



Journal of Medical Sciences

ISSN 1682-4474

science
alert

ANSI*net*
an open access publisher
<http://ansinet.com>

JMS (ISSN 1682-4474) is an International, peer-reviewed scientific journal that publishes original article in experimental & clinical medicine and related disciplines such as molecular biology, biochemistry, genetics, biophysics, bio-and medical technology. JMS is issued eight times per year on paper and in electronic format.

For further information about this article or if you need reprints, please contact:

Osagie Akhionbare
Department of Periodontology,
School of Dentistry,
University of Benin,
Benin City, Edo State,
Nigeria

The Palliative Effects of Lidocaine with Adrenaline on Recurrent Aphthous Stomatitis (RAS)

Osagie Akhionbare and Patrick Imioshor Ojehanon

To study the beneficial effect of lidocaine with adrenaline used for alliviation of pain in routine dental procedures on patients with Recurrent Aphthous Stomatitis (RAS). Thirty RAS patients with no known history of any systemic conditions, who reported for the first time for treatment between 2003/2004 at the Dental Centre of the University of Benin Teaching Hospital, Benin City, Nigeria, were selected for this study. The patients had ulcers located on the tongue, floor of the mouth and the buccal mucosa. They were randomly selected into two groups of fifteen each. The first group was taught how to apply the solutions, using the syringe, of 2% lidocaine and the second group 2% lidocaine in 1:80000 adrenaline. The time the solution was applied and the resultant effect before the start of their meals and when the feeling of pain became apparent, were noted. Graphic word rating scale was used to access the level of pain before and after solution application. Complete relief of pain associated with the ulcer after the application of either solutions of lidocaine was reported by 86.7%. 66.7% of patients who used lidocaine solution had a shorter period of onset of pain relief while the reverse was the case with the other group. Patients that used lidocaine with adrenaline solution, reported a longer period of pain relief as compared to lidocaine without adrenaline. During this period the patients under study took their meals in comfort. Lidocaine with adrenaline solution could be incorporated with other methods of managing RAS. This is mostly important in the early period of the ulcers, since it gives a faster and almost complete relief of pain during mealtime.

Key words: Effects, lidocaine, recurrent aphthous stomatitis

INTRODUCTION

Recurrent Aphthous Stomatitis (RAS) is one of the most common oral mucosal inflammatory ulcerative diseases worldwide (Rees and Binnie, 1996). Epidemiological studies indicate that the prevalence of RAS is between 2 and 50% in the general population; most estimates fall between 5 and 25% and three-month recurrence rates as high as 50% (Barrons, 2001). It has been observed with a frequency as high as 50-60%. The peak age of onset for RAS is between 10 and 19 years. After childhood and adolescence, it may continue throughout the entire human lifespan without geographic or age-, sex-, or race-related preference (Ship *et al.*, 2000).

Considerable research attention has been devoted to elucidating the causes of RAS. Local and systemic conditions, genetic, immunologic and infectious microbial factors have all been identified as potential aetiopathogenic agents. However, to date, no principal aetiology has been discovered. Since the aetiology is unknown, diagnosis is entirely based on history and clinical criteria. No laboratory procedures exist to confirm the diagnosis (Natah *et al.*, 2004).

There are three clinical subtypes on the basis of ulcer size and number as minor, major and herpetiform. Minor aphthous ulcers are the most common subtype, representing 80-90% of all recurrent aphthous ulcers. The ulcers, which usually occur on the nonkeratinized oral mucosa, can cause considerable pain and may interfere with eating, speaking and swallowing. Clinically, it presents as shallow ulcerations with an erythematous halo on unattached oral mucosa (Shashy and Ridley, 2004).

The lack of clarity regarding the aetiology of aphthous ulcers has resulted in treatments that are largely empirical. These treatments include the use of antibiotics (Graykowski and Kingman, 1978; Henriksen and Axell, 1985; Kerr *et al.*, 2003), anti-inflammatories (Vincent and Lilly, 1992; Saxen *et al.*, 1997; Rhodus and Bereuter, 1998; Rhodus *et al.*, 2001; Gonzalez-Moles *et al.*, 2002), immune modulators (De Cree *et al.*, 1978; Drinnan and Fischman, 1978; Olson and Silverman, 1978; Matsuda *et al.*, 2003), anaesthetics, alternative (herbal) remedies (Paulo Filho *et al.*, 2000; McBride, 2001) and bioadhesives. (Kutcher *et al.*, 2001; Kutcher, 2001; Andriani *et al.*, 2000).

