AN APPROACH TOWARDS PAINLESS ADMINISTRATION OF LOCAL ANAESTHETIC AGENTS IN PEDIATRIC DENTISTRY: IN VIVO STUDY

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Abstract

Three topical anesthetic agents namely Eutectic mixture of Local anesthetic 5% cream, Produit Dentaire (20% benzocaine) and Lignocaine 15% spray used in pediatric patients during various dental procedures requiring local anesthesia administration were evaluated in terms of onset of action and clinical efficacy for pain perception.

In this study 210 patients aged between 6-14 years were randomly divided into three groups and were subjected to the test agents. The onset of action was analyzed using stop watch and dental probe and response of the patients to pain was evaluated using visual analogue scale.

Results showed that Eutectic Mixture of Local Anesthetic agent 5% had the highest onset of action and superior in pain reduction followed by Produit Dentaire and Lignocaine Spray 15%.

Clinical article (J Int Dent Med Res 2012; 5: (2), pp. 96-101)

Keywords: Pain, topical anaesthetic agents, EMLA, Produit Dentaire, Lignocaine Spray.

Received date: 10 May 2012 **Accept date:** 06 June 2012

Introduction

Behavior management in pediatric dentistry encompasses various elements ranging from creating a “pain-free” environment to acceptance of treatment by a child.[1] Fear of syringes and needles has been reported as one of the major causes of apprehension and anxiety in dental patients. For this reason, pediatric dentists are on a constant search of tools for painless administration of local anaesthesia and topical anesthetics have proven to be a boon in this attempt.[2]

Various agents are available today for topical analgesia. While lignocaine serves as the gold standard, benzocaine is also known for its excellent surface anaesthetic properties. A new topical anesthetic agent Eutectic Mixture of Local Anesthetics 5% cream (EMLA) contains Lignocaine and Prilocaine as its active ingredients which when combines facilitates increased absorption of local anesthetic agents and expose tissue to exceptionally high local anesthetic concentration, thus has rapid onset of action. Though, it was introduced as a topical anesthetic agent for medical applications, it has been found to possess a local anesthetic effect on oral mucosa also.[3]

As there are very few studies that have been taken into consideration the effectiveness of the recent topical anaesthetic agents, an attempt has been made to analyze the clinical effectiveness of varied topical anesthetic agents namely Xylocaine, Produit Dentaire and EMLA.

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Materials and methods

Two hundred ten patients between six to fourteen years in age, who were attending the Pediatric Dental Clinic at Sardar Patel Post Graduate Institute of Medical and Dental Sciences, Lucknow, India were randomly selected for the study. The approval of ethical committee was obtained. The permission of each patient and parents were obtained after fully informing them about the study.

Care had been taken to select the children without any allergic history to local anaesthesia and without any pathology and inflammation in the oral mucosa.

Test agents were divided into three groups (Figure 1-3):
Group I: Eutectic Mixture of Local Anaesthetic 5% cream (EMLA) (Astra Zeneca Pharma Inc. Ontario)
Group II: Produit Dentaire (PD Pharma Switzerland)
Group III: Lignocaine 15% spray (ICPA Health Product, India)

Figure 1. Eutectic Mixture of Local Anesthetic 5% cream.

Figure 2. Produit Dentaire gel (20% Benzocaine).

Figure 3. Lignocaine 15% spray.

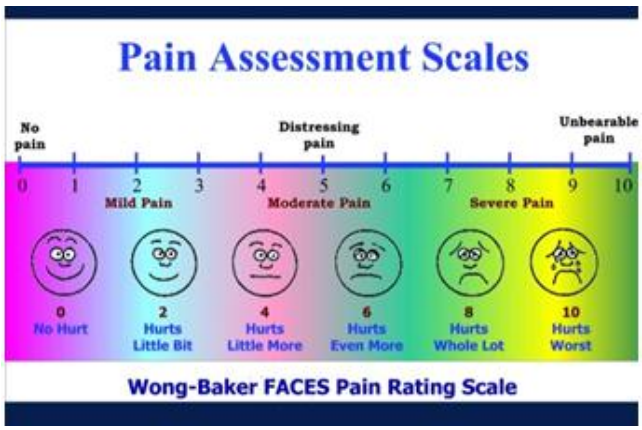

Figure 4. Visual Analogue Scale.

