Semiology of the Pain Syndrome - Identifying the Ideal Methods of Locoregional Anesthesia Based on Their Rationale and Features

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Anesthesia and the degree of control over the perception of pain depends on the personality of the individual, the socio-economic conditions, potential previous painful experiences and, last but not least, on fatigue and fear of the dentist. The perception of pain in patients is closely connected to their mental state. Pain is defined as a sensation of discomfort, with wide variations, both in quality and intensity, for different people in seemingly identical conditions; an unpleasant sensitive and emotional phenomena connected to the threat of a wound or caused in the tissues or described in the terms of this disease. The essential element of any type of anesthesia is analgesia, an effect which in some cases cannot be achived, due to the patient's particularities or the physician's lack of experience in anesthesia. Locoregional anesthesia (LRA) represents the blocking of the nociceptive sensitive and sympathetic autonomic afferents as well as that of motor efferents at the level of peripheral nerves' axons, by means of local anesthetic. To achieve the set purpose, we carried out a study on a representative human sample comprised of 10.123 patients treated in the Oral and Maxillofacial Surgery Clinic (Ambulatory) from the County Clinic Emergency Hospital St. Spiridon Iasi, between 01.01.2015-31.12.2016. The reason for the exclusion of certain categories of patients in the reseach was: the patients with a special conditions background require individual pre-anesthesia schemes, personalised for the nature of the pre-existing general condition, which must be further approved by the attending specialist physician : cardiologist, internist, diabetologist; children under 18 years old, with a high degree of anxiety; a high precentage of elderly patients, over 60 years old, possess a combination of general issues, thus requiring a special approach. The thoroughness lying at the core of the anesthetic practice, most especially the safegurading of a technical accuracy in the performance of anesthesia [12,], instead of improvisations, the lack of anatomical and stomatological training in general and the resulting inefficiency as such, is the underlying in-depth structuring element of this paper.

Keywords: Diagnosis, locoregional anesthesia, pain, anxiety, sedation, semiology, painkillers, emergency

Pain is a purely functional phenomenon, arising due to an excitation of certain intensity acting on the surface nerve terminations or on those inside the organism; it is the result of stimulation of specialised nociceptor receptors and/or their related nerve fibres [3]; it is a global phenomenon requiring two essential and distinctive aspects, the perception of and the reaction to pain. The perception is a neurologic phenomenon, while the reaction to pain is a group of somatic, vegetative, mental phenomena; each of these aspects has its own programme. The threshold of pain perception is the lowest intensity of a stimulus which is recognised as pain. The threshold of the reaction to pain is represented by the intensity of the painful sensation triggering somatic phenomena.

Pain represents an important alarm system in the protection of the organism; it triggers defense reactions towards the removal of the harmful agent; it gives useful guidelines for the establishing of the diagnosis.

The decoding and acknowledgement of a painful message, which has reached the superior nerve centers by different sensitive-sensory ways, bears the generic term of sensation of pain. Pain is a multidimensional experience, caused by characteristic properties of the *neuroprint* of nervous impulses type, generated and distributed by a neurocerebral network: *the body's own neuromatrix*. This *Neuromatrix* is genetically determined and modified by sensory experiences, representing the primary mechanism inducing the neuronal character of the pain (Melzack, 1986).

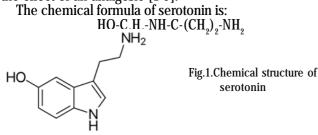
The neurochemistry of pain refers to the endogenous chemical substances intervening in the triggering process of the pain signal and the transmission of specific information to the brain and also in the descending control of the brain over the intensity of this signal.

The brain exercises a descending control over the intensity of the pain signal by means of neurons containing opioid peptides, catecholamine, serotonin.

