A Study on the Penetration of Lidocaine into Oral Mucosa by Iontophoresis

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I. INTRODUCTION

Iontophoresis is a process which causes an increased penetration of ionized substances into tissues with the assistance of an electrical current. One electrode should assist the penetration of a charged compound during iontophoresis, i.e., negative ions are delivered by cathodal (−) iontophoresis, and positive ions are delivered by anodal(+) iontophoresis.[1]

Iontophoresis has many advantages as a drug administration method. Systemic toxicity is virtually eliminated since only a minute amount of drug is delivered. Nevertheless, a relatively high drug concentration is administrated locally. Patient acceptance is excellent, and fear of administration is eliminated, especially in comparison to administration by syringe and needle.[2] Thus, in the medical literature, iontophoresis is used to indicate the process of increasing the penetration of electrically charged drugs into surface tissues by the application of the electric current.[3, 4]

Although iontophoresis was apparently first described in 1747 by Veratti, this technic lost its popularity toward the end of the 19th century when more sophisticated inventions in the field of electricity were made. Iontophoresis was revived at the beginning of the 20th century by Leduc, who introduced the term iontherapy and formulated laws that govern this process. Leduc's elegant experiment provided convincing evidence that iontophoresis was a powerful technic for the introduction of drugs into and through the surface tissues.[3, 5, 6]

Iontophoresis is old process that has received new life by application of sophisticated technology, scientific principles, and modern drugs. Iontophoresis has been used primarily as a research tool in clinical investigations, and now there are several valid uses of iontophoresis in medicine and dentistry. Iontophoresis has been in clinical use to diagnose and treat various diseases.[3, 5] The iontophoretic application of drugs has been used to treat dentinal hytersensitivity, as well as some other dental problesm.[7]

Iontophoretic medication is the process of introducing ionic drugs into surfaces of the body for therapeutic purposes. Many ionic pharmaceuticals are available, including fluoride,[3, 7-12] lidocaine hydrochloride,[3, 7, 13-18] epinephrine hydrochloride[19-21] methylprednisolone sodium succinate,[22-27] several ionic antibiotics,[3] and other specific pharmacological agents. These durgs offer potential for the development of new dental therapies. Iontoporetic medication is highly suited to dentistry because most of the

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conditions treated in the dental offices are near the body surface.

Pain is one of the most commonly experienced symptoms in dentistry and, as such, pain control is a major concern to dentists. In dentistry, pain control is obtained primarily by the injection of local anesthetic solution for acquiring nerve blocks, field blocks, and local infiltration. But, most patients have a fear and anxiety of needle injection. For these patients, iontophoresis will be a better method for anesthesia of surface tissues than needle injection. Although several clinical studies[3,7,13-18] have reported the possibility of lidocaine iontophoresis for anesthesia of oral mucosa, the study about quantitative comparison between iontophoresis and topical administration of lidocaine was sparse.

The aims of this study were to evaluate : (1) the efficacy of lidocaine iontophoresis in oral mucosa and (2) the influence of epinephrine on lidocaine adminstration using radiolabelled lidocaine and measurement of radioactivity.

Ⅱ. MATERIALS AND METHODS

Animals

Sixteen rabbits, weighing approximately 2kg each, were anesthetized with Ketamine (Ketalar inj., Yu Han Corp., Korea) by intramuscular injection(50mg/kg).

Materials

[1-carbony-^{14}C] Lidocaine hydrochloride [specific activity(S.A.)=55.0 Ci/mmol, Dupont, U.S.A.] was used. When carbon labelled lidocaine was dissolved in distilled water, 0.1ml of the solution had 5μCi of isotope.

Bosmin^{R}(epinephrine hydrochloride 0.1g/100ml), added to lidocaine to obtaine the final concentration of 1 : 50,000 epinephrine solution, was used as a vasoconstrictive agent.

Drug application

Rabbits were divided into four groups as follows.

Group 1. The lidocaine in distilled water was applied in 0 mA for 5 minutes(topical application).

Group 2. The lidocaine in distilled water with 1 : 50,000 epinephrine was applied in 0 mA for 5 minutes.

Group 3. The lidocaine in distilled water was applied in 4 mA for 5 minutes.

