ORIGINAL RESEARCH PAPER

Volume-7 | Issue-9 | September-2018 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

EFFICACY OF A NOVEL HERBAL FORMULATION AS A TOPICAL ANESTHETIC IN VARIOUS INTRAORAL PROCEDURES IN PEDIATRIC PATIENTS: A RANDOMIZED PLACEBO CONTROLLED SINGLE-BLINDED TRIAL

Dental Science

Neelisha Pandey Ex. Junior Resident, Department of Paediatric and Preventive Dentistry, Faculty of Dental Sciences, King George's Medical University, Lucknow.

Ramesh Kumar Pandey Ex. Professor and Head, Department of Paediatric and Preventive Dentistry, Faculty of Dental Sciences, King George's Medical University, Lucknow.

Rajeev Kumar Singh* Associate Professor, Department of Paediatric and Preventive Dentistry, Faculty of Dental Sciences, King George's Medical University, Lucknow. *Corresponding Author

Ajay Kumar Singh Rawat Scientist E2 and Head, Pharmacognosy and Ethnopharmacology Division, National Botanical Research Institute, Lucknow.

Sharad Srivastava Senior Scientist, Pharmacognosy and Ethnopharmacology Division, National Botanical Research Institute, Lucknow, India

ABSTRACT

BACKGROUND: Topical anesthetics have been widely used to alleviate the fear and anxiety associated with the administration of the local anesthetic injections in children. The increasing incidences of systemic adverse reactions reported with the use of topical anesthetics have propelled the clinicians to seek for safer alternatives. This study sought to determine whether a novel herbal formulation was as effective as the commercially prepared 2% Lignocaine gel as a topical anesthetic in various intra oral procedures in children.

METHODS: This was a single center, stratified (3 to 6 years and 7 to 12 years of age), single-blinded, placebo-controlled study. Sixty children were enrolled in the study. All the patients were administered with all the three topical agents at various time intervals and in a random order. Patients were assessed for reduction in the mean pain scores with the Wong Bakers Faces Pain Scale.

RESULTS: Sixty children (n=60) were divided into two age groups 3-6 years (n=30) and 7-12 years (n=30). Equal randomization with respect to gender (1:1) was done in both the age groups (n=15).Reduction of mean pain scores were assessed. It was eventually concluded that the total pain scores were highest in the control agent (8.73+1.43). There was no statistically significant difference between 2% Lignocaine gel and the herbal extract group (p=0.059)

CONCLUSION: In this study, it was concluded that the novel herbal formulation could be used as an effective and a safe alternative to the currently available commercial topical anesthetics.

KEYWORDS

INTRODUCTION:

Administration of local anesthetics remains perhaps the single most important fear inducing stimulus for children undergoing various dental and medical procedures.[1,2] The sight of injection causes a great amount of physiologic arousal and is often considered to be the root cause of disruptive behavior in children. Managing a highly anxious child patient in the dental chair can be extremely taxing, leading to delivery of suboptimal quality treatment. Thus, a number of techniques have been developed to overcome such untoward psychogenic responses including reassurance, warming the anesthetic solution, slow speed of injection, larger gauge of needles and conscious sedation. The use of topical anesthetics is thought to be one of the most important pharmacological treatment strategies to alleviate pain and anxiety of a child before injecting the anesthetic.[3] Topical anesthetics are widely used in many medical procedures like anesthetization of skin before intravenous cannulation, in maxillary sinus punctures and for harvesting of skin graft.[4] Intraorally, they are widely used to reduce the discomfort associated with the administration of local anesthetic injections, to alleviate the pain in cases of superficial and ulcerative mucosal lesions, as oropharyngeal anesthetics in cases of endoscopic procedures and in various other operative dental procedures in pediatric patients.

Recently, concerns have been raised regarding increased incidence of adverse reactions arising due to the systemic absorption of the topical anesthetics. Yaman and Kisnisci reported three cases of idiopathic swelling of the lower lip associated with topical anesthesia.[5] Feng lin et al described the cardiovascular complications resulting from topical Lidocaine application.[6] Benzocaine is a widely used topical anesthetic and has been reported to cause toxic Methaemoglobinaemia in otherwise healthy individuals with no predisposing risk factors.[7] The popularly used EMLA (eutectic mixture of local anesthetics) cream, which is used to provide topical anesthesia for a variety of painful superficial procedures, may cause potential life threatening complications.[8] Oral mucosa is highly vascularized and drugs that are absorbed through the oral mucosa directly enter the systemic circulation, bypassing the gastrointestinal tract and first-pass metabolism in the liver. For some drugs, this results in a rapid onset of action, often faster than the intravenous route. Due to the rich vascular supply of the non-keratinized portion of the oral mucous membrane and low body weight of the children these have become a matter of concern in the pediatric fraternity. This has lead to an increasing trend of exploration of alternative options to synthetic topical anesthetics, such as use of topical refrigerants.[9] Athbi Alqueer reported in 2005 the efficacy of a homemade clove topical anesthetic gel in comparison to 20% Benzocaine gel in reducing the pain of the intraoral injection.[10]