Serotonin's role in modulating the pain is: a slight electric stimulation of the gigantocellular reticular nucleus, facilitating the transmission of painful information through the spine, by means of a serotonergic mechanism in which 5HTI receptors are involved. The global effect of serotonin (an indole derived amine) on pain is an algebraic sum between the exaggeration tendencies and the diminishing

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tendencies of the pain sensation, ensuring one the whole the effect of an analgesic [1-5].



The patient is first and foremost afraid of pain, pain being an experience each person encounters more or less frequently, in a higher or lower intensity.

It is thus normal to have the patient be preoccupied with the method, technique and quality of the anesthesia and the surgical performance, the possibility of deficiences in the induction or the duration of the anesthesia, which might cause pain during the intervention or in the period afterwards [6,7]. The perception of pain in patients is strongly correlated with their mental state. A solitary therapy is not 100% self-sufficient in dental practice. Only the combination of several factors has a cummulated positive effect: mental preparation, pharmaco-therapeutical sedation, locoregional anesthesia.

Although the modern anesthesia procedures have considerably changed the working environement in the dental practices and the ambulatory care for oral and maxillofacial surgery, the emotion and the anxiety, the concerns persist still with patients that will have to be subjected to dental treatments and care; pain relief represents a highly important objective for the dentist or the oral surgeon.

Locoregional anesthesia entered current practice after 1905, when Einhorn synthesized procaine (novocaine). Step by step, anesthesia methods and techniques were perfected, new anesthetic substances were synthesized, which allowed all the surgical branches, and of course maxillofacial surgery, as well as other stomatological specialties, to develop intensly.

After this date, general anesthesia was replaced by locoregional anesthesia, considered to be *a method of anesthesia with the lowest risks*, provided the indications and warnings are closely followed.

Locoregional anesthesia is the method in which the use of chemical, physical substances or electricity creates a temporary desensitization of the anatomical region on which one intervenes, while retaining intact consciousness. Due to the fact that this anesthesia abolishes only pain sensitivity, preserving the thermic, tactile and pressure sensibilities, American authors called it locoregional analgesia [5,6].

The most used methods for pain control in stomatological practice consist of the blocking the ways of pain impulses [7]. This blocking is made by depositing an adequate chemical agent extraneurally, close to the nerve or the nerves to be anesthesied. The chemical agent, represented by the anesthetic solution, is absorbed by the lipoid tissue of the nerve, thus preventing the depolarization of the nerve membrane.

To achieve a maximal effect, the local anesthesic must be in contact with at least 8-10 mm of nerve, in order to block 2-3 Ranvier nodes. If however, a smaller part of the nerve is the focus, it is believed that the anesthesia will be incomplete.

The thickness of the nerve's fibre is another important factor in locoregional anesthesia; the thicker nerve fibers

are more difficult to block, requiring a higher concentration and quantity of anesthetic solution. This is the result of a larger surface, in relation with the volume and the size of the internodal distance. If an inappropriate concentration of local anesthetic makes contact with the nerve fibre or if less than a minimum number of fibres is affected, the anesthesia may be incomplete [8-10]. This manifests itself by insensitivity to a single stimulus, but a possible painful response to a repeated series of stimuli. If a nerve or nerve fibres are unable to transmit impluses, because of a local anesthetic agent, it means that the regional analgesia is functioning well over the area innervated with these nerves.

Anesthesia ensures the relief of pain, the undettered functioning of the vital systems and apparatus, facilitating the surgical performance.

The usage of analgesic-anesthesic substances preceded, by far, the anatomical and physiological research and discoveries on pain.

Today, modern anesthesia allows the adjustment of methods and techniques for each specific case individually, so that it ensures a perfect operating security, with minimal risks.

A good local or locoregional anesthetic should be harmeless to the tissues, should not have a local or general toxicity, should determine a qualitative and enduring anesthesia, and should not cause injuries at the level of nerve terminations. It should also be hydrosoluble and not cause allergic phenomena [11].

