condition continuation of infusion weekly.

Follow up: Stepwise reduction of pain until VAS 1-2, successful reduction of pain medication, including Otezla®, much better general condition, mood distinctly brightened, energy feeling significantly better, swelling and restriction of movement in affected joints markedly improved, control CRP < 5 mg/l. After 20 procaine infusions, the patient is almost painless, happy, has stopped using NSAR and Otezla®.

Additional complementary treatment: start with alkaline-rich nutrition, supplementation with Vitamin E (800 IE) and antioxidant complex, frankincense (Bosvay®, 3x800 mg), Harpagophytum (3x480 mg).

Comment: The positive effect of neural therapy and intravenously injected procaine is mentioned in old literature [105].

Case 2

Deep foot ulceration and chronic osteomyelitis: Patient H.S, 56 years old, state after kidney transplantation, cytostatic therapy.

State before procaine treatment (17th April 2009): All together 12 (!) operations during four months stay at the university hospital, multiple rejection reactions after autologous skin transplantations, wound healing disorders on harvesting points, CRP 98.5 mg/l, highly inflammatory ulceration of the dorsum of foot, partly extensor tendons and bones are visible, buffy test with metabolic acidosis.

Therapeutic procedure: 2x per week procaine-base-infusion (titration until 500 mg procaine and 120 ml 8.4% sodium bi-carbonate).

Follow up: 25.5.09: CRP: 23.3 mg/l, wounds on forearm and upper leg completely healed, ulceration foot 80% closed, pain reduced from VAS 8 to 2-3, Opioid drug (Tilidin ret. 200 mg) discontinued, 17.6.09: CRP: 6.8 mg/l, foot wound also completely dry, increase of motion training, 4.10.09: maintenance dose 1 tablet ProcCluster® 50 mg, very beneficial, no recurrence.

Additional complementary treatment: exposure to ozone gas locally (two month), homeopathic remedies, anti-oxidative acting supplement complex, alkaline-rich and hypo-allergic food.

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Comment: Together with the anti-inflammatory and vasodilating features of procaine, the known problem of metabolic alkalosis in patients with chronic kidney diseases and after transplantation can be solved by a combination with sodium bi-carbonate [106,107].

Case 3

Acute batch of multiple sclerosis: Patient ZR, 38 years old, disease known since 2003, relapsing-remitting, last in April 2011 (3 weeks stay in hospital for corticoid and interferon-treatment were necessary).

State before procaine treatment (7th May 2013): He reports double vision, rotary vertigo, right side of face with intensive dysesthesia, general exhaustion, stress syndrome, MRI (25.4.2013) showed a clear demyelination in white matter periventricular right more than left.

Therapeutic procedure: 1st week every other day, 2nd to 3rd week procain-base-infusion in rising dosage (total 8 x).

Follow up: Rapid symptom improvement, after two weeks already free of any complaints, complete period of disability only 4 weeks, his impression is very well and energetic, last clinical control in November 2014 without any change, control MRI (28.7.2013).

Additional complementary treatment: Neural therapy of neuro-modulative foci (Tonsils, Sinuses), brain organ cell extract weekly (Curafaktur), homeopathy with conium D12 2x3 globuli over 10 days and Gelsemium C30 1x3 globuli (1 day).

Case 4

Rheumatoid arthritis: Patient HR, women 34 years old, diagnosis known since 4 years, oral treatment with cortisol (10mg), MTX and NSAR (ibuprofen 3x600 mg) over three years.

State before procaine treatment (14th October 2016): Increasing drug side effects (stomach, flatulence, weakness), weather dependent pain in the small joints, swelling of metacarpophalangeal joints with warmness, stiffness in the morning, CRP: 11.2 mg/l.

Therapeutic procedure: At the beginning, weekly procain-base-infusion, after two months, reduction to twice a month, currently ProcCluster® capsule (50 mg) every other day and one infusion per month.