The present study was undertaken to prepare a novel herbal formulation comprising of five well known medicinal plants under standardized conditions and to test the efficacy of the formulation for its topical anesthetic activity in comparison to 2% Lignocaine gel with a placebo as a control.

MATERIALS AND METHODS:

The herbal plants selected for the study included Spilanthes acmella, Zanthoxylum alatum , Urtica dioica , Berberis aristata and Cloves**.** Samples of plant materials were collected from the foothills of Uttarakhand region in India. The herbal specimens were deposited and taxonomic identification and authentication was carried out in the National Botanical Research Institute, Council of Scientific Research, India.

PREPARATION OF EXTRACT:

Equal amounts of selected plant materials (200 grams each) were coarsely powdered for extraction with 50% Hydroalcoholic solvent. Extracts were concentrated using Rotatory evaporator (Buchi) and lyophilized after complete evaporation of solvent residue. The condensed residue free extract was further subjected to gel formulation using 0.5% Carbopol 934 as a stabilizer. The gel was prepared and

stored in airtight containers, sealed with parafilm, and stored at 4oC for the clinical trials. The selection of plants and the procedure of extract preparation were as per Ayurvedic and traditional texts and all the above plants are listed in the "Ayurvedic Pharmacoepia of India" and the "Indian pharmacopeia". These plants have been widely used in humans for various ailments and their benefits are well documented, thus they were considered absolutely safe for topical application.

CLINICAL TRIALS:

In the present study, sixty children were selected in the age group of 4-12 years, irrespective of racial or ethnic variations. To avoid gender bias, we selected an equal number of girls and boys. In the present study, the buccal aspect of the maxillary arch was selected as the site of topical anesthetic application and children who required multiple intra oral procedures in the maxillary arch and thus indicated for infiltrative anaesthesia were enrolled in the study. Patients having chronic systemic debilitating conditions, acute oral afflictions, a history of sensitivity to anesthetics or contact dermatitis and suffering from disturbances in physical and/or mental growth were excluded from the study. Extremely anxious patients or patients with behavior management problems were also not included in the study. The study protocol, aims, objectives, and the procedure to be performed in the trial were explained to the patient's parents/guardians. A written informed consent was obtained from the parents/guardians after they were reassured of the ethical aspect of the trial and the safety of their wards on the usage of the herbal drugs as topical anesthetics. The safety and efficacy of herbal formulation was authenticated by the Department of National Botanical Research Institute, Council of Scientific Research, India. The guardians of the participating child subjects were instructed to ensure a good night's sleep of their wards before the procedure. On arrival in the dental operatory the children were made to relax in the dental operatory with a friendly and efficient staff around so as to allay any fear or apprehension of the child. The study followed the consort guidelines. The present study was conducted in a single blinded fashion where the subjects were not aware of the agent being tested.

DESIGN OF THE STUDY:

The study was conducted in two phases.

PHASE 1:

Phase 1 was undertaken as a pilot study to assess the rapidity of onset and duration of action of the two agents being used in the present study, i.e, the herbal formulation and 2% Lignocaine topical gel.A sample size of 12 was chosen for this phase of the study. The selected patients were divided into three groups of four children each. The three groups were assigned one of the three tests agents each i.e, herbal extract gel, Lignocaine gel and a placebo.The gingiva in relation to the maxillary right central incisor was chosen as the test site in all the subjects. This site was chosen due to ease of access and isolation so that the time of onset of action of the drugs could be accurately determined. Following isolation, the test area was dried using sterile gauze. Approximately 0.5 gm of the test agent was applied to the area using a cotton applicator. Care was exercised 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 anesthesia every 30s for a period of 3 minutes. The blunt end of a periosteal elevator was used to check for objective signs of surface anesthesia. The children were instructed to indicate pain by raising their right hand and the investigator noted eye movements for signs of discomfort. Time was regulated using a stop watch. The time of onset of surface anesthesia was noted. Following the 3-minute period, the test area was wiped free of the agent. The mucosa was inspected for any signs of local irritation. An average time of application for each agent was derived from this phase.