Most studies done, have involved the evaluation of the topical and systemic therapeutic agents that basically suppress or modulate immune system function. For example, levamisole (Graykowski and Kingman, 1978; De Cree *et al.*, 1978; Drinnan and Fischman, 1978; Olson and Silverman, 1978) thalidomide (Barrons, 2001; Jacobson *et al.*, 1997) colchicine (Viguer *et al.*, 2000;

Fontes *et al.*, 2002; Katz *et al.*, 1994). However, topical agents are preferred because they have fewer associated side effects; but the inability to obtain adequate contact time may limit their effectiveness.

Various topical analgesics have been tried previously such as benzydamine hydrochloride (Matthews *et al.*, 1987; Edres *et al.*, 1997) diclofenac (Saxen *et al.*, 1997) and 5-aminosalicylic acid (Collier, 1992) which have resulted in various degrees of pain reduction.

It is important to note that the effects of these agents are not immediate and not much attention has been focused at alleviating the pain that occurs when the ulcers first appear in the oral cavity. This initial period before the symptomatic effects of topical and systemic therapy begin to manifest, it is important that palliative measures are taken which allow these patients to eat, drink and swallow their meals in comfort.

The value of lidocaine in the management of ulcer pains, has been demonstrated in some studies with the use of anaesthetic lidocaine-prilocaine cream, EMLA (Eutectic Mixture of Local Anaesthetics). This has been used in the management of numerous medical and surgical procedures, such as anaesthesia for superficial surgery and debridement of infected ulcers (Adeoti *et al.*, 1998; Blanke and Hallern, 2003; Rosenthal *et al.*, 2001; Holm *et al.*, 1990).

Lidocaine (2% concentration), which is commonly used in various dental procedures to achieve anaesthesia, was used in this study because of its ease of availability and ability to prevent the generation and propagation of action potentials at any point along a nerve without resultant loss of consciousness but loss of pain. This is due to its surface analgesic properties when applied locally or specifically to the ulcer surface. Because of its intrinsic vasodilator effect with the resultant rapid systemic absorption, combination with adrenaline (1:80000) was used.

MATERIALS AND METHODS

Thirty patients who had their Recurrent Aphthous Stomatitis (RAS) located on the tongue, floor of the mouth, the buccal mucosa, reported for the first time for treatment, were selected at random for this study. This is from amongst all those seen at the University of Benin Teaching Hospital, Dental Center, between year 2003 and 2004. They all had great difficulty in eating their meals due to the nature of pain associated with the ulcer. They had no known history of any systemic condition and conditions that maybe affected by any component of the agents used. Two of the patients had major ulcers, while the rest had minor ulcers.

Patients were randomly selected into two groups (15 patients per group). The first group was taught on how to apply the solutions of 2% lidocaine while the second group used 2% lidocaine with 1:80000 adrenaline. These were applied onto the ulcer surface with the use of aspirating syringe. Two to three drops of the solution were applied directly into the ulcer surface after the patient had swallowed most of the saliva in the mouth. They were instructed to allow the mouth remain opened for about 2 minute to permit the solution to remain in contact with the ulcer before closing the mouth to swallow accumulated saliva. This was repeated a second time. The patients were asked to record the time the solution was applied and the resultant effect before the start of their meal and to note the time when the feeling of the effect of pain became apparent. They were, to access and record their level of pain, using the Graphic Word Rating Scale before and after application of the solutions.

RESULTS

The results of this study showed that 53.3% followed by 36.7 and 10% of the patients felt medium, intense and severe pain, respectively from their ulcers before the applications of the agents. Complete relief of pain associated with the ulcer after the application of either form of lidocaine was reported by 86.7% of the patients. Only 13.3% still felt light pain. However, during the early part of taking meal, 80% reported complete pain relief and 20% felt light pains from their ulcers (Table 1).

A higher proportion of the patients (66.7%) who used lidocaine solution had a shorter period of onset of pain relief (within 0-2 min) while the reverse was the case where

80% of the other group that used lidocaine with adrenaline solution had a longer period of onset of pain relief (2-4 min) (Table 2).

The patients who used the solution of lidocaine with adrenaline reported to have had a longer period of pain relief as compared to those that used only lidocaine solution. Gradually reappearance of pain by both groups was experienced. During this period the patient took his/her meals without difficulty (Table 3).

