A STUDY ON THE PENETRATION OF DEXAMETHASONE INTO ORAL MUCOSA WITH THE USE OF IONTOPHORESIS

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CONTENTS

I. INTRODUCTION

Iontophoresis is a process which causes an increased penetration of ionized substances into tissues with the assistance of an electrical current. Thus, it involves the transfer of ions into the body by electromotive force. Ions with positive charge are driven into the skin at the anode and those with negative charge at the cathode.[1]

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. Since Leduc's elegant experiment provided convincing evidence that iontophoresis was a powerful technic for the introduction of drugs into and through the surface tissues, iontophoresis had been employed rather frequently in the 1930s and 1940s for the transport of substances into the skin. The use of iontophoresis declined in subsequently years, and it became primarily a research tool in clinical investigations. However, there are several valid uses of iontophoresis in medicine and dentistry and iontophoresis has been in clinical use to diagnose and treat a variety of diseases.[2,3]

Iontophoresis has been utilized as a method of choice for the administration of pilocarpine in a diagnostic test for cystic fibrosis[4] and of local anesthetics and epinephrine for the minor surgery of surface tissues[5]. And, iontophoresis has been used for the delivery of various compounds for the treatment of hyperhydrosis[3].

Iontophoresis frequently has been used in dentistry as a method of choice to aid in the penetration of fluoride ions for the treatment of exposed hypersensitive dentin.[6-10] Loose deciduous teeth have been extracted following a profound surface anesthesia induced by iontophoretic application of a local anesthetic containing epinephrine to the oral mucosa[11]. Treatment of recurrent herpes labialis using idoxuridine iontophoresis resulted in abortion of the lesions and rapid healing.[1,12-14]

In many previous reports, the clinical results suggested the possibility of steroid iontophoresis for the treatment of inflammatory lesions of the skin, oral mucosa, musculoskeletal system, and other pathology.[1,13,15-21] And, a pharmacokinetic study of percutaneous iontophoresis of prednisolone was undertaken[22] and the efficacy of steroid iontophoresis into the skin and joint structure was

* This paper was supported by S.N.U. POSSCO Research Fund in the year of 1990.

demonstrated using radiolabeled dexamethasone[23]

However, there is an almost total lack of information about the actual quantity and tissue distribution of corticosteroid administered by iontophoresis in the oral mucosa.

The present investigation has been undertaken to determine the efficacy of steroid iontophoresis in the oral mucosa using radiolabeled dexamethasone and autoradiographic technic. In addition, influences of polarity and buffer solution on dexamethasone iontophoresis were investigated.

II. MATERIALS AND METHODS

Animals

Thirty-six rabbits, weighing approximately 2 kg each, were anesthetized with Ketamine (50 mg / kg) by intramuscular injection.

Radioactive materials and chemicals

[1, 2, 4, 6, 7 $-^3$H] Dexamethasone [specific activity (S.A.)=94 Ci / mmol, Amersham Corporation, United Kingdom] was used. When tritiated dexamethasone was dissolved in 0.1 M sodium phosphate buffer solution(pH 7.0) or distilled water, 0.35 ml of the solution had 40μCi of isotope.

Drug application

Rabbits were divided into four groups as follows.

Group 1, 2, 3. The dexamethasone in 0.1M sodium phosphate buffer solution was applied in 2.0 mA for 6 minutes.

Group 4. The dexamethasone in distilled water was applied in 2.0 mA for 6 minutes.

Each group included nine rabbits and was divided into three subgroups(anodal, cathodal, and topical). The right buccal mucosa was chosen as drug application site. For drug application, the buccal mucosa of rabbit was dried with gauze. An active electrode (diameter : 8mm) was made up of polymerizing resin and a snap which could be attached to clip on electrode(Model No. 6543. Life-Tech, Texas, U.S.A.). An active electrode containing sterile cotton was saturated with 0.35 ml of solution and placed on the buccal mucosa. For anodal (+) iontophoresis, the active electrode was connected to the anode of iontophoretic unit (Dentaphor, Life-Tech, Texas, U.S.A.), while the cathode was connected to the abdomen of the rabbit. For cathodal (-) iontophoresis, the electrodes were reversed. For topical application, the drug was applied with same electrode but no current was used. During the application of drug, the cotton rolls was 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 remaining on the mucosa touching electrode was throughly washed with a gentle stream of distilled water. In Group 1 and 4, tissue samples were obtainted 40 minutes later after iontophoretic or topical drug application. In group 2, tissue samples of buccal mucosa were obtained at 4 hours after drug application, and at 24 hours in group 3.