Previously, a pilot study was carried out in the same departments, to overview the proper study design and to take care of the possible constraints during the main study. The study was divided into two phases.

Phase I: It was carried out to find the onset of action of the three test anaesthetic agent used. Ninety patients were selected and divided into three groups of thirty patients each and were assigned to one of the three test agents.

In all the study subjects, gingiva in relation to maxillary left incisors was chosen as the test site. Following isolation, the test area was dried using sterile gauze and care was taken to see that no undue pressure was exerted on the tissue during the application of the drug. The area was checked for the onset of surface anaesthesia every 30 seconds for a period of 3 minutes. A dental probe was used to check for objective signs of anaesthesia. Time of onset of action of anaesthetic agents was recorded. An average time of application was derived from this study for all the three anaesthetic agents.

Phase II: It was carried out to evaluate the efficacy of the three anaesthetic agents in reducing pain of intraoral injections. One hundred and twenty patients between six to fourteen years and a mean age of eight to nine years were chosen for this part of the study. The anaesthetic agents were applied on the test area inside the oral cavity. The duration of anaesthetic agent was derived from first phase of the study.

After this, infiltration anaesthesia (1ml of 2% Xylocaine with vasoconstrictor) was administered on the test site. During administration of anaesthesia the investigator observed the response of the child. Each child quantified the pain perception during the injection using a visual analogue scale (VAS) scale (Figure 4). No information regarding the scale was given to the child prior to the study in order to eliminate bias due to anticipated pain. The pain score was recorded for each of the agent.

Statistical analysis The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 15.0 Statistical Analysis Software. The chi square test, analysis of variance(ANOVA), student 't' test, Wilcoxon signed rank statics, Mann-Whitney U test were performed to know effect of each variable and to reveal statistical significance. The confidence level of study was proposed to be 95%; hence a P value < 0.05 has been considered significant, P value <0.01 has been considered highly significant and a P value < 0.001 has been considered very highly significant.

Results

Table 1 shows distribution of subjects to compare the three groups for time taken for onset of analgesia. In group I, all except one patient demonstrated onset of analgesia to be within 1 minute whereas in Group II and III the onset was within 1 minute for 83.3% patients and after 1 minute for the rest respectively. The mean time taken for onset of analgesia ranged from 36.70±8.23 (Group I) to 112.97±3.76 seconds (Group III). This difference was statistically significant (p<0.001).

Table 2 shows the analysis of variance for mean time taken for onset of analgesia in different groups. Analysis of variance and box plot show a statistically significant intergroup difference (p<0.001).

SN	Time taken	Group I (n=30)		Group II (n=30)		Group III (n=30)	
		No.	%	No.	%	No.	%
1.	≤1 min	29	96.7	25	83.3	0	0.0
2.	>1 min	1	3.3	5	16.7	30	100.0
Mean±SD (sec)		36.70±8.23		55.90±5.37		112.97±3.76	

Table 1. Distribution of subjects to compare the three groups for time taken for onset of analgesia. $\chi 2=68.611$ (df=2); p<0.001

	Sum of Squares	Df	Mean Square	F	Sig.
Between Groups	94418.49	2	47209.24	1280.31	<0.001
Within Groups	3207.97	87	36.87		
Total	97626.46	89			

Table 2. Analysis of Variance for mean time taken for onset of analgesia.

Table 3 shows the inter group comparison for mean time taken for onset of analgesia in different groups. All the three comparisons were significant statistically. It was observed that mean time taken by Group I was significantly lower as compared to that of Group II and Group III (p<0.001) whereas Group II showed significantly lower values as compared to that of Group III (p<0.001).

S.No.	Comparison	"t"	"p"
1.	Group I vs Group II	–10.704	<0.001
2.	Group I vs Group III	–46.196	<0.001
3.	Group II vs Group III	-47.692	<0.001

Table 3. Between group comparison of mean time taken for onset of analgesia in different group.