Group 4. The lidocaine in distilled water with 1 : 50,000 epinephrine was applied in 4 mA for 5 minutes.

Each group included 4 rabbits, and drug application site was right buccal mucosa. Because the lidocaine is positively charged, drug was delivered by anodal(+) iontophoresis. For drug application, the buccal mucosa of rabbit was dried with gauze, and cleansed with alcohol wipe. An active electrode(diameter : 10mm) was made up of polymerizing resin and a snap which could be attached to clip on electrode (Phoresor Ⅱ, PM700, Motion Control, U.S.A.). An active electrode containing sterile cotton was saturated with 0.1ml of solution and placed on the buccal mucosa. For anodal(+) iontophoresis, the active electrode was connected to the anode of iontophoretic unit(Fig.1 Phoresor Ⅱ, PM700, Motion contol, U.S.A.), while the cathode was connected to the abdomen of rabbit. For affixing the indifferent electrode, rabbits's skin of abdomen was carefully shaved. For topical application, the drug was applied with same electrode but no current was used. During the application of drug, the cotton rolls were used for keeping the periphery of field dry and preventing saliva contamination which might shunt the current. Area touching the active electrode was outlined with indelible pencil. After application, radioactivity remanining on the mucosa touched by the electrode was thoroughly washed with a gentle stream of distilled water.

Measurement of radioactivity

Tissue samples of the same diameter as the

electrode were obtained at 30 minutes after drug application. Tissue samples of the buccal mucosa were divided into three layers, i.e., superficial, middle, and deep layers. The thickness of the tissue samples was approximately 3mm, therefore that of the sliced pieces was approximately 1mm. Sliced samples were weighed and homogenized in 2ml of 4% NaOCl solution. This homogenate was mixed with cocktail solution in counting vial. The radioactivity of lidocaine was determined using a Beckman Liquid Scintillation Counter (Fig. 2, LS 5000TA, Beckman, U.S.A.). Because the weights of the sliced samples were somewhat different, the radioactivity per milligram of sliced sample(cpm/mg) was used for comparing the differences among groups.

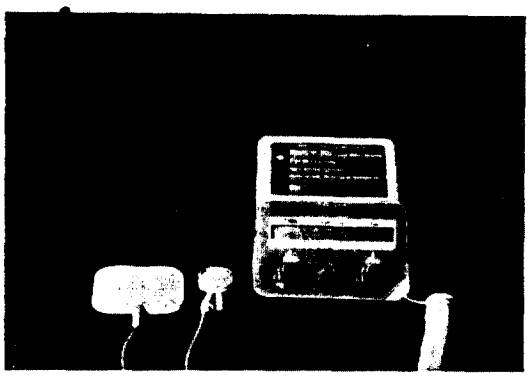

Fig 1. Phoresor Ⅱ, PM700, Motion Control, U.S.A.

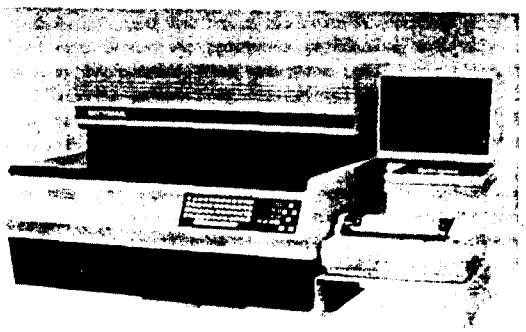

Fig 2. Beckman Liquid Scintillation Counter, LS 5000TA, Beckman, U.S.A.

Statistical analysis

Data were inputed on an IBM PC and all statistical analyses were performed by SPSS PC+ (Microsoft Corp., U.S.A.). Analysis of variance (ANOVA) was used to compare the mean values.

Ⅲ. RESULTS

Table 1 and Fig. 3 show the means and standard deviations of radioactivity according to the depth of tissue in topical application and iontophoresis of [^{14}C] lidocaine.

Table 2−4 show the means and comparative amounts of [^{14}C] lidocaine, and statistical differences in superficial, middle, and deep layers. In all layers, the means of radioactivity increased in order of topical application groups, iontophoresis without epinephrine group, and iontophoresis with epinephrine group.