Follow up: Better general condition within two weeks, all pharmaceutical drugs were stopped after 6 weeks, no more joint pain, still little morning stiffness, much better general mobility and no progress of deformation.

Additional complementary treatment: Change of diet (vegetarian), supplementation with anti-oxidants, removal of all irritating root-canal teeth, amalgam sanitation, probiotics for intestinal health.

Comment: Procaine was used as additive to penicillin for intraarticular treatment of pyogenic arthritis over two decades [108-110]. Perhaps the local anesthetic component had more influence to control the inflammation than expected before.

Case 5

Sclerodermia: Patient HS, women 48 years old, diagnosed in June 2014.

State before procaine treatment (24th January 2015): Joint pain permanently (VAS between 4-5), coldness of fingers, dysaesthesia, dry eyes, beginning of radiologic changes on distal finger phalanges.

Therapeutic procedure: Two infusions procaine-base per week (titration to 300 mg procaine and 80 ml 8.4% sodium bi-carbonate), after one month reduction of infusion interval to twice per month.

Follow up: Very good response, almost free of symptoms over a period of two years.

Additional complementary treatment: Change of diet (vegetarian), supplementation with anti-oxidants, detox of Aluminum load, probiotics for intestinal health.

Comment: The case confirmed some hints from previous literature [111-113].

Case 6

Breast cancer with lung and bone metastasis: Patient RM, women 53 state after lumpectomy left breast (May 2010) $T_2 N_1(2-16) M_x E+P+$, HER2 negative, no chemotherapy, no radiotherapy, anti-hormonal treatment (Tamoxifen 10 mg) stopped after 5 months due to side effects, relapse with multiple bone and lung metastasis in February 2012.

State before procaine treatment (29th March 2012): Very weak and depressive mood, diffuse back pain (VAS 6-7), problems in climbing stairs, five kilogram loss of weight within last 6 weeks, laboratory: AP: 324 U/l, CA 15-3: 344 kU/l, CA 125: 76 kU/l, CEA: 7.5 mcg/l, pain medication with Tramadol ret. 100 mg (2x1), Novaminsulfon (2x500 mg) and Ibuprofen (2-3x400 mg), buffy with compensated metabolic alkalosis.

Therapeutic procedure: Series of 12 infusions with dosage titration over 6 weeks (optimal range 350 mg Procaine and 60 ml 8.4% sodium bi-carbonate), then weekly and meanwhile one to two per month.

Follow up: Within a scope of a holistic complementary concept completely free of pain, general better condition (appetite, energy, range of movement), distinct increase of weight, tumor markers significantly diminished, the pharmaceutical pain killers were stopped completely, last PET-CT (November 2016) has shown partial remission with complete disappearance of lung spots and reduced activity (SUV) into the skeleton.

Additional complementary treatment (stepwise made after first diagnosis): Change of diet (vegetarian), supplementation with anti-oxidants, intestinal support, removal of metal fillings in teeth and one root-canal tooth, mistletoe treatment over one year, whole body hyperthermia every three months, use of silver willow and aspen extract (Phytodolor®) for natural analgesic as needed.

Comment: The case underlines the importance to treat also the tumor-associated inflammation which is achievable with Procaine and other natural remedies [114,115].

Conclusion and Outlook

After the empirical start twenty years ago, procaine-base-infusion treatment has reached a well-accepted level of clinical importance and has advanced into a routine therapy in many hospitals and outpatient departments for pain treatment, rehabilitation and natural medicine.

Even if scientific findings convincingly confirm the procaine-base mechanism of action, spectrum of indications and the individualized application, more research and scientific studies are warranted.

It is very important for the authors of this article to emphasize that the treatment method of procaine is conducted properly, especially to individualize the therapy according to the acid-base-homeostasis and clinical parameters of the patient. Finally, it is noticeable that the method is not a replacement for neural therapy injections, especially for treatment of neuro-modulative triggers.

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