Locoregional anesthesia is successfully used for patients with a balanced mental state, calm and cooperative. For anxious, aggitated and non-cooperative patients one recommends as an ideal anesthesia method, for extended oral surgical interventions, that can be both timeconsuming and traumatising, the locoregional anesthesia in combination with a safe and efficient pre-anesthesia. During the intervention, an intravenous infusion is carried out to administer the anxiolytic medication or those meant to prevent and treat potential side effects.

Pre-Anesthesia comprises all the measures taken to better prepare the organism for anesthesia; knowledge of safe pre-anesthesia methods, of pain and anxiety control, establishing a good relation with the patient are the most important managing methods for the patient harbouring negative emotions in the dentist's practice. The purpose of premedication must be unconditionally determined by the anxiolytic effect and the analgesic one for the improvement of pain toleration.

The objectives of premedication – inducing calmness, a certain degree of amnesia, causing induction, the preservation of the anesthesia; reducing salivary secretion. To remove the reflex hyperactivity, vegetative hyperactivity, using a vagal as well as a sympathetic-adrenaline pathway. Both manifest themselves by rhythm disturbances. To increase the threshold of pain sensitivity; to reduce the painful effects of certain substances used in premedication (atropine, antispasmodic substances or barbiturates). During operation the basal metabolic rate must be decreased.

Pre-anesthesia is carried out by combining four fundamental drugs: (alone or in various association): 1. Analgesics (opiates); 2. Vagolytics (atropine, scopolamine – cerebral depressor); 3. Sedatives (barbiturates); 4. Tranquilizers (derivatives of phenothiazine).

Mental and drug-related preparation (pre-anesthesia premedication) do not have as a primary objective the control of intraoperative pain (covered by the anesthesia), but mainly the control of the mental reaction to pain [12, 13]. There can be no premedication if there is no infrastructure in place with a surgical treatment room and a *waking* room, in which the patient can be supervised by qualified staff and has at its disposal oxygen therapy equipment and instruments, keeping the breathing airways free, with monitors for the vital functions and cardio-respiratory analeptic functions [14]. We bear witness thus to the limits of dental medicine practice, especially for the stomatological specialists.

The search for, the research and the assessment of optimal methods of locoregional anesthesia to successfully address distressed patients as an alternative to the combined anesthetic method implies thorough knowledge of the physiologic, physiopathologic and, last but not least, the psychological aspects of pain.

Knowledge of pharmacology and pharmacodymanics of sedative, analegesic and anesthetic medication is a major prerequisite in the creation of alternative preanesthesia schemes.

For a surgical intervention the anesthetic is more dangerous for the patient than the scalpel itself.

Analgesia is a peripheric anesthesia; regional analgesia refers to the loss of pain sensation for an anatomical area, without affecting the patient's consciousness [15].

Basic anesthesia: is a very strong pre-anesthesia, a partial anesthesia. The hypnotic effect of the medication is surpassed, without reaching the stage of anesthesia without reflexes. The characteristic of analgesia is the action on the fiber.

Regional anesthesia represents more than the loss of the pain sensation for a specific anatomical area, without affecting the consciousness; regional anesthesia interrupts all other sensations, including temperature, pressure, contact, motor function.

The terms of regional analgesia and regional anesthesia are presented as an expression of local anesthesia and are often used indiscriminately. As long as the pain is the main sensation of the tooth, the analgesia may offer a satisfactory state for the patient. If one wishes to interrupt the painful sensibility, the motor function, the thermic and pressure sensation, then regional anesthesia offers the best results.

Analgesia and regional anesthesia do not exclude one another. They interfere with one another, completing each other, with the ultimate purpose of relieving pain for the patient's comfort and security.

A few criteria are to be considered in selecting the method of locoregional anesthesia, on which the success or failure of the method often depends. These criteria are : the anesthesia area, the necessary depth, the duration of the anesthesia, the presence of infection, the patient's age, the general state of the patient, hemostasis, if it is absolutely necessary.