PHASE 2:

This phase was conducted to evaluate the efficacy of herbal extract in comparison with the topical 2%Lignocaine gel and a control agent. The present study was a randomized, one centre, cross over, single-blind, placebo-controlled study. Sixty healthy, cooperative and treatment experienced children participated in the study. The selected subjects were divided into two groups (n=30) according to their age i.e., group 1 (3-6 year) and group 2 (7-12 years).The order of the combinations which were used in the children was randomised. The sequence of allocation was randomly chosen through a lottery system. The combinations of the anaesthetic agents were numbered as follows:

- o Herbal extract vs lignocaine- 1
- o Lignocaine vs placebo -2
- o Placebo versus herbal extract- 3

Three chits were prepared with the above numbering of 1 2 3 and were double folded and kept in three envelopes. Each participant was asked to pick out the envelopes and the order in which the numbers were selected was the order in which the agents were administered to the children. This allocation sequencing was conducted by a disinterested dental nurse who was not allowed to interact with the parents and the children at any time of the study. The patients were tested on three different visits four days to one week apart. Since the threshold of pain in every individual is different and varies from person to person, all the sixty children were tested for all the three agents. The selected children were divided into groups purely for finding if there were any significant differences between the different age groups and between the genders. All the patients were suffering from multiple caries in maxillary arch and had to be administered with infiltration anaesthesia. On the first visit, the test areas were dried using a sterile gauze piece following adequate isolation. The investigator applied approximately 0.5 gm of the placebo for the stipulated time to the sites using a cotton applicator. Subsequently, the test areas were wiped so that no traces of the test agent could be identified.

The investigator then infiltrated 1 ml of 2% Lignocaine with vasoconstrictor using a 26 gauge needle at the prepared test site. The needle was concealed in an attempt to eliminate a fear promoting situation that could alter the subject's pain perception. The use of fear promoting words was discouraged. During the injection procedure, an observer recorded the response of the child according to Wong Baker Scale. The site to be tested was dried with cotton gauge and strict isolation condition was maintained. The children were asked to complete a face pain scale with values from 2(smiling) to 10(crying). The participants rated the pain scales per trial. The ratings were performed after each application. The participants were then allowed to rinse their mouth before leaving the operatory.

After one week all the participants received the next combination of the agents in the same manner as described above for the first visit. The parents/guardians were asked to report immediately in case of any changes or symptoms as told by the child on the test site due to the topical material. One week later the third combination was administered.

The obtained data were summarized in a master chart and subjected to statistical analysis {**illustrated in figure 1}.**

RESULTS:

The present study was carried out with an aim to compare the efficacy of a herbal preparation as topical anesthetic for dental procedures in child patient. A total of 60 children were enrolled in the present study and divided in group 1(3-6 years) and group 2 (7-12 years).Out of 60 patients enrolled in the present study, 30 were aged between 3-6 years and remaining 30 were aged between 7-12 years and designated as Group I and II of the study. The distribution of patients in both the age groups was similar in either of sex. Both the groups having an equal number (n=15; 50%) of males and females. All the patients required multiple procedures in the maxillary arch necessitating the use of infiltration anesthesia. All the patients were tested randomly for the placebo, Lignocaine gel, and herbal anesthetic extract at different time intervals on the buccal aspect of maxillary teeth. Assessments were done for different sites (control, Lignocaine and herbal extract) and then amongst groups for gender. Pain was assessed using Wong Baker Scale Faces Pain Rating Scale for both the groups.

Assessment on Wong Baker Scale

The total pain scores in Control group ranged from 6 to 10 with a mean value of 8.73±1.43. In Group I, mean pain score was 9.20±1.13 (range 6-10) whereas mean pain score in Group II was 8.27±1.55 (range 6-10) thus showing a significant difference between two groups (p=0.015) whereas mean pain scores among males were 8.93±1.36 (range 6-10) as compared to 8.53±1.48 (range 6-10) in females thus showing no significant difference between two groups (p=0.275).The comparison of pain scores in two age groups showed mean pain scores among females to be lower as compared to males for both the age groups yet the difference was not significant statistically for both the age groups (p>0.05). The comparison of pain in two age groups gender wise showed mean value of age Group II to be lower as compared to that of age group I but the difference was not found to be significant statistically in either of two gender (p>0.05)**{illustrated in table 1}.**

The values were represented in Number (%) and Mean±SD and statistical tests used were Friedman ANOVA test and Mann- Whitney U test.