There was no significant difference between the topical application groups. The addition of ephinephrine 1/50,000 did not affect the uptake of lidocaine in topical administration.

Significant differences were found between topical application groups and iontophoretic groups($p<0.05$). Compared with topical application, the amounts of lidocaine absorbed were increased about twice to seven times by iontophoresis. In the case of lidocaine without ephinephrine group, the amount of lidocaine absorbed was five times greater with iontophoresis than topical application in superficial layer. In middle and deep layers, the penetration of lidocaine was increased above twice by iontophoresis. When epinephrine 1/50,000 was added, the amount of lidocaine absorbed by iontophoresis was incressed. The penetration of lidocaine was enhanced above six times by iontophoresis than topical application when epinephrine 1/50,000 was added.

There was also significant difference between

the iontophoresis without epinephrine group and the iontophoresis with epinephrine group($p<0.05$). Co-iontophresis of epinephrine 1/50,000 significantly enhanced the penetration of lidocaine. This phenomenon was markedly observed in middle and deep layers.

Table 1. The mean counts and standard deviations of radioactivity(cpm/mg) of [^{14}C] lidocaine in the layers of specimens.(mean±SD)

	Topical		Iontophoresis	
Group*	1	2	3	4
Superficial	76.61 ±9.44	76.75 ±19.43	403.74 ±72.09	517.03 ±87.12
Middle	33.09 ±6.64	48.39 ±12.70	71.17 ±4.06	210.21 ±17.20
Deep	22.45 ±3.62	23.87 ±5.92	61.95 ±15.16	147.46 ±28.84
Total	132.16 ±8.67	149.00 ±36.62	536.86 ±83.21	874.70 ±93.11

Group 1, 3 : lidocaine alone. 2, 4 : lidocaine with epinephrine 1/50,000.

*Each group included 4 rabbits.

Table 2. The means(cpm/mg) and comparative amounts of [^{14}C] lidocaine and statistical significance in the superficial layer.

Group	Mean	Comparative amount	ANOVA
1	76.61	1**	
2	76.75	1.00	(1,3)* (1,4)*
3	403.74	5.27	(2,3)* (2,4)*
4	517.03	6.75	(3,4)*

*$p<0.05$ **76.61 cpm/mg

Group 1 : topical application, lidocaine alone.

2 : topical application, lidocaine with epinephrine 1/50,000.

3 : iontophoresis, lidocaine alone.

4 : iontophoresis, lidocaine with epinephrine 1/50,000.

Table 3. The means(cpm/mg) and comparative amounts of [^{14}C] lidocaine and statistical differences in middle layer.

Group	Mean	Comparative amount	ANOVA
1	33.09	1**	
2	48.39	1.46	(1,3)* (1,4)*
3	71.17	2.15	(2,3)* (2,4)*
4	210.21	6.35	(3,4)*

*$p<0.05$ **33.09 cpm/mg

Group 1 : topical application, lidocaine alone.

2 : topical application, lidocaine with epinephrine 1/50,000.

3 : iontophoresis, lidocaine alone.

4 : iontophoresis, lidocaine with epinephrine 1/50,000.

Table 4. The means(cpm/mg) and comparative amounts of [^{14}C] lidocaine and statistical differences in the deep layer.

Group	Mean	Comparative amount	ANOVA
1	22.45	1**	
2	23.87	1.06	(1,3)* (1,4)*
3	61.95	2.76	(2,3)* (2,4)*
4	147.46	6.59	(3,4)*

*p<0.05 **22.45 cpm/mg

Group 1 : topical application, lidocaine alone.
2 : topical application, lidocaine with epinephrine 1/50,000.
3 : iontophoresis, lidocaine alone.
4 : iontophoresis, lidocaine with epinephrine 1/50,000.