Autoradiographic procedures

The biopsy of the treated area under electrode was made down to the connective tissue. Tissue samples of the buccal mucosa were immediately placed in OCT compound(Lab-Tek Products) and frozen. Frozen sections of 10μm thick were picked up directly from microtome knife with gelatin coated glass slide. The air-dried sections were then dipped in liquid emulsion (NTB-3, Eastman Kodak Company).[24] After 2 months of exposure at -20℃, autoradiographs were developed for 1 minute in D-19 developer(Kodak) at 20℃, fixed and then stained with toluidine blue.

Examination and quantitation

Histologic sections were examined under light microscope. And, separate counts of grains within 2,500μ^2 over the superficial, intermediate, basal epithelium, and upper part of lamina propria were performed.

Statistical analysis

Data were inputed on a 16 bit IBM PC and all the statistical analyses were performed by SPSS PC$^+$(Microsoft Corp., U.S.A.). T-test was used

to compare the mean values.

Ⅲ. RESULTS

Table 1 shows the mean counts and standard deviations of grains according to mucosal layer at 40 minutes, 4 hours, and 24 hours after administration of [^{3}H] dexamethasone in 0.1M sodium phosphate buffer solution.

Table 1. The mean counts and standard deviations of grains at 40 minutes (group 1), 4 hours (group 2), and 24 hours (group 3) after administration of [^{3}H] dexamethasone in 0.1M sodium phosphate buffer solution.

Group	Polarity	Epithelium			Lamina Propria (upper)	Total
		Superficial	Intermediate	Basal		
1	anodal	10.9(1.54)	10.7(3.16)	11.0(4.92)	6.3(2.78)	38.9(10.3)
	cathodal	10.8(4.02)	8.9(5.51)	6.7(4.03)	2.3(2.35)	28.7(8.78)
	topical	9.2(2.22)	5.0(2.60)	0.9(1.17)	0.0(0.00)	15.1(4.57)
2	anodal	10.4(1.81)	8.0(2.50)	10.0(3.24)	6.7(1.00)	35.1(4.46)
	cathodal	9.8(2.59)	8.1(3.06)	8.8(3.53)	5.4(1.24)	32.1(7.13)
	topical	7.6(1.42)	4.2(1.64)	3.9(1.62)	0.3(0.50)	16.0(3.12)
3	anodal	2.9(1.17)	3.4(1.01)	3.9(2.03)	2.3(1.50)	12.6(5.20)
	cathodal	2.4(0.53)	3.0(0.40)	3.3(0.50)	0.7(0.50)	9.4(0.53)
	topical	2.0(1.50)	1.6(0.88)	2.0(2.00)	0.7(0.71)	6.2(3.56)

Fig. 1. The number of grains at 40 minutes after administration of [^{3}H] dexamethasone in 0.1M sodium phosphate buffer solution according to mucosal layer.

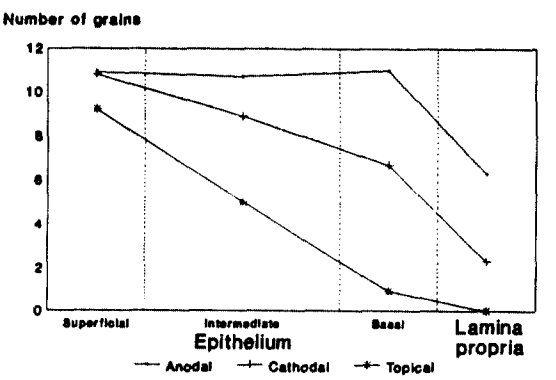


Table 2. Level of statistical significance for comparison of numbers of grains at 40 minutes after adiminstration of [^{3}H] dexamethasone in 0.1M sodium phosphate buffer solution.