The total pain scores in Lignocaine group ranged from 0 to 4 with a mean value of 1.40±1.14. In Group I, mean pain score was 1.53±1.01 (range 0-4) whereas mean pain score in Group II was 1.47±1.28 (range 0-4) showing no significant difference between two groups (p=0.711). Mean pain scores among males were 1.60±1.10 (range 0-4) as compared to 1.40±1.19 (range 0-4) in females thereby showing no significant difference between two groups (p=0.468).The comparison of pain scores in two age groups showed mean pain scores among females to be lower as compared to males for age group II and to be higher as compared to males for age group I. The difference was not significant statistically for both the age groups (p>0.05). The comparison of pain in two age groups according to gender showed mean value in age Group I to be lower as compared to that of age group II for males. Mean value of age group I was higher as compared to that of age group II among females but the difference was not found to be significant statistically for either of two gender (p>0.05) **{illustrated in table 2}.**

The total pain scores in Herbal extract group ranged from 0 to 4 with a mean value of 1.77±0.91. In Group I, mean pain score was 2.00±0.74 (range 0-4) whereas mean pain score in Group II was 1.53±1.01 (range 0-4) showing a significant difference between two age groups (p=0.043). The mean pain scores among males were 1.73±0.87 (range 0-4) as compared to 1.80±0.96 (range 0-4) in females thereby showing no significant difference between two groups (p=0.797).The comparison of pain scores in two age groups showed mean pain scores among females to be higher as compared to males for group I and to be lower as compared to males for group II. The difference was not significant statistically for both the age groups (p>0.05). The comparison of pain in two age groups according to gender showed mean value of age Group I to be lower as compared to that of age group II for males and mean value of age group I to be higher as compared to that of age group II among females but the difference was not found to be significant statistically for either of two gender (p>0.05) **{illustrated in table 3}.**

When the group comparisons of mean pain scores was done it was found that the there was a significant difference in the mean pain reduction between control and Lignocaine and control and herbal formulation (p<0.001 in both) whereas the difference was not significant between the herbal extract and the Lignocaine sites (p=0.059) **{illustrated in table 4 and table 5}.**

DISCUSSION

The procedures involving the administration of local anesthesia have been cited as being more stressful and painful than disease related or post-operative pain as stated by Humphrey *et al* (1992)[11] and Cummings *et al* (1996)[12]. Topical anesthetics have proved to be a boon for the clinicians in this regard. A number of herbal plants with significant anesthetic properties have been identified and researched extensively. Previously, herbal anesthetic formulation which could be used in surgical and dental procedures have been prepared and patented.[13] The present study was an attempt to prepare a herbal formulation and evaluate its efficacy by comparing it with the conventionally used 2% Lignocaine gel in children.

The herbal formulation comprised of plants of Spilanthes acmella, Zanthoxylum alatum, Cloves, Berberis aristata and Urtica dioica, all of which have been traditionally used in treating various human ailments. The above plants also possessed excellent antimicrobial properties, thereby providing an additional benefit of creating an aseptic field at the site the of procedure.[14,15,16,17,18]

The present study was designed in two phases so, as to evaluate the clinical application time of the herbal formulation and the 2% Lignocaine gel in the first and assess the quantitative reduction of pain in terms of numeric data before the administration of infiltration anesthesia in the second. The Lignocaine 2% gel showed the mean time of onset of action of 3-5 minutes in accordance with previous studies (International Medication Systems, Limited, 2006)[19] and the herbal formulation begin to exert its effect approximately after three minutes. Previous studies have reported that an already fearful, anxious or an uncooperative child patient with or without severe mental retardation would not be able to correctly quantify the pain in terms of the scores of pain scales.[20,21] Since the present study was entirely based on the subjective perception of pain evaluated in terms of pain scores recorded solely by the child, hence, only cooperative and healthy patients with minimal or no signs of anxiety were selected.

The phase two of the study was designed to evaluate the actual efficacy of the herbal agent as a topical anesthetic in comparison with 2% Lignocaine gel. The study was done in a placebo controlled, single blinded randomized manner following the consort guidelines. All the subjects were administered the three topical agents in a random order at various time intervals. The subjects were blinded to eliminate bias. The anesthetic agents were evaluated on the basis of the degree of reduction of pain of the needle prick in the present study. A placebo was introduced as the control drug. Although Goodenough *et al* suggested[22] that older children may have a greater potential to experience a placebo effect from the inert medicines and in the presence of low pain scores, a placebo effect may lead to lower scores, and small differences between groups, still, a placebo had to be incorporated in the present study to establish a baseline data of the anesthetic properties of the herbal extract which was being evaluated for the first time.