Table 4 shows distribution of subjects according to grade of pain perception. Majority of subjects in Group I had no pain, in Group II had moderate pain whereas in Group III had severe pain. There was a striking difference among groups as regards the pain score. On comparing the data the intergroup difference was statistically significant (p<0.001).

SN	Grade of Pain	Group I (n=30)		Group II (n=30)		Group III (n=30)	
		No.	%	No.	%	No.	%
1.	No pain	17	56.7	0	0.0	0	0.0
2.	Mild pain	13	43.3	10	33.3	1	3.3
3.	Moderate pain	0	0.0	20	66.7	2	6.7
4.	Severe pain	0	0.0	0	0.0	27	90.0

Table 4. Distribution of subjects according to grade of pain perception. $\chi 2=73.656$ (df=2) p<0.001 (Kruskall Wallis test)

Table 5 shows between group comparisons of grades of pain in different groups. All the between group comparisons of grade of pain perception were statistically significant (p<0.001). Group I had significantly lower grade of pain perception as compared to both Groups II and III while Group II had significantly lower grade as compared to Group III (p<0.001).

S.No.	Comparison	"z"	"p"
1.	Group I vs Group II	–6.053	<0.001
2.	Group I vs Group III	–7.015	<0.001
3.	Group II vs Group III	–6.481	<0.001

Table 5. Between group comparison of Grade of pain perception in different groups (Mann-Whitney U test).

Table 6 shows the results of between group comparisons of three groups for mean VAS scores. Results of between group comparisons revealed to be significant statistically (p<0.001). It was observed that mean pain scores of Group I were significantly lower as compared to that of Groups II and III while that of Group II were significantly lower as compared to that of Group III. Group III had significantly higher mean scores compared to both Group I and II.

S.No.	Comparison	"t"	"p"
1.	Group I vs Group II	-15.745	<0.001
2.	Group I vs Group III	-21.932	<0.001
3.	Group II vs Group III	-11.592	<0.001

Table 6. Between group comparisons of Mean VAS scores for pain in different groups.

Discussion

Pain control is an integral part of modern dentistry.[2] Prevention of pain during dental procedures can nurture the relationship of the patient and dentist, building trust, allaying fear and anxiety and promoting a positive dental attitude. Hence, it is important to resort to a pain free method of administering local anaesthesia for pediatric patient's as it is an important consideration in their behaviour guidance.[4] Local anesthetic agents can be injected or they can be applied topically. Topical anaesthetic agents have been used in dentistry for a number of years, mainly for reducing the pain experienced during administration of local anesthetic injections.[5]

Xylocaine is today the standard against which all topical anesthetic are compared. It has Lidocaine as the main active ingredient and is the most preferred topical anesthetic by the dentist. However, as stated, it is not favorable regarding bioadhesion, analgesic potential and taste characteristics. Hence, its use has been limited by concerns about local irritation, systemic toxicity and inadequate analgesia.[6]

Produit Dentaire and Eutectic Mixture of Local Anaesthesia 5% cream (EMLA) are new systems in the field of topical anesthetic agents. Produit Dentaire, a topical anesthetic agent that contains benzocaine has a low water solubility and consequent slow absorption from the area of topical application. It not only prolongs the anaesthesia but also reduces its toxicity but can also produce toxic symptoms if absorbed into the systemic circulation in sufficient quantities.[7] A new topical anaesthetic agent Eutectic Mixture of Local Anaesthesia 5% cream (EMLA) was introduced and approved for medical applications in 1980 by Holst and Evers. The cream has been studied extensively and found to have maximal analgesic effect due to its rapid absorption.[3]

To ascertain effective topical anesthetic agents, an attempt has been made to analyze the clinical effectiveness of varied local anesthetic agents namely Xylocaine, Produit Dentaire and EMLA. Hence the present study was taken to clinically evaluate the onset of action and efficacy of different topical anesthetic agents for pain perception in pediatric dental patients.