Tissue	Level of statistical significance		
	Anodal compared to cathodal	Anodal compared to topical	Cathodal compared to topical
Superficial epithelium	n. s.	n. s.	n. s.
Intermediate epithelium	n. s.	****	n. s.
Basal epithelium	n. s.	****	****
Lamina propria (upper layer)	***	****	****
Total	*	****	****

n. s. : $p>0.05$, * : $P\leqq0.05$, ** : $p\leqq0.01$, *** : $p\leqq0.005$, **** : $p\leqq0.001$

Fig. 1 shows the number of grains according to mucosal layer at 40 minutes after the iontophoretic application of [^{3}H] dexamethasone in 0.1M sodium phosphate buffer solution. At 40 minutes after administration of [^{3}H] dexamethasone in 0.1M sodium phosphate buffer solution (Table 2), there were significant differences in the number of grains over the upper layer of lamina propria($p \leqq 0.005$) and total ($p \leqq 0.05$) between the anodal and cathodal iontophoresis. In anodal iontophoresis, we found that counts of grains over the intermediate, basal epithelium, upper layer of lamina propria, and total showed significant differences ($p \leqq 0.001$) compared to those in topical application. Similar results were found between cathodal iontophoresis and topical application, and significant differences ($p \leqq 0.001$) were noted in basal epithelium, upper layer of lamina propria, and total. Both cathodal and anodal iontophoresis resulted in significantly increased uptake of [^{3}H] dexamethasone into oral mucosa compared to topical application. It should be noted that maximum amount of [^{3}H] dexamethasone movement occurred during anodal iontophoresis, especially into deeper layer of epithelium and upper layer of lamina propria.

Fig. 2 and 3 show the number of grains according to mucosal layer at 4 hours and 24 hours after the iontophoretic application of [^{3}H] dexamethasone in 0.1M sodium phosphate buffer solution, respectively. Table 3 and 4 show the level

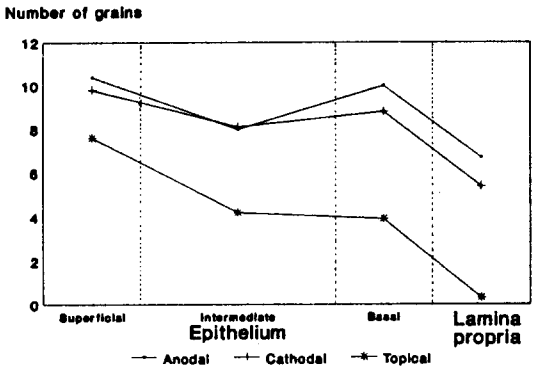


Fig. 2. The number of grains at 4 hours after administration of [^{3}H] dexamethasone in 0.1M sodium phosphate buffer solution according to mucosal layer.

of statistical significance in the numbers of grains at 4 hours and 24 hours, respectively after administration of [^{3}H] dexamethasone in 0.1M sodium phosphate buffer solution. Anodal iontophoresis compared to cathodal one resulted in a small, not statistically significant, increased drug concentration after 4 hours except in upper layer of lamina propria($p \leqq 0.05$). But, both anodal and cathodal iontophoresis were still greatly effective ($p \leqq 0.001$) compared to topical application up to 4 hours after administration. And, although the number of grains was decreased in order of anodal, cathodal, and topical application after 24 hours, the differences were markedly reduced. Significant differences in total counts of grains were found

Table 3. Level of statistical significance for comparison of numbers of grains at 4 hours after administration of [^{3}H] dexamethasone in 0.1M sodium phosphate buffer solution.