The action of local anesthesics is represented by the blocking of Na channels. From a chemical viewpoint, they are categorised in 2 large groups: aminoesters: procaine, tetracaine • aminoamides: lidocaine, prilocaine, mepivacaine, bupivacaine, ropivacaine, etidocaine.

The choice of the local anesthetic is made depending on the size of the nerve to be blocked and the type of block we want to achieve.

The purpose of the study is to demonstrate the value of locoregional anesthesia methods. In order to apply these locoregional anesthesia techniques as accurately and as efficiently as possible, the knowledge of anatomical features of the oral-maxillofacial territory becomes a vital prerequisite, one without which the effect of the locoregional anesthetics leaves much to be desired. We believe that, although the local anesthetics used today do not meet all the criteria, they do comprise the majority.

Experimental part

Material and method

In order to meet the set objective, we carried out a study on a representative human sample comprised of 10,123 patients, treated in the Oral and Maxillofacial Surgery Clinic (Ambulatory Care), from the County Clinic Emergency Hospital, 3 St.Spiridon3 Iasi, between 01.01.2015-31.12.2016.

Results and discussions

The selection of cases was random, in relation with the addressability of the patients for the duration of the research.

The 10,123 patients had dentoalveolar surgical interventions.

The investigation algorithm of the general sample involved the analysis of a multitude of data concerning the patient and the recommended intervention.

Before establishing the indication of anesthesia, a general compulsory clinical examination was carried out, in order to assess whether the patient's state does not contraindicate any of the substances used; three compulsory stages are followed: the psychological study stage, the anamnesis stage and the patient's organic state.

The fear of pain is most often triggered by influence exercised even before entering the dentist's practice; the impact of the waiting room in a dentist's practice; the overall outlook of the waiting room, the agitation of the medical staff, noises, the specific odour.

Anxiety, fear of a dental treatment that may cause pain are frequently indicated factors in DASS. The reasons for this fear are plenty, starting with previous traumatising medical-surgical experiences of any type, therapeutic stomatological experiences and, last but not least, the mental-affective load particular for each patient.

The importance of identifying the source factors for the negative emotion is of high practical interest, since this state of anxiety is characterised by an extremely powerful vasovagal response, sometimes with dramatic consequences for the patient.

During stomatological therapy or dentoalveolar surgical therapy, for the anxiety- ridden patients, with DASS-2, DASS-3, DASS-4, the negative emotion's main source lies with the anticipation of pain (28%), followed by fear of the specialist physician (22.3%), fear of anesthesia (20.6%), fear of surgical intervention (17.3%) and the sight of blood (11.6%).

A patient, even a mentally balanced one, confident in his/her emotional reactions, may become anxiety-ridden when unexpectedly introduced in the dentist's office, surrounded by instruments, seringes, blood soaked dressings, imprinting materials, high rotating equipment, enhancing and internalising his/her concerns.

The general state of health, reflected in the waist and the weight, allowes for an objective study, unlike general notions such as obesity and weight loss, since both are deemed as organic defects.

Complementary examinations are guided based on the data obtained from the anamnesis, the careful examination of the oral cavity, so as to control and remove potential mobile dental prostheses, decemented prostheses, easily detachable tooth fillings, macroglossia, possible causes of serious accidents, such as mechanical obstruction of airways.

If the medical background and the general clinical examination highlighted organic and functional defects or

deficiencies, paraclinical laboratory examination will always be requested.

We suggested the improvement of locoregional anesthesia methods through : substitution : technique – intraosseouss anesthesia or the anesthetic agent; combined : topical anesthesia or pre-anesthesia medication.

The value of the proposed anesthesia methods was demonstrated by a cross-comparative analysis, whose assessement was based on the following indexes: tolerance score of intraoperative pain; onset of an unpredictable medical event (allergy, a cardiovascular one); onset of postoperative pain -the patients' statements.