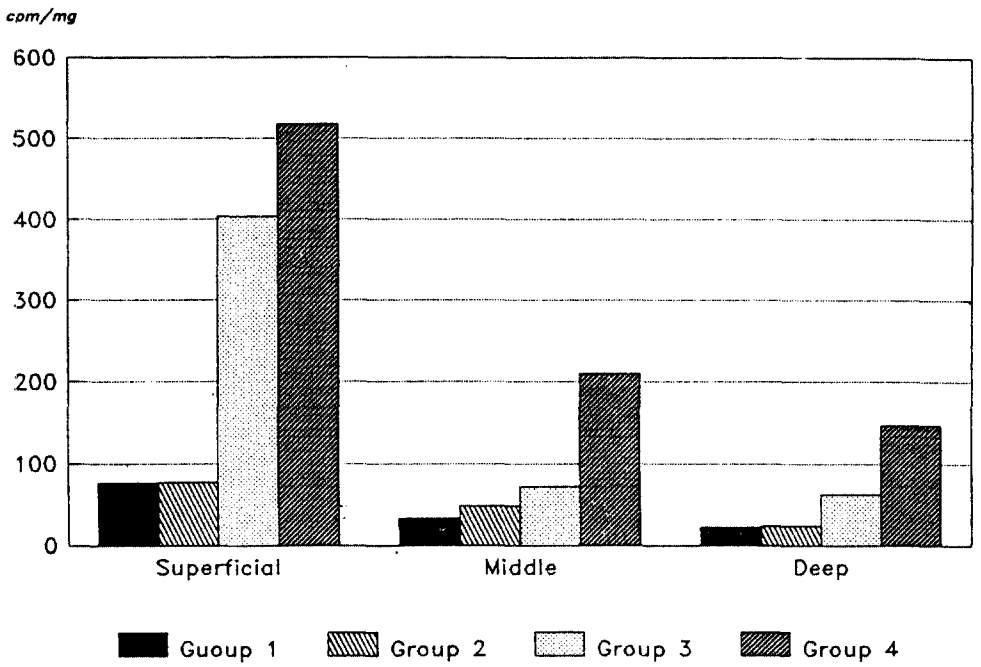

Fig 3. The means of radioactivity(cpm/mg) of [^{14}C] lidocaine in the layers of specimens.

Group 1 : topical application, lidocaine alone.
2 : topical application, lidocaine with epinephrine 1/50,000.
3 : iontophoresis, lidocaine alone.
4 : iontophoresis, lidocaine with epinephrine 1/50,000.

Ⅳ. DISCUSSION

Iontophoretic delivery provides a means of noninvasive administration of drugs to the body. This method minimize the potential trauma and visible distortion of tissue due to injection and the risk of injection associated with it. Iontophoretic drug delivery also avoids the pain and anxiety caused by needle insertion.[4, 28] For local or topical treatment, iontophoretic delivery has the advantage of reduced systemic side effects because only minute amounts of the drug delivered reach the systemic circulation while a high local drug concentration is achieved. Also, the amount of medication delivered can be accurately regulated by controlling the quantity of electric current supplied. This fact can also be utilized to deliver the drug at programmable rates so that the dosage regimen can be tailored to the needs of individual patients.[3, 4, 28]

The disadvantage include the possibility of electric shock, skin irritation or burns.[4, 28] Iontophoretic delivery has a limit to the quantity of medication that can be delivered. and introduction of ionized solutes with molecular weight greater than 8,000 to 12,000 results in a very uncertain rate of delivery.[28]

The factors which affect the iontophoretic delivery of durgs can be classified as physicochemical and electronic factors. Among the physicochemical factors, the first factor is charge of the drug. For iontophoretic delivery, the drug molecules must be in ionized state with either a positive or a negative charge. Nonionic drugs may also be delivered iontophoretically provided that a charge can be induced on them, or otherwise by iontohydrokinesis. Thus the possible mechanisms of iontophoresis may inclued the direct electrostatic repulsion and electroosmosis.[1, 4, 6] In this study, because both lidocaine and epinephrine are positively charged, drug was delivered by anodal(+) iontophoresis. Next factor is conductivity of drug. One study[2] reported the specific conductivity for a number of drugs, the hydrochloride salts of local anesthetics and vasoconstrictors were found highly conductive. This fact was in agreement with the results of this study. Presence of buffer species or salt ions has a negative effect on the iontophoretic delivery of drug molecules with moderate to strong conductivity, since these extraneous ions compete with charged drug molecules for the electric current. The greater the ionic strength, the higher the concentration of extraneous ions, which will result in more competition for the electric current. The pH is an important factor for drugs whose degree of ionization is pH dependent, for exemple, the hydrochloride salt of a local anesthetic is effectively delivered by iontophoresis at approximately pH 5 since the molecules are positively charged at this pH.[2, 4, 6, 29, 30] However, iontophoresis of local anesthetics can be performed successfully even when the pH is close to the pKa since there will be adequate numbers of local anesthetic ions to carry the current.[2] Iontophoretic delivery increases when the concentration of drug is increased. In general, the effect of concentration may be predicted by the Nernst-Planck equation.[4, 6, 31]