Tissue	Level of statistical significance		
	Anodal compared to cathodal	Anodal compared to topical	Cathodal compared to topical
Superficial epithelium	n. s.	* * *	*
Intermediate epithelium	n. s.	* * *	* * *
Basal epithelium	n. s.	* * * *	* * *
Lamina propria (upper layer)	*	* * * *	* * * *
Total	n. s.	* * * *	* * * *

n. s. : $p > 0.05$, * : $p \leqq 0.05$, * * : $p \leqq 0.01$, * * * : $p \leqq 0.005$, * * * * : $p \leqq 0.001$

in anodal ($p \leqq 0.01$)and cathodal iontophoresis ($p \leqq 0.05$) compared to topical application.

The reduction of counts which could reflect the resorption of drug by blood vessel mainly occurred between 4 and 24 hours after administration (Table 1, Fig. 2, and 3).

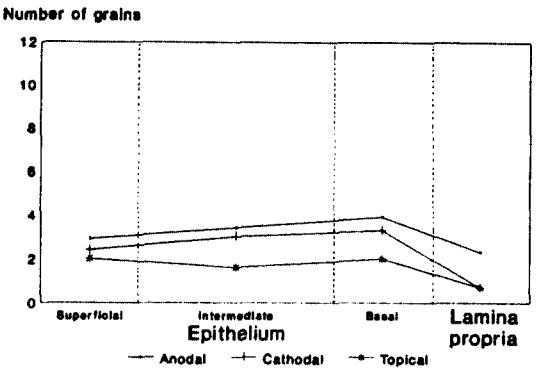


Fig. 3. The number of grains at 24 hours after administration of [^{3}H] dexamethasone in 0.1M sodium phosphate buffer solution according to mucosal layer.

Table 4. Level of statistical significance for comparison of numbers of grains at 24 hours after administration of [^{3}H] dexamethasone in 0.1M sodium phosphate buffer solution.

Tissue	Level of statistical significance		
	Anodal compared to cathodal	Anodal compared to topical	Cathodal compared to topical
Superficial epithelium	n. s.	n. s.	n. s.
Intermediate epithelium	n. s.	****	****
Basal epithelium	n. s.	n. s.	n. s.
Lamina propria (upper layer)	**	**	n. s.
Total	n. s.	**	*

n. s. : $p > 0.05$, * : $p \leqq 0.05$, ** : $p \leqq 0.01$, *** : $p \leqq 0.005$, **** : $p \leqq 0.001$

In the iontophoresis of [^{3}H] dexamethasone in distilled water, anodal iontophoresis also greatly enhanced the penetration of drug at 40 minutes after administration (Table 5 and 6). There was a significant difference ($p \leqq 0.01$) in total counts of grains between anodal and cathodal iontophoresis. And, significant differences in total counts of grains were found in anodal ($p \leqq 0.001$) and cathodal iontophoresis ($p \leqq 0.05$) compared to topical application.

Table 5. The mean counts and standard deviations of grains at 40 minutes after administration of [^{3}H] dexamethasone in 0.1M sodium phosphate buffer solution (group 1) and [^{3}H] dexamethasone in distilled water (group 4).

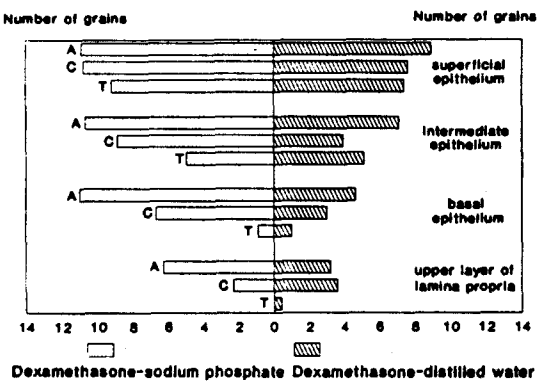
Group	Polarity	Epithelium			Lamina Propria (upper)	Total
		Superficial	Intermediate	Basal		
1	anodal	10.9(1.54)	10.7(3.16)	11.0(4.92)	6.3(2.78)	38.9(10.3)
	cathodal	10.8(4.02)	8.9(5.51)	6.7(4.03)	2.3(2.35)	28.7(8.73)
	topical	9.2(2.22)	5.0(2.60)	0.9(1.17)	0.0(0.00)	15.1(4.57)
4	anodal	8.9(2.76)	7.1(1.97)	4.6(1.24)	3.2(0.97)	23.8(4.35)
	cathodal	7.6(1.01)	3.9(1.45)	3.0(1.12)	3.6(1.67)	18.0(3.35)
	topical	7.4(2.79)	5.1(0.78)	1.0(1.00)	0.4(0.73)	14.0(2.92)

Table 6. Level of statistical significance for comparison of numbers of grains at 40 minutes after administration of [^{3}H] dexamethasone in distilled water.

Tissue	Level of statistical significance		
	Anodal compared to cathodal	Anodal compared to topical	Cathodal compared to topical
Superficial epithelium	n. s.	n. s.	n. s.
Intermediate epithelium	* * * *	*	*
Basal epithelium	*	* * * *	* * * *
Lamina propria (upper layer)	n. s.	* * * *	* * * *
Total	* *	* * * *	*

n. s. : $p>0.05$, * : $p\leqq0.05$, * * : $p\leqq0.01$, * * * : $p\leqq0.005$, * * * * : $p\leqq0.001$

Table 5 and Fig. 4 show the comparison of numbers of grains between in the iontophoresis of [^{3}H] dexamethasone in 0.1M sodium phosphate buffer solution and [^{3}H] dexamethasone in distilled water. Iontophoresis of dexamethasone in sodium phosphate buffer solution was more effective than that of dexamethasone in distilled water. Table 7 shows the statistical differences of the effect of buffer solution in the anodal and cathodal iontophoresis, and topical application of dexamethasone. Addition of buffer solution was effective both in the anodal ($p\leqq0.005$) and cathodal iontophoresis ($p\leqq0.01$) but not in topical application ($p>0.05$). Thus, addition of buffer solution greatly influenced the anodal iontophoresis of dexamethasone.



A : anodal, C : cathodal, T : topical

Fig. 4. The number of grains at 40 minutes after administration of [^{3}H] dexamethasone in 0.1M sodium phosphate buffer solution and [^{3}H] dexamethasone in distilled water according to mucosal layer.

Table 7. Level of statistical significance for comparison of numbers of grains between [^{3}H] dexamethasone in 0.1M sodium phosphate buffer solution and [^{3}H] dexamethasone in distilled water at 40 minutes after administration.

Tissue	Level of statistical significance		
	Anode	Cathode	Topical
Superficial epithelium	n. s.	*	n. s.
Intermediate epithelium	*	*	n. s.
Basal epithelium	* * *	*	n. s.
Lamina propria (upper layer)	* *	n. s.	n. s.
Total	* * *	* *	n. s.

n. s. : $p>0.05$, * : $p\leqq0.05$, * * : $p\leqq0.01$, * * * : $p\leqq0.005$, * * * * : $p\leqq0.001$

Fig. 5 allows the comparison of total counts of grains in anodal and cathodal iontophoresis, and topical application of [^{3}H] dexamethasone in 0.1M sodium phosphate buffer solution and [^{3}H] dexamethasone in distilled water.

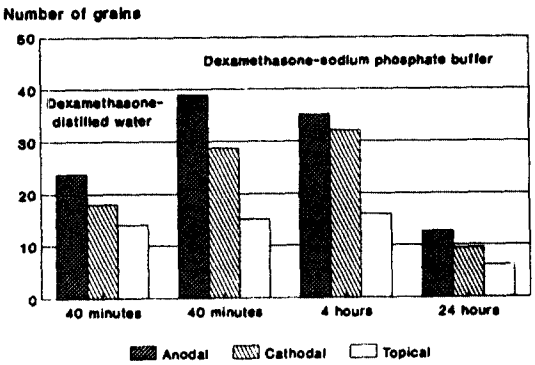


Fig. 5. The number of total grains.

Ⅳ. DISCUSSION

Iontophoresis is the introduction, by means of an electric current, of ions of soluble salts into the tissues of the body for therapeutic purposes. Fluoride iontophoresis has been used in dentistry as a treatment modality for dentinal hypersensitivity.[6-10] Gangarosa[11] reported the extractions of loose deciduous teeth following a profound surface anesthesia induced by iontophoretic application of a local anesthetic containing epinephrine to the oral mucosa. And, idoxuridine iontophoresis into mouse skin was performed by Gangarosa et al.[25] Also, many authors[1,12-14] reported relief of discomfort and reduction in healing time of herpes simplex lesions in a small group of patients treated by idoxuridine iontophoresis. And, Lekas[13] reported promising results in the treatment of both herpes simplex and recurrent aphthae by levamisole iontophoresis.

Corticosteroid iontophoresis has been used successfully in the treatment of Peyronie's disease (plastic induration of the penis).[15] And, Lekas[13] reported a small group of patients with aphthous stomatitis who were treated with iontophoresis of triamcinolone acetonide. Another study of corticosteroid iontophoresis for the treatment of aphthous stomatitis and lichen planus was conducted by Gangarosa.[1] Several authors[16-18,21] have documented the treatment of a variety of musculoskeletal inflammatory conditions including temporomandibular disorders using corticosteroid iontophoresis. Glass et al.[23] suggested that iontophoresis might be an efficacious and desirable method for the administration of steroids to a localized regions of inflammation. Using radiolabeled dexamethasone sodium phosphate, they demonstrated the dexamethasone could be delivered iontophoretically into all tissue layers underlying the electrode down to, and including tendinous structures and cartilaginous tissue. However, a study,[26] using in vitro and in vivo experiments, failed to demonstrate the permeability of corticosteroids through the skin by iontophoresis. In our experiment, dexamethasone could be efficiently delivered by iontophoresis, and iontophoresis enabled the dexamethasone to penetrate into deeper layer of oral mucosal epithelium of rabbit. For example, over a ten fold increase in the penetration of [^{3}H] dexamethasone in sodium phosphate buffer solution by anodal iontophoresis compared to topical application was found in basal epithelium at 40 minutes after administration (Table 1 and Fig. 1).

Results from different penetration periods suggested that drug concentration by iontophoresis was still higher than that of topical application up to 4 and 24 hours. And, reduction in the number of grains between 4 and 24 hours might explain that resorption by blood vessel mainly occurred during this period.

Steroids are usually uncharged unless they have been chemically modified for high water solubility (intravenous use). But, it was hypothesized that during iontophoresis of indifferent ions (Na^+, Cl^-, etc.) movement of water into tissues may occur by one or more mechanisms. The term iontohydrokinesis (IHK) was coined to describe transport

of water into tissue as a result of iontophoresis irrespective of the mechanism of the transport.[27] Gangarosa et al[27] described that the possible mechanisms of water movement during iontophoresis might include an electrophoretic effect, electro-osmotic effect, transport of water by hydrated-ion-movement, and solvent and solute drag. And, the most likely explanation for the mechanism of IHK is that iontophoretic movement of hydrated ions requires transfer of water attracted to the ion by dipoles. Thus, the hydrated ion hypothesis of water movement during IHK predicts that both positive and negative ions would carry water during iontophoresis and that sodium ions, which have a larger hydration shell, would carry more water due to anodal current than chloride ions due to cathodal current. Gangarosa et al[25] reported increased penetration of idoxuridine (IdUrd) by either anode or cathode which, although not highly ionized, forms anions in aqueous solution requiring introduction under the cathode. And, Gangarosa et al[27] showed that nonelectrolytes such as [^{3}H] 9-β-D-arabinofuranosyladenine (Ara-A) and [^{3}H] thymidine (dThd) could be iontophoretically delivered to mouse tissues in aqueous NaCl solutions. Thus, increased penetration of nonelectrolytes might occur due to increased water movement.

This hypothesis was in agreement with our results. In iontophoresis of dexamethasone in sodium phosphate buffer solution, anodal iontophoresis was more effective than cathodal one. And, addition of buffer solution showed the most significant difference in anodal iontophoresis. This could be explained by iontohydrokinesis that nonelectrolyte drugs could be introduced into surface tissues by iontophoresis of electrolytes, especially sodium ions. Previously, it was thought that only charged drugs could be introduced by this technique. Thus, the prerequisite of iontophoretic treatment that the drug must be charged can be modified to include nonelectrolyte drugs in solutions of charged molecules. But, it is also possible that there is a slight degree of ionization of the nonelectrolytes and that the ions formed would move into the tissue by the normal process of iontophoresis[27] This might explain partly the difference between anodal and cathodal iontophoresis in the penetration of [^{3}H] dexamethasone in distilled water.

Dermatologic studies[28,29] on the permeability and penetration concluded that during iontophoresis, the greatest concentration of ionized substances was expected to move into some regions of the skin where either the skin was damaged, or along the sweat glands and hair follicles, as the diffusion resistance of the skin to permeation was lowest in the regions. Thus, hair follicles and sweat ducts could act as diffusion shunts. Our results agreed with that fact. Fig .11 shows the penetration path of isotope into hair follicle in the skin adjacent to the buccal mucosa of rabbit. And, many authors suggested a difference in the nature of the intercellular barrier in keratinized and non-keratinized tissue[30-32] Therefore, the characteristics of oral mucosa which shows different degree of keratinization and permeability between the oral mucosal regions and lacks hair follicles and sweat glands must be considered in the penetration study of chemicals in oral mucosa. And, the differences of permeability between species must be considered in the application of experimental results to human[33] Also, control of saliva which prevents effective current flow must be performed in the application of iontophoretic technic in the oral cavity[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 administered locally where it shoud achieve the maximum benefit. Patient acceptance is generally excellent, and fear of injection is eliminated[1,34,35] And, it is reasonable to assume that the therapeutic efficacy of drugs which are nonelectrolytes can be improved by increasing their penetration into surface tissues during electrolyte iontophoresis.

However, the ultimate suitability of a given drug for iontophoretic application must be tested in vivo. And, selection of drugs appropriate for such testing can be based on their specific conductivity. Gangarosa et al.[34] provided specific conductivity values for a number of local anesthetics, vasoconstrictors, corticosteroid hormones, antineoplastic drugs, nucleotides, and antiviral agents.

Iontophoretic drug delivery has gained growing acceptance for local therapy.[1-3,36] And, iontophoresis in dental practice can be widely accepted because of possibility of iontophoresis of local anesthetics and steroids. Systematic approaches, including investigation of the basic scientific aspects of this technic, its mechanism of action, and case-controlled clinical studies, may lead to wider and more effective use of this simple, but versatile, technic.

V. CONCLUSIONS

The many clinical studies reported the possibility of corticosteroid iontophoresis for the treatment of mucocutaneous inflammatory lesions and several experimental studies were undertaken to support the clinical results.

However, the information on the iontophoretic delivery of corticosteroid into oral mucosa in literature is sparse.

We have investigated the efficacy of corticosteroid iontophoresis in the buccal mucosa of rabbit using radiolabeled dexamethasone and autoradiography. The authors came to the following conclusions :

1. Iontophoresis was highly effective method in the penetration of dexamethasone in sodium phosphate buffer solution into oral mucosa of the rabbit, compared to topical application, and anodal current was more effective than cathodal one.
2. Anodal iontophoresis was still more effective up to 4 and 24 hours after administration of dexamethasone in sodium phosphate buffer solution and reduction in the number of grains was mainly occurred between 4 and 24 hours.
3. Addition of sodium phosphate buffer was effective in anodal and cathodal iontophoresis, but did not influence the topical application. And, the anodal iontophoresis was greatly influenced by the addition of sodium phosphate buffer solution.
4. Steroid iontophoresis could be regarded as reliable treatment modality for the inflammatory lesions of oral mucosa as well as skin.

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이온영동법에 의한 Dexamethasone의 구강점막에의 침투에 관한 연구

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[국문초록]

이온영동법은 전기력의 도움으로 이온화된 물질의 신체조직내 침투를 증가시키는 술식으로서 전신적 부작용은 줄어드는 반면, 국소부위의 약물농도를 증가시킬 수 있다는 장점때문에 효과적인 국소요법으로 인정받고 있다. 치의학 분야에서는 과민상아질의 치료를 위해 불소 이온영동법이 빈번히 이용되어져 왔으며, 국소마취제나 항바이러스 제재의 도포시에도 이용되었다. 또, 이온영동법에 의한 스테로이드 투여로 피부나 구강점막의 염증성 질환의 효과적 치료를 보고한 많은 문헌이 있으나, 이온영동법에 의한 스테로이드의 구강점막에의 침투량이나 분포에 관해서는 거의 소개된 바가 없는 실정이다.

본 연구는 방사선 동위원소가 부착된 dexamethasone을 이온영동법을 이용하여 가토의 협점막에 침투시킨후 자기방사선 술식에 의해 그 침투량과 분포를 대조군과 비교 평가하였으며 다음과 같은 결과를 얻었다.

1. 이온영동법은 단순 국소도포에 비해 dexamethasone과 0.1M 인산소다 완충용액의 혼합액(dexamethasone in 0.1M sodium phosphate buffer solution)의 가토 협점막 침투량을 증가시켰으며, 양극을 사용하였을 때 더 효과적이었다.
2. Dexamethasone과 0.1M 인산소다 완충용액의 혼합액 투여 4시간, 24시간후 까지도 양극 이온영동법이 효과적이었으며 은입자의 감소는 투여 4시간 부터 24시간 후 사이에 주로 일어났다.
3. 인산소다 완충용액의 첨가는 양극 및 음극에 의한 이온영동법 모두에 효과적이었으며, 양극에 가장 효과적이었고 단순도포군에는 영향을 미치지 않았다.
4. 이온영동법에 의한 스테로이드 투여는 피부뿐만 아니라 구강점막 염증성 병소의 효과적 치료술식으로 여겨질 수 있다.

주요어 : 이온 영동법, dexamethasone, 구강점막, 침투

EXPLANATION OF FIGURES

Fig. 6. An autradiograph of buccal mucosa obtained at 40 minutes after administration of [^{3}H] dexamethasone in 0.1M sodium phosphate buffer solution by anodal iontophoresis. Note the numerous silver grains over the epithelium and underlying lamina propria. Toluidine blue X200.

Fig. 7. An autoradiograph of buccal mucosa obtained at 40 minutes after administration of [^{3}H] dexamethasone in 0.1M sodium phosphate buffer solution by topical application. Note that most silver grains are over the superficial epithelium. Toluidine blue X200.

Fig. 8. An autoradiograph of buccal mucosa obtained at 24 hours after administration of [^{3}H] dexamethasone in 0.1M sodium phosphate buffer solution by anodal iontophoresis. Note few grains over the epithelium. Toluidine blue X200.

Fig. 9. An autoradiograph of buccal mucosa obtained at 40 minutes after administration of [^{3}H] dexamethasone in distilled water by cathodal iontophoresis. Toluidine blue X200.

Fig.10. An autoradiograph of buccal mucosa obtained at 40 minutes after administration of [^{3}H] dexamethasone in distilled water by topical application. Toluidine blue X200.

Fig.11. An autoradiograph of the skin adjacent to the buccal mucosa obtained at 40 minutes after administration of [^{3}H] dexamethasone in 0.1M sodium phosphate buffer solution by anodal iontophoresis. Note the penetration path of drug. Toluidine blue X200.

Fig. 6

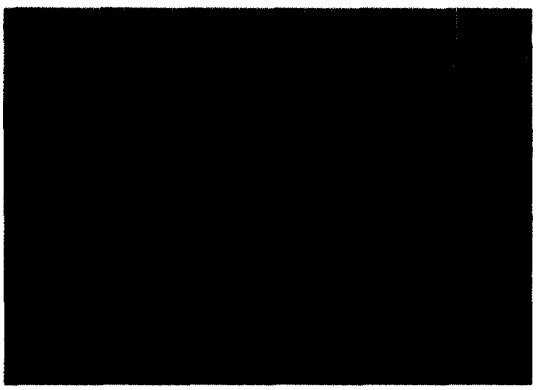

Fig. 7

Fig. 8

Fig. 9

Fig. 10

Fig. 11