Pain is a subjective attribute which is difficult if not impossible to quantify. Children vary greatly in their cognitive and emotional development, medical condition, response to painful interventions and to the experience of pain, as well as in their personal preferences for care in comparison to adults making the assessment of pain very difficult in them.[20] Children's self-reports of pain intensity are a valuable source of information, but their interpretation must be considered together with observation of the behavior, reports by parents, clinical data and information on the child's social environment. Pain intensity scores serve a very useful purpose in sensitively evaluating the effects of pain-relieving and pain-producing interventions. Self-report is the desired method of pain assessment. Obtaining an accurate measurement of pain is vital to gauging baseline discomfort and response to therapy.

Multiple scales have been developed for the assessment of pain in children. One of the most widely used and best-validated pain scales is now the Wong Bakers Faces Pain Rating Scale (WBFPRS). A Wong Baker Scale has the potential to be an excellent measure of treatment effect in school-aged children and adolescents according to Gregory Garra D *et al* (2010).[23] The Wong Baker Faces Pain Scale combines pictures and numbers to allow pain to be rated by the user. It can be used in children over the age of 3, and in adults. The faces range from a smiling face to a sad, crying face. A numerical rating is assigned to each face, of which there are 6 total. Clinicians have noted that topical anesthetics do not work for every child in every instance. Several investigators have attempted to determine the factors that predict the effectiveness of topical anesthetics.

Kleiber *et al*[24] found that younger age was one of the important predictors determining the effectiveness of analgesics in children. They stated that for every year younger, children were 1.5 times more likely to be in the higher pain group indicating that despite higher reported anesthetic effectiveness in this group, younger children still report higher pain. Tanya Wrzosek[25] performed a literature search of all the medical databases and summarized that topical anesthetics may be associated with higher magnitude of benefit for managing pain during common needle stick procedures in 4-6 year old children when compared to younger (1-3 year old) and older (7-11 year old) children. This observation was consistent with anecdotal reports by clinicians that topical anesthetics are more effective in this age group and are increasingly utilized for needle stick pain management in 4-6 year old children as compared to other age groups as stated by Chambers *et al.*[26] It has been suggested that the reason topical anesthetics are effective in this particular age group is that the nociceptors are more densely packed in the mucous membranes of small children resulting in a higher number being activated during clinical procedures.[22,27] In addition, it has been demonstrated that younger children self-report more pain than older children for the same stimulus.[22,27,28] Younger children also favor the extreme ends of pain scales when self-reporting pain[20,22,27]; taken together, these factors could lead to larger differences in scores between anesthetic and placebo-treated groups, resulting in larger effect sizes.

All the above facts lead us to segregate the selected sample into two age groups of 3-6 and 7-12 years so that an equivalent comparison could be drawn and no intra group bias would be present. Studies also suggest

that there are important sex-related influences on the experience of pain.[29,30] Hence, to avoid any gender bias, an equal number of female and male subjects were chosen in each group. In the present study, assessments were done gender wise and according to the age groups. After a careful evaluation of the results of statistical analysis it was concluded that the mean pain scores recorded in the patients were higher with the placebo (8.73+-1.43) than with the 2% lignocaine gel(1.40+-1.14) and the herbal formulation(1.77+-0.91) in both the age groups and gender. The p value (p=0.059) indicated that the difference between the herbal extract and the Lignocaine group was not significant.

The limitation of this study included the apprehension and the subjective bias of the children with every visit depending on how little or more pain was felt by the child in the previous visit. In addition, the herbal preparation was a crude product in a concentrated yet raw form being applied to the oral mucous membrane. The standard drug being used in comparison was 2% Lignocaine gel which is a synthetically derived pure product. However in analyzing the results of the study it was found that there was no significance difference ascertained between the two. Thus, the present study if further followed up could lead to the preparation of a novel herbal anesthetic gel which can not only be used in dental set up but also in other medical situations too.

The herbal anesthetic gel might be beneficial to specific patient groups such as hemophiliacs, pediatric patients, patients suffering from needle phobia, and in patients suffering from long standing infections.