Electronic factors influencing iontophoretic drug delivery are electrodes and iontophoretic devices. One concern in iontophoretic drug delivery is to prevent any pH shifts in the drug solution and the prevention of any possibility of skin burns.[4, 6] Principal consideration for an iontophoresis device are : safety, convenience and reliability.[4] Because impedence of living tissue is affected by seasonal variations, blood flow, cardiac activity, blood pressure etc,[32] iontophoretic device should monitor the resistivity of tissues and fluids. Phoresor^{R}(Motion Control Inc., Salt lake City, Utah), used in this study, fulfills to perfection all these requirements.

Iontophoresis has had a long history of use in dentistry. Iontophoresis has been frequently

used in dentistry as a method of choice to aid in the penetration of fluoride ions for the treatment of exposed hypersensitive dentin[7-12] Loose deciduous tooth have been extracted following a profound surface anesthesia induced by iontophoretic application of a local anesthetic containing epinephrine to the oral mucosa.[7,18] Treatment of recurrent herpes labialis using idoxuridine iontophoresis resulted in abortion of the lesions and rapid healing.[7,12,33,34] In the treatement of aphthous stomatitis and lichen planus, corticosteroid iontophoresis appears to give a very beneficial effect.[7]

Lidocaine iontophoresis was used in dermatology for minor surgery of surface tissues[14,15] and painless venipunture[16], and in otolaryngology for myringotomy.[17] In dentistry, lidocaine iontophoresis was used for extraction of loose deciduous teeth or gingival therapy.[7,18] Gangarosa and Mahan[22] discussed the use of the iontophoretic modality in the treatment of TMD-MPDS using iontophoresis of lidocaine and epinephirine followed by methyl prednisolone succinate. Other studies reported successful uses of dexamethasone sodium phosphate combined with lidocaine by iontophoresis in treatment of various musculoskeletal inflammatory conditions.[23-27] In the treatment of postherpetic neuralgia, lidocaine iontophoresis was effective.[35] Russo et al.[36] studied the duration and depth of anesthesia produced by lidocaine with iontophoresis, injection, and swabbing. The results showed that lidocaine iontophoresis was an effective method of producing local anesthesia. This fact was in agreement with the results of this study. Compared with topical application, the amounts of lidocaine absorbed were increased about twice to seven times by iontophoresis.

Lidocaine produces some vasodilation and epinephrine may be added to slow vascular absorption and prolong the duration of action of the anesthetic.[29,30] Because vasodiatory effects of lidocaine and irritative electric current can induce startling increases in tissue perfusion, the addition of epinephrine reduces this effect with a probable correlative decrease in the local clearance of lidocaine.[14] In this study, obvious hyperemia was produced with lidocaine iontophoresis and blanching effect was produced by adding the epinephrine 1 : 50,000 solution. Vasoconstriction would reduce lidocaine uptake by cutaneous vasculature, so the amount of lidocaine absorbed by iontophoresis was increased when epinephrine 1/50,000 was added.