In order to assess the manner in which the proposed anesthetic option manages to modulate the patient's reception of the maneuvers considered to be painful a system was put in place to assess the degree of pain during surgery.

The main purpose of our research was to identify the *ideal method of anesthesia.*

In our study we included the following surgical interventions, generically referred to as: surgical intervention by appointment : dental extraction, apical resection, canine or molar odontectomy, regularization of alveolar ridge, gingivectomy.

We deemed as necessary the removal of 3131 patients from the sample, presenting : a special conditions background, children under 18 years old, elderly persons over 60 years old.

The reason for excluding from research these categories of patients was: the patients with special conditions background require personalised pre-anesthesia schemes correlated with the nature of their general preexisting condition, and even more so, approved by the attending specialist physician : cardiologist, internist, diabetologist; children under 18 years old have a high threshold of anxiety; a high percentage of elderly patients over 60 years old have a combination of general problems, thus requiring a special approach.

We selected an optimal number of patients – 6992 (69.07%), aged between 20-60 years old, in order to apply a coherent comparative statistical method with a practical and scientific conclusion.

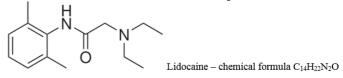
Owing to the multiple advantages presented, locoregional anesthesia is considered a common method in routine stomatological care.

The fundamental principles and the clinical data support the anesthesia techniques, indicating the fact that it can successfully replace the sensation of pain arising during the surgical intervention, depending on the various clinical situations, so as to ensure the optimal comfort of the patient during surgery.

In the past years new intraosseouss anesthesia techniques were developed and launched on the market, and progress was made on the injection method of anesthetics, with the introduction on the market of electronic computer systems for the administration of anesthetics. Some of these are : the Confort Control Syringe system from Dentsply, The Wand system, SleeperOne system from Dental HITEC. Some of these systems are adjusted for the administration of intraosseouss anesthesia as well.

The locally applied anesthetic is absorbed and carried into the blood flux. This is important, since the incorrect use of anesthetics may induce toxicity, by a single application or by association with an injection-conducted anesthesia. The quantity of anesthesia is important when discussing topical reactions. The concentration of the anesthetic in topical medicine is higher than those in the injectable versions. Topical administration reaches high levels in comparison with slow intravenous injection. Although the plasmatic level is of 1/3 of the one obtained by intravenous administration, the speed with which it enters the blood flux is faster. What is certain is the fact that toxic reactions caused, even in the case of topical application, death.

The use of a topical anesthetic before the anesthetic puncture is something common in stomatology. Lidocaine and benzocaine are the most used topical anesthetics.



Lidocaine, aslo known commercially as xylocaine, is a local amide anesthetic, derivative of cocaine but without the euphoric or addiction effect of cocaine.

Benzocaine is a local anesthetic used for pain relief at mucosa level.

The principle on which intraosseouss anesthesia systems are based is common and consists of the insertion of the anesthetic solution in the periradicular cancellous bone of the treated tooth, after a previous perforation of the cortical bone; the following advantages of the intraosseouss anesthesia are confirmed: immediate anesthesia of a number of teeth (2-6) from the maxilla and the mandible via a single anesthetic puncture, without an additional palatal or tongue injection; eliminates the numbness sensation in soft parts (tongue, cheeks, lips); the use of vasoconstrictors without the risk of necrosis.

The technical limitation lies exclusively in the inability to penetrate the cortical bone, due to its density or rigidity. In these rare cases (aprox. 4% of cases), another locoregional anesthetic technique is recommended.

The surgical intervention ranking at the top was: dental extraction -3241 cases (46.35%); apical resection -1720 cases (24.59%), odontectomy-621 cases (8.88%); periapical curretage -583 cases (8.33%); removal of small tumors -507 cases (7.25%); regularization of alveolar ridge -320 cases (4.57%).