TABLE 1: Assessment of Pain on Wong Bakers Faces Pain Rating Scale for Control Sites

S No.	Variable	No. of cases	Mean Score	SD	Range	Significance of association
1.	Overall	60	8.73	1.43	6-10	-
2.	Group I	30	9.20	1.13	6-10	z=2.427;
3.	Group II	30	8.27	1.55	6-10	p=0.015
4.	Male	30	8.93	1.36	6-10	z=1.092;
5.	Female	30	8.53	1.48	6-10	p=0.275
Group I (3-6 Yrs) (n=30)						
6.	Male	15	9.33	0.98	8-10	z=0.492;
7.	Female	15	9.07	1.28	6-10	p=0.683
Group II (7-12 Yrs) (n=30)						
8.	Male	15	8.53	1.60	6-10	z=0.976;
9.	Female	15	8.00	1.51	6-10	p=0.367
Males (n=30)						
10.	Group I	15	9.33	0.98	8-10	z=1.408;
11.	Group II	15	8.53	1.60	6-10	p=0.217
Females (n=30)						
12.	Group I	15	9.07	1.28	6-10	z=1.978;
13.	Group II	15	8.00	1.51	6-10	p=0.067

TABLE 2: Assessment of Pain on Wong Bakers Faces Pain Rating Scale for Lignocaine Sites

S No.	Variable	No. of cases	Mean Score	SD	Range	Significance of association
1.	Overall	60	1.40	1.14	0-4	-
2.	Group I	30	1.53	1.01	0-4	z=0.371;
3.	Group II	30	1.47	1.28	0-4	p=0.711
4.	Male	30	1.60	1.10	0-4	z=0.725;
5.	Female	30	1.40	1.19	0-4	p=0.468
Group I (3-6 Yrs) (n=30)						
6.	Male	15	1.47	0.92	0-2	z=0.551;
7.	Female	15	1.73	1.28	0-4	p=0.653
Group II (7-12 Yrs) (n=30)						
8.	Male	15	1.60	1.12	0-4	z=0.993;
9.	Female	15	1.20	1.27	0-4	p=0.389
Males (n=30)						
10.	Group I	15	1.47	0.92	0-2	z=0.285;
11.	Group II	15	1.60	1.12	0-4	p=0.838
Females (n=30)						
12.	Group I	15	1.73	1.28	0-4	z=1.160;
13.	Group II	15	1.20	1.27	0-4	p=0.305

TABLE 3: Assessment of Wong Bakers Faces Pain Rating Scale for Herbal Extract Sites

S No.	Variable	No. of cases	Mean Score	SD	Range	Significance of association
1.	Overall	60	1.77	0.91	0-4	-
2.	Group I	30	2.00	0.74	0-4	z=2.019;
3.	Group II	30	1.53	1.01	0-4	p=0.043
4.	Male	30	1.73	0.87	0-4	z=0.258;
5.	Female	30	1.80	0.96	0-4	p=0.797
Group I (3-6 Yrs) (n=30)						
6.	Male	15	1.87	0.52	0-2	z=0.983;
7.	Female	15	2.13	0.92	0-4	p=0.567
Group II (7-12 Yrs) (n=30)						
8.	Male	15	1.60	1.12	0-4	z=0.285;
9.	Female	15	1.47	0.92	0-2	p=0.838
Males (n=30)						
10.	Group I	15	1.87	0.52	0-2	z=0.924;
11.	Group II	15	1.60	1.12	0-4	p=0.539
Females (n=30)						
12.	Group I	15	2.13	0.92	0-4	z=1.882;
13.	Group II	15	1.47	0.92	0-2	p=0.174

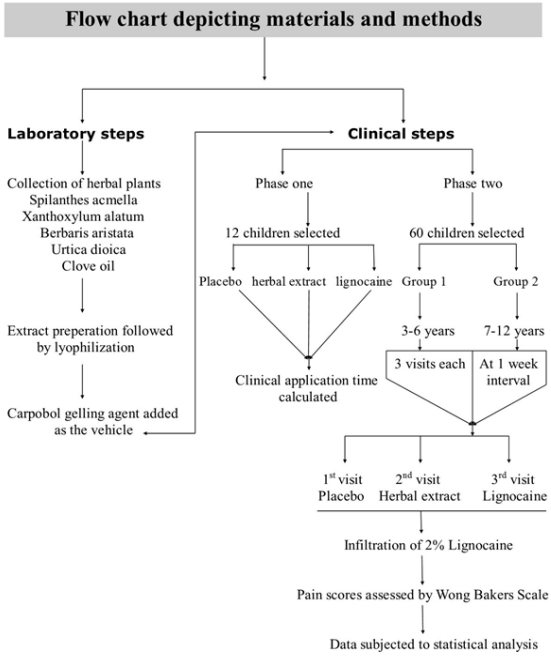
TABLE 4: Comparison of Mean Pain Scores in Different Groups