In the present study when group of children were tested for different topical anesthetic agents, the results inferred that Eutectic Mixture of Local anaesthesia 5% Cream (Group I) had rapid onset of action when compared to Produit Dentaire (Group II) and Lignocaine spray 15% (Group III). This may be because EMLA is a mixture of Lignocaine (2.5%) and Prilocaine (2.5%) in their base forms having melting points of 69^0C and 37^0C, respectively. However, when these agents are combined together in eutectic form, the melting point of the mixture is lowered to 17^0C. This new physical property allows the anesthetic agents to form oil at mouth temperature (37^0C) and thus facilitates increased absorption of the local anesthetic

agents.[3] The results of the present studies were in accordance with earlier studies conducted by Munshi *et al.* (2001)[8], Vickers *et al.* (1993)[9] and Al-Melh (2007)[10].

On the other hand, results of the present study also indicated that Produit Dentaire (that contains 20% Benzocaine) had better onset of action when compared to Lignocaine spray 15%. This may be because Benzocaine has low dissociation constant (pKa= 3.4) and penetrates through mucosa, exerting its anesthetic effect and providing intimate contact between dosage form and absorbing tissue which may result in high drug concentration in local area and high drug flux through the absorbing tissue. (Nayak *et al.* 2006, Jelvehgari *et al.*, 2006).[2, 11]

Even though Xylocaine (Lignocaine spray 15%) is the most preferred topical anesthetic agent by dentists, in the present study, Xylocaine (Lignocaine spray 15%) demonstrated delayed onset of action. This may be attributed to its unfavorable bioadhesion, analgesic potential and taste characteristics.[1] Altogether; in spray form it is not always possible to confine the expelled amount of solution to the preferred site. Lignocaine spray has delayed onset of action of 112 seconds because of its relatively weak surface anesthetic activity, hence 1-2 minutes of contact with the mucosa is required.[2] The results of the present study were in accordance with Tulga *et al.* (1999)[12], Bennett (1984)[13] and Cawsen and Spector (1990).[14]

When the groups of children were evaluated for pain perception the results inferred that Eutectic Mixture of local anesthetic 5% cream, which is a mixture of Lignocaine and Prilocaine, had low grade of pain perception when compared to Produit Dentaire and Lignocaine spray 15%. As the active drugs in the eutectic mixture are in liquid phase, the release rate is favorable. Thus, ideal circumstances for skin penetration by the active base are achieved with the EMLA preparation having high concentration gradient, small micro droplet size and a satisfactory release rate.[3] Another reason for low grade of pain perception of EMLA 5% cream could be attributed to its high pH of 9.6, the potency of the topical anesthetic agents increases by increasing the pH.[2, 3, 15] The results of the present study was consistent with results of Meechan and Winter (1996)[16], Meechan and Thomason (1999)[17], Shiau *et al*.(2008)[18]and Singh *et al.*(2012).[19]

It was also inferred from the present study that Produit Dentaire (Benzocaine) produced a lesser pain perception when compared to Lignocaine spray 15%. This may be because Produit Dentaire (benzocaine) has been found to be effective at a 20% concentration when applied for atleast 1minute, but ineffective with 30 seconds applications. Similar results seemed to confirm with that of Nusstein *et al.,* 2003[20], Vongsavan *et al.,* 1996[21] and Fukayama *et al.,* 2002.[22] As regard to pain perception Lignocaine spray 15% was least effective when compared to EMLA 5% cream and Produit Dentaire as it has been found to be effective at concentration of 5%, 10%, 20% and 60% when applied for longer duration of 2-20 minutes. Studies reported by Carrel *et al.*, 1974[23] , Carr *et al.,* 2001[24] and Wahl *et al.,* 2001[25] were in accordance with results of the present study.

Conclusions

Hence, from the present study it can be inferred that Eutectic Mixture of Local Anesthetic 5% cream is a better topical anesthetic agent when compared to Produit Dentaire and Lignocaine Spray 15% in regards to onset of action and pain perception. As the numbers of studies on this subject are sparse and clinical results are mixed, an attempt has been made to explain the results on a pharmacological basis. However, further studies are required for EMLA cream with an improved formulation more suitable for mucosal application before its routine use in dentistry.

Acknowledgements

I wish to express my sincere thanks to Dr. Jaishree Bogra (MD, Anesthesia) and Dr. Nishita Garg Jain (MDS, Pedodontist) without whose help I could not have completed this study.

Declaration of Interest

The authors report no conflict of interest and the article is not funded or supported by any research grant.

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