The locoregional anesthesia methods used were: locoregional anesthesia – 57%; locoregional anesthesia + topical anesthesia – 19%; locoregional anesthesia + preanesthesia medication – 24 %.

Regardless of the accuracy of the stomatological technique and the skill of the medical practitioner, a faulty anesthesia indication – disregarding the specific conditions of each patient may result in complications carrying hidden risks.

The value of the proposed anesthesia methods was demonstrated by means of a cross-comparative analysis, whose assessement was based on the following indexes: the tolerance score of intraoperative pain; onset of an unpredictable medical event (allergy, a cardiovascular one); onset of postoperative pain -the patients' statements.

Out of a total of 6992 patients examined and treated, we were interested in their distribution on the medical emergency variable.

The computer statistical deductions led to the following percentage scores: 37% triggered an acute hypotonia failure (vasovagal syncopes, ortostasis syncopes, pregnancy syncopes, carotid sinus syndrome); 36% triggered cardio-circulatory emergencies (rhythm disturbances, HTA crises, angor pectoris crises); 12% triggered allergic accidents; 8% triggered neurologic emergencies; 7% triggered other types of emergencies.

The analysis of data on variable: indication of anesthesia vs. onset of the medical emergency, revealed the following preliminary data: locoregional anesthesia vs. emergencies – 94%; locoregional anesthesia + topical anesthesia vs. emergencies – 5%; locoregional anesthesia + preanesthesia medication vs. emergencies – 1%.

Three major factors may alter the indication of anesthesia with the immediate consequence of a medical emergency: dental anxiety score - holds the highest percentage; the appearance of a general state of health; incomplete anamesis.

Locoregional anesthesia is far from being a perfect anesthetic technique. If one forgoes the patient's general state of health and his mental state at the moment of surgery, the LRA cannot eliminate the risk of an unpredicted medical accident.

The alternative in indication of anesthesia is the combined method of locoregional anesthesia and preanesthesia medication.

The indication of anesthesia + premedication (with a computerized average of 70%) is the method that proved to be most efficient in managing postoperative pain.

After correlating all the analysed indexes, we can conclude that the combined method of locoregional anesthesia + pre-anesthesia medication is the closest to the ideal anesthesia technique in dental practice or in the oral surgery ambullatory care, managing to reduce to a minimum the risks associated with the performance of anesthesia.

Conclusions

During stomatological or dentoalveolar surgery, the onset of a medical emergency is influenced by the indication of anesthesia.

The potential of the locoregional anesthesia represents the most physiological anesthesia method and has the widest indications in stomatology.

Anesthetic substances, rather numerous at the moment, have common properties, distinguished only by the swiftness of onset, the power of action, the duration, secondary reactions and the maximal posology of each and every one of them.

The purpose of premedication must unconditionally be determined by the anxiolytic and analgesic effect on the improvement of tolerance to pain, and the administered doses must be correlated with the DASS anxiety score, the manner in which it is used, the probable duration of the intervention.

The thoroughness lying at the core of the anesthetic practice, most especially the safegurading of a technical accuracy in the performance of anesthesia, instead of improvisations, the lack of anatomical and stomatological training in general and the resulting inefficiency as such, is the underlying in-depth structuring element of this paper.

The dentist must choose wisely the best anesthetic, recommending caution in its administration, the restricted posology, personalized for each patient.

References

1.ADLER R., 2007: Intraosseouss Dental Anesthesia, Patent Cooperation Treaty Application.

2.AGGARWAL V., JAIN A., KABI D., 2009:Anesthetic Efficacy of Supplemental Buccal and Lingual Infiltrations of Articaine and Lidocaine after an Inferior;Journ. Of Endodontics, 35(7):925-929.

3.AGGARWAL V., JAIN A., KABI D., 2009:Articaine added to inferior alveolar nerve block, Dental Abstracts, 54(4):190-191.