DISCUSSION

Various studies have reported that the aetiology of Recurrent Aphthous Stomatitis (RAS) which usually causes considerable pain and interferes with eating, speaking and swallowing is unknown (Natah *et al.*, 2004; Burruano and Tortorici, 2000; Zunt, 2003; Petersen and Baughman, 1996). This therefore means that various methods of management are geared towards relief of symptoms (Rhodus and Bereuter, 1998; Kutcher *et al.*, 2001; Kutcher, 2001). Reports have also indicated that these methods of managements results in the early remission of signs and symptoms of the conditions and in some cases increases the interval between reoccurrences (Barrons, 2001; De Cree *et al.*, 1978; Muzio *et al.*, 2001). This involves the use of single or a combination (Ylikontiola *et al.*, 1997) of various methods such as, antibiotics, anti-inflammatories, immune modulators, anaesthetics and alternative (herbal) remedies (Paulo Filho *et al.*, 2000; McBride, 2001) and bioadhesives (Kutcher *et al.*, 2001; Kutcher, 2001; Andriani *et al.*, 2000).

Not much have been reported on the use of lidocaine as a form of pain relief in RAS while attention has not even been focused on combination of lidocaine with adrenaline, which is usually used to achieve local anaesthesia in various dental procedures. This study has shown that combination of lidocaine with adrenaline gives a longer period of pain relief, which allows the patients enough time to take their meals. This was an indication that adrenaline may have had a role to play in the period of pain relief.

It is important to note that most of the management methods apart from the use of anaesthetics like lidocaine only reduces the intensity of pain after a certain period (Saxen *et al.*, 1997) and not eliminating it, as is in this case which allows the patients to eat their meals with some comfort.

Previous studies with the use of lidocaine for ulcer pains did not incorporate adrenaline in their formulation (Blanke and Hallern, 2003; Rosenthal *et al.*, 2001; Holm *et al.*, 1990).

The use of benzydamine hydrochloride mouthwash which is available in the UK as an over the counter

Table 1: Pain severity of ulcers of patients

Characteristics	Before appt	After appt	During meals
	No. (%)	No. (%)	No. (%)
No pain	-	26 (86.7)	24 (80.0)
Light pain	-	4 (13.3)	6 (20.0)
Medium pain	16 (53.3)	-	-
Intense pain	12 (36.7)	-	-
Severe pain	2 (10.0)	-	-
Unbearable pain	-	-	-
Total	30 (100.0)	30 (100.0)	30 (100.0)

Table 2: Onset of pain relief

Time	Lidocaine solu (%)	Lidocaine with adren. solu. (%)
0-2 min	10 (66.7)	3 (20)
2-4 min	5 (33.3)	12 (80)
>4 min	None	None
Total	15 (100.0)	15 (100)

Table 3: Period of pain relief

Time	Lidocaine solu (%)	Lidocaine with adren. solu. (%)
0-5 min	13 (86.7)	None
5-10 min	2 (13.3)	11 (73.3)
10-15 min	None	4 (26.7)
>15 min	None	None
Total	15 (100.0)	15 (100.0)

preparation has been used. It contains some degree of local anaesthetic properties; this produces transient topical anaesthesia thereby giving symptomatic relief only to patients with ulcers of minor severity (Edres, 1997). But its adverse effects of numbness or stinging sensation of the oral mucosa makes this study important because the effect of numbness in this study is only located in the immediate locality of the ulcer which is of benefit to patients in terms of oral activities.

Cyanoacrylate (2-octyl cyanoacrylate), which is topical medical adhesive formulation (Narang, 2001) has also been used as a form of pain relief. It polymerizes instantly upon application into a thin, flexible polymer film thereby creating a mechanical barrier and providing pain relief of oral ulcerations and irritations and maintains a natural healing environment for the area to heal. However, it is important to note that this is only a mechanical barrier that prevents substances getting to the surface of the ulcer but does not affect the generation and propagation of impulses in an inflammatory environment of RAS, as in the case of lidocaine in this study. Further studies can be undertaken to see the beneficial effect of lidocaine/adrenaline with any other method of managing both major and minor RAS.

CONCLUSIONS

This study has indicated the ability of lidocaine in relieving pain associated with Recurrent Aphthous ulcers and combination with adrenaline further increase the period of pain relief which allows the patients enough time to take their meals.

Lidocaine with adrenaline solution can be incorporated with other methods of managing RAS. This is most important in the early period of the ulcers, since it gives a faster and almost complete relief of pain during mealtime.

REFERENCES