S. No.	Variable	No. of cases	Control		Lignocaine		Herbal extract		Significance of association (Friedman test)
			Mean	SD	Mean	SD	Mean	SD	p
1.	Overall	60	8.73	1.43	1.40	1.14	1.77	0.91	<0.001
2.	Group I	30	9.20	1.13	1.53	1.01	2.00	0.74	<0.001
3.	Group II	30	8.27	1.55	1.47	1.28	1.53	1.01	<0.001
4.	Male	30	8.93	1.36	1.60	1.10	1.73	0.87	<0.001
5.	Female	30	8.53	1.48	1.40	1.19	1.80	0.96	<0.001
Group I (n=30)									
6.	Male	15	9.33	0.98	1.47	0.92	1.87	0.52	<0.001
7.	Female	15	9.07	1.28	1.73	1.28	2.13	0.92	<0.001
Group II (n=30)									
8.	Male	15	8.53	1.60	1.60	1.12	1.60	1.12	<0.001
9.	Female	15	8.00	1.51	1.20	1.27	1.47	0.92	<0.001
Male (n=30)									
10.	Group I	15	9.33	0.98	1.47	0.92	1.87	0.52	<0.001
11.	Group II	15	8.53	1.60	1.60	1.12	1.60	1.12	<0.001
Female (n=30)									
12.	Group I	15	9.07	1.28	1.73	1.28	2.13	0.92	<0.001
13.	Group II	15	8.00	1.51	1.20	1.27	1.47	0.92	<0.001

TABLE 5: Inter Group Comparisons of Mean Pain Scores by Wilcoxon Signed Rank Test

S. No	Variable	No. of cases	Control vs Lignocaine		Control vs Herbal Extract		Lignocaine vs Herbal extract	
			z	p	z	p	z	P
1.	Overall	60	6.835	<0.001	6.870	<0.001	1.886	0.059
2.	Group I	30	4.884	<0.001	4.893	<0.001	2.646	0.008
3.	Group II	30	4.846	<0.001	4.883	<0.001	0.302	0.763
4.	Male	30	4.850	<0.001	4.902	<0.001	0.707	0.480
5.	Female	30	4.852	<0.001	4.858	<0.001	1.897	0.058
Group I (n=30)								
6.	Male	15	3.477	0.001	3.508	<0.001	1.732	0.083
7.	Female	15	3.475	0.001	3.472	0.001	2.000	0.046
Group II (n=30)								
8.	Male	15	3.455	0.001	3.508	<0.001	0.447	0.655
9.	Female	15	3.447	0.001	3.453	0.001	0.816	0.414
Male (n=30)								
10.	Group I	15	3.477	0.001	3.508	<0.001	1.732	0.083
11.	Group II	15	3.455	0.001	3.508	<0.001	0.447	0.655
Female (n=30)								
12.	Group I	15	3.475	0.001	3.472	0.001	2.000	0.046
13.	Group II	15	3.447	0.001	3.453	0.001	0.816	0.414

FIGURE 1: Flow chart



REFERENCES:

1. Bernstein DA, Kleinknecht RA, Alexander LD: Antecedants of dental fear. J Public Health Dent 1979;39:113-124.
2. Gale EN: Fears of the dental situation. J Dent Res 1972;51:964-966
3. Martin MD, Ramsay DS, Whitney C, Fiset L, Weinstein P: Topical anesthesia: differentiating the pharmacological and pschychological contributions to efficacy. Anesth Prog 1994; 41:40-47.
4. Ohlsen L, Englesson S, and Evers H: An aesthetic lidocaine/prilocaine cream (EMLA) for epicutaneous application tested for cutting split skin grafts. Scand J Plast Reconstr Surg1985; 19:201-209.
5. Yaman Z, Kisnisci RS. : Idiopathic swelling of the lower lip associated with topical anesthesia: Report of three cases. Australian Dental Journal 1998; 43(5):324-7.
6. Lin F, Chang WH, Su YJ, Tsai CH: Cardiovascular complications resulting from topical lidocaine application. Int J Gerontology 2008;2(4):229-32
7. Adriani J. Reactions to local anesthetics. JAMA 1966: 196:405–408.
8. Adriani J, Campbell D. Fatalities following topical application of local anesthetics to mucous membranes. JAMA 1956: 162: 1527–1530.
9. Abott K, MN, Kerry SF: The use of a topical refrigerant anesthetic to reduce injection pain in children. J Pain and Symptom Management 1995; 10(8):584-90.
10. Alqareer A, Alyahya A, Andersson L: The effect of clove and benzocaine versus placebo as topical anesthetics. Journal of Dentistry 2006; 34: 747-50.
11. Humphrey GB, Boon CM, Van Linden Van Den Heuvell GF, Van de Wiel HB. The occurrence of high levels of acute behavioral distress in children and adolescents undergoing routine venipunctures. Pediatrics 1992; 90: 87-9.
12. Cummings EA, Reid GJ, Finley GA, McGrath PJ, Ritchie JA.Prevalence and source of pain in pediatric inpatients.Pain 1996; 68:25-31.
13. Palpu P, Rao CV, Rawat AKS, Ojha SK. 2006.Herbal formulation useful as local anesthetic. India. Publication number: US 2006/0141064.December 28, 2004. June 29, 2006.
14. Veershekhar T. Study of analgesic and anti-inflammatory effects of the plant Spilanthes acmella var; oleracea Rajiv Gandhi University of Health Sciences 2005; 45: Chapter 2.
15. Batool, F., Mubashir S., Rocha JBT, Hussain A., Saied Z., Dilnawaz S. Evaluation of antioxidant and free radical scavenging activities of fruit extract from Zanthoxylum alatum: A commonly used spice from Pakistan. Pakistan Journal of Botany 2010; 42 (6):4299-311.
16. Kumar P, Jaiswal P, Singh VK, Singh DK. Medicinal, therapeutic and pharmacological effects of syzygium aromaticum (laung) Pharmacology online 2011; 1: 1044-55.
17. Sabir M, Bhide NK.In vitro antiheparin action of Berberine on the dog and human blood. Indian Journal of Physiological Pharmacology. 1971; 15: 97-100.
18. Gülçin I, Küfrevioglu OI, Oktay M, Büyükokuroglu ME.Antioxidant, antimicrobial, antiulcer and analgesic activities of nettle (Urtica dioica L.).Journal of Ethnopharmacology 2004; 90(2-3):205-15.
19. Lidocaine hydrochloride jelly [International Medication Systems, Limited] Permanent Link:http://dailymed.nlm.nih.gov.
20. Chambers CT, Johnston C. Developmental differences in children's use of pain scales. Journal of Pediatric Psychology 2002; 27:27-36.
21. Von Baeyer CL. Children's self-reports of pain intensity: scale selection, limitations and interpretation. Pain Research and Management 2006; 11(3): 157–62.
22. Goodenough B, Kampel L, Champion GD, Laubreaux L, Nicholas MK, Ziegler JB, McInerney M.An investigation of the placebo effect and age-related factors in the report

of needle pain from venipuncture in children.Pain 1997; 72:383-91.
23. Garra G, Singer A J, Taira BR, Chohan J, Cardoz H, Chisena E, Thode Jr, HC.Validation of the Wong- Baker FACES Pain Rating Scale in Pediatric Emergency Department Patients. Academic Emergency Medicine 2010; 17(1):50-4.
24. Kleiber C, Schutte DL, McCarthy AM, Floria-Santos M, Murray JC, Hanrahan K. Predictors of topical anesthetic effectiveness in children. Journal of Pain 2007; 8: 168-74.
25. Wrzosek T, Hogan ME, Taddio A. Age and efficacy of topical anesthetics.Pediatric Pain Letter 2009; 11(2).
26. Chambers CT, Giesbrecht K,Craig KD, Bennett SM, Huntsman E. A comparison of faces scales for the measurement of pediatric pain: children's and parents' ratings. Pain 1999; 83:25-35.
27. Arts SE, Abu-Saad HH, Champion GD, Crawford MR, Fisher RJ, Juniper KH, Ziegler JB.Age-related response to lidocaine-prilocaine (EMLA) emulsion and the effect of music distraction on the pain of intravenous cannulation. Pediatrics 1994;93:797-801.
28. Tak JH, Van Bon WH. Pain and distress-reducing interventions for venepuncture in children. Child Care Health Development 2006; 32:257-68.
29. Guinsburg R, de Araújo Peres C, Branco de Almeida MF, de Cássia Xavier Balda R, Cássia Berenguel R, Tonelotto J, Kopelman BI.Differences in pain expression between male and female newborn infants. Pain 2000; 85(1-2):127–33.
30. Fuller BF. Infant gender differences regarding acute established pain. Clinical nursing research 2002; 11(2):190-203.