Epinephrine is a positively charged and highly conductive drug. In ophthalmologic studies,[19-21] epinephirine iontophoresis to the cornea can induce ocular herpes simlex virus type-1(HSV-1) shedding from latently infected rabbits. Bezzant et al.[14] discussed the use of iontophoretic local anesthesia in the cauterization of spider veins. They compared the patients anesthetized with iontophoresis of lidocaine and with lidocaine plus epinephirine 1/50,000. The results achieved with lidocaine and epinephirine 1/50,000 were superior in duration of anesthesia, and eliminated the inevitable increased edematous papules caused by transcutaneous cauterization procedures. Gangarosa[7] reported that in treating aphthous lesions near the tongue, or in highly vascular areas, two step method(epinephrine iontophoresis for vasoconstriction follwed by Solu-Medrol^{R} iontophoresis was more effective than Solu-Medrol^{R} iontophoresis. Riviere et al.[37] reported that co-iontophoresis of vasoactive compounds may significantly alter the transdermal delivery of lidocaine. They compared the electrical impedance with the presence or absence of vasoactive compounds. The lowest impedance was seen when norepiephrine is present, an intermediate value when lidocaine alone is iontophoresised, and the highest impedance was seen with tolazoline. These findings mean that ionic concentration was highest when norepinephrine was present. In this study, the amounts of lidocaine absorbed increased in order of topical application groups, iontophoresis with-

out epinephrine group, and iontophoresis with epinephrine group. When epinephrine 1/50,000 was added, the penetration of lidocaine was enhanced above six times by iontophoresis than topical application. Comparing between iontophortic groups, co-iontophoresis of epinephrine 1/50,000. significantly enhanced the penetration of lidocaine.

Many variables can influence the iontophoresis of a drug. The strength of the current (4 mA), solution concentration(50μ Ci/ml), duration of iontophoresis(5minutes) were constant in this study. Differences among subjects in regional blood flow, skin thickness, quantity of hair follicles and sweat glands per unit surface area, thoroughness of cleansing of the skin before iontoporesis, and the method of attachment of the electrodes may contribute to a variable amount of lidocaine. The effects of the last two factors were constant and drug application site lacked hair follicles and sweat glands in this study. Although epinephrine ions may compete with lidocaine ions, it is considered that vasoconstrictive effect was more dominant than competition effect was more dominant than competition for the electric current, in this concentration of 1/50,000. Co-iontophoresis of epinephrine 1/50,000 significantly enhanced the penetration of lidocaine. In topical application, the additon of epinephrine 1 : 50,000 did not increase the penetrated amount of lidocaine. This finding means that only a minute amount of epinephrine was delivered by topical application in this concentration of 1/50,000.

In the application of experimental results to human, the differences of permeabilty between species[31, 38] and the characteristics of oral mucosa[39, 40] must be considered. Also, the control of saliva which prevents effective current flow must be performed in the application of iontophoretic technic in oral cavity. For the iontophoretic drug delivery in dental practice, and electrode should be made to be well adapted to the contour of oral mucosa.

Because most of conditions treated in the dental offices are near the body surface, iontophoresis can be widely accepted in dental practice. It is considered that lidocaine iontophoresis can be an effective method of producing local anesthesia in oral mucosa. Iontophoresis will be a better method of drug admistration avilable which can aid in dental pain control

Ⅴ. CONCLUSIONS

The author measured the quantities of radiolabeled lidocaine administered by iontophoresis and topical application into the oral mucosa of sixteen rabbits.

The obtained results were as follows :

1. Compared with topical application, iontophoresis was a highly effective method in the penetration of lidocaine into oral mucosa($p < 0.05$)
2. The addition of epinephrine 1/50,000 did not affect the uptake of lidocaine in topical application.
3. Co-iontophoresis of epinephrine 1/50,000 significantly enhanced the penetration of lidocaine.($p < 0.05$)

REFERENCES

1. Gangarosa, L.P., Park, N.H., Wiggins, C.A. and Hill, J.M. : Increased penetration of nonelectrolyte into mouse skin during iontophoretic water transport(Iontohydrokinesis). J Pharmacol Exp Ther, 212(3) : 377-381, 1980.
2. Gangarosa, L.P., Park, N.H., Fong, B.C., Scott D.F. and Hill J.M. : Conductivity of drugs used for iontophoresis. J Pharmacol Sci 67 : 1439-1443, 1978.
3. Sloan, J.B. and Soltani, K. : Iontophoresis in dermatology. J Am Acad Dermatol 15 : 671-684, 1986.
4. Banga, A.K. and Chien, Y.W. : Iontophoretic delivery of drugs : Fundamentals, devel-

opments and biomedical applications. J Controlled Release, 7 : 1−24, 1988.
5. Lee, S.W., Kim, Y.K. and Kho, H.S. : A study on the penetration into oral mucosa with the use of iontophoresis. J Korean Acad Oral Med, 16(1) : 9−23, 1991.
6. Ahn, H.A. and Shim, C.K. : Iontophoretic delivery of drugs across the skin. Seoul University Journal of Phamaceutical sciences, 15 : 79−99, 1990.
7. Gangarosa, L.P. : Iontophoresis in dental practice. Quintessence Publishing Co. Inc. Chicago, 1983.
8. Murthy, K.S., Talim, S.T. and Singh, I. : A comparative evaluation of topical application and iontophoresis of sodium fluoride for desensitization of hypersensitive dentin. Oral Surg, 36(3) : 448−458, 1973.
9. Jensen A.L. : Hypersensitivity controlled by iontophoresis : double blind clinical investigation. JADA, 68 : 216−225, 1964.
10. Lee J.Y. Kim H.S. : A comparison study on the efficacy between dentifrices and iontophoresis in treatment of dentinal hypersensitivity. J Korean Acad Periodontol, 19(2) : 147−158, 1989.
11. Gangarosa, L.P. and Park, N.H. : Practical considerations in iontophoresis of fluoride for desensitizing dentin. J Prosthet Dent, 39 (2) : 173−178, 1978.
12. Gangarosa, L.P. : How modern iontophoresis can improve your practice. Quintessence Int., 10 : 1027−1038, 1982.
13. Gangarosa L.P. : Newer local ansesthetics and techniques for administration. J Dent Res, 60(8) : 1471−1480, 1981.
14. Bezzant, J.L., Stephan, R.L., Petelenz, T.J. and Jacobsen, S.C. : Painless cauterization of spider veins with the use of iontophoretic local anesthesia. J Am Acad Dernatorl, 19 (5) : 869−875, 1988.
15. Sisler, H.A. : Iontophoretic local anesthesia for conjunctival surgery. Am Ophthalmol, 10(5) : 597−598, 1978.
16. Arvidsson, S.B., Ekroth, R.H., Hansby, A. M.C., Lindholm A.H. and Olsson, G.W. : Painless venipunture. A clinical trial of iontophoresis of lidocaine for veimpunture in blood donors. Acta Anaesthesiol Scand, 28 : 209−210, 1984.
17. Epley, J.M. : Modified technique of iontophoretic anesthesia for miringotomy in childen. Arch Otolaryngol, 103 : 358−361, 1977.
18. Gangarosa, L.P. : Iontophoresis for surface local anesthesia. JADA, 88 : 125−128, 1974.
19. Hill, J.M., Shimomoro, Y., Kwon, B.S. and Gangarosa, L.P. : Iontophesis of epinephrine isomers to rabbit eyes induced HSV−1 ocular shedding. Invest Ophthalmol Vis Sci 26 : 1299−1303, 1985.
20. Shimomoro, Y., Dudley, J.B., Gangarosa, L. P. and Hill, J.M. : HSV−1 quantitation from rabbit neural tissues after epinephrine-induced reactivation. Invest Ophthalmol Vis Sci 26 : 121−125, 1985.
21. Shimomoro, Y., Gangarosa, L.P., Kataoka, M. and Hill, J.M. : HSV−1 shedding by iontophoresis of 6−hydrodopamine followed by topical epinephrine. Invest ophthalmol Vis Sci 24 : 1588−1594, 1983.
22. Gangarosa, L.P. and Mahan, P.E. : Pharmacologic management of TMJ−MPDS. ENT J., 61 : 30−41, 1982.
23. Delacerda, F.G., : A comparative study of three methods of treatment for shoulder girdle myofascial syndrome. J Orthopaed Sports Phys Ther, 4(1) : 51−54, 1982.
24. Harris, R. : Iontophoresis : Clinical research in musculoskeletal inflammatory conditions. J Orthopaed Sports Phys Ther, 4(2) : 109−112, 1982.
25. Bertolucci, L.E. : Introduction of antiinflam -matory drugs by iontophoresis : double blind study. J Orthopaed Sports Phys Ther, 4(2) : 103−108, 1982.
26. Stralka, S.W. and Newsome, L.S. : The use

of physical modalities and electrotherapy in the treatment of patients with low-back pain. Forum medicum, Inc., 1-13, 1989.
27. Lark, M.R. and Gangarosa, L.P. : Iontophoresis : An effective modality for the treatment of inflammatory disorders of the temporomandibular joint and myofascial pain. J Craniomandib Prac, 8(2) : 108-119, 1990.
28. Stephen, R.L. : Answer to question on iontophoretic delivery of drugs, JAMA, 256 (6) : 769, 1986.
29. Bennett, C.R. : Monheim's local anesthesia and pain controul in dental practice. 7th ed. The C.V. Mosby Co., St. Luise, 1984.
30. ADA : Council on dental therapeutics of American Dental Association. : Accepted dental therapeutics, 40th ed., 181-209, 1984.
31. Schalla, W. and Schaefer, H. : Mechanism of penetration of durgs into the skin : Dermal and transdermal absorption, Wissenschaftliche Verlagsgesellschaft mbH Stuttgart, 41-72, 1982.
32. Geddes, L.A. and Baker, L.E. : Principles of applied biomedical instrumentation, 3rd ed., A Wiley-Interscience Pub. New York, 537-651, 1989.
33. Gangarosa, L.P., Merchant, H.W., Park, N. H. and Hill, J.M. : Iontophoretic application of IdUrd for recurrent herpes labialis (RHL). J Dent Res, 56 : B194, Abst. #569, 1977.
34. Henley-Cohn, J. and Hausfeld, J.N. : Iontophoretic treatment of oral herpes. Laryngoscope, 94 : 118-121, 1984.
35. Gangarosa, L.P., Haynes, M., Qureshi, S., Selim, M.M, Qzawa, A., Hayakawa, K., Ohkido, M. and Mahan, P.E. : Treatment of postherpetic neuralgia by iontophoresis. Proceeding 3rd International Dental Congress on Modern Pain Control : 263-265, 1985.
36. Russo, J., Lipman, A. G., Comstock, T. J., Page, B.C. and Stephen, R.L. : Lidocaine anesthesia : Comparison of iontophoresis, injection, and swabbing. American Journal of hospital Pharmacy 37 : 843-847, 1980.
37. Riviere, J.E., Sage, B. and Williams, P.L. : Effects of vasoactive drugs on transdermal lidocaine iontophoresis. J. Parm Sci 80 : 615-620, 1991.
38. Bartek, M.J., LaBudde, J.A. and Maibach, H.I. : Skin permiability in vivo : Comparison in rat, rabbit, pig and man. J Invest Dermatol 58 : 114-125, 1972.
39. Squier, C.A. and Hall, B.K. : The permeabiltiy of skin and oral mucosa to water and horeseradish peroxidase as related to the thikness of the permeabilty barrier. J Invest Dermatol 84 : 176-179, 1985.
40. Squier, C.A. and Lesch, C.A. : Penetration pathways of different compounds through epidermis and oral epithelia. J Oral Pathol 17 : 512-516, 1988.

이온영동법에 의한 Lidocaine의 구강점막 침투에 관한 연구

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[국문초록]

저자는 방사선 동위원소가 부착된 lidocaine을 이온영동법과 국소도포법을 이용하여 16마리의 가토의 구강점막에 침투시켜 그 침투량을 측정한 후 상호 비교하였으며, ephinephrine의 첨가가 lidocaine 침투에 미치는 영향에 대해 조사한 바, 다음과 같은 결론을 얻었다.

1. 이온영동법은 국소도포에 비하여 Lidocaine의 구강점막으로의 투여에 매우 효과적이었다.($p<0.05$)
2. Ephinephrine 1/50,000 용액의 첨가는 국소도포법에 의한 lidocaine 침투량에 영향을 미치지 않았다.
3. Ephinephrine 1/50,000 용액을 첨가하여 이온영동법을 실시하였을때, 모든 층에서 lidocaine의 침투량이 증가하였다.($p<0.05$)

주요어 : 이온영동법, lidocaine, 구강점막, epinephrine