4.ANDERSON R. The Puzzle of Pain. 2nd ed. London, New York: Gordon &Breach ; 2004.

5.BABL F, BARNETT P, PALMER G, et al. A pilot study of inhaled methoxyflurane for procedural analgesia in children. Paediatr Anaesth 2007;17:148-53.

6.BRAD R, BANCILA R, LAZARESCU F. Anxietatea în corelaie cu manevrele de igienizare: rezultatele ultimului studiu realizat în S. U. A. Rev Med Stom. 2001 ;5(2):87-90.

7.BUCUR A., VILA C.N., LOWRY J., ACERO J., 2009:Compediu de chirurgie oro-maxilo-faciala.Edit., Q Med.Publishing, Bucuresti.

8.BOATCA, R.M., SCUTARIU, M.M., RUDNIC, I., STEFANACHE, M.A.M., HURJUI, L., REZUS, E., MARTU, S., Evolution of Inflammatory Biological Markers Within periodontal Therapy to patients with Rheumatoid Arthritis, Rev. Chim. (Bucharest), **67**, no. 4, 2016, p. 741

9.CARACAS H.C., MARTINS P.M., 2009: The use of lidocaine as an antiinflammatory substance: A systematic review, Journ. of Dentistry, 37(2):93-97.

10.CHIRITA R, SZALONTAY A, ILIESCU D. Interrelatiile dintre tulburările anxioase si tratamentul stomatologic. Rev Med Stom. 2001;5(1):276–279.

11.COSTAN V.V., CIOFU M., TOADER P.M., FILIOREANU A. M., POPA C., POPESCU E. Specific treatment in the diagnostis and treatment of malignant transformed leukoplakias-Oral Oncology, May 1, 2013, Vol.49, suppl.1, S 66

12.DAU M., BUTTERCHEREIT I., GANZ C., FRERICH B., ANISIMOVA E.N., DAUBLANDER M., KAMMERER P.W., Influence of needle bevel design on injection pain and needle deformation in dental local infiltration anaesthesia – randomized clinical trial, International Journal of Oral and Maxillofacial Surgery, volume 46, Issue 11, Iunie 2017

13.DOUKETIS, JAMES D. MD; SYED, SUMMER MD; SCHULMAN, SAM MD, PhD Periprocedural management of Direct Oral Anticoagulants: Comment on 2015 American Society of regional Anesthesia and Pain medicine Guidelines Regional Anesthesia & Pain Medicine: March/ April 2016 - Volume 41 - Issue 2 - p 127–129

14.HILA EPSTEIN-BARASH L, KWON A.H., 2009:Prolonged duration local anesthesia with minimal toxicity,Proceeding of the National Academy of Sciences.

15.***Medical Developments International Ltd. Penthrox (methoxyflurane) inhalation. Product information, May 2009.

16.MARTU, S., NICOLAICIUC, O., SOLOMON, S., SUFARU, I., SCUTARIU, M., REZUS, C., POPESCU, E.. The Evaluation of the C Reactive Protein Levels in the Context of the Periodontal Pathogens Presence in Cardiovascular Risk Patients, Rev. Chim. (Bucharest), **68**, no. 5, 2017, p. 1081

17.DIMOFTE M, CHOUKROUN J, MOSCALU M, POPESCU E. Quality of Life after using of Platelet Rich Fibrin (PRF) in Patients with Alveoloplastic Extraction. Revista de Cercetare si Interventie Sociala 2016; 55 : 31-46. IF 0,380

18. SAVA, A; FURNICA, C; PETREUS, T; CHISTOL, RO; MOTOC, AGM. Trigeminal nerve: MRI anatomy and case presentation of trigeminal neuralgia due to arterial compression, Romanian Journal of Morphology and Embryology, 2012, 53(4): 1097-1102

19.WIENER R.C., 2009:Local anesthetic syringe ergonomics and student preferences, J Dent.Educ., 73(4):518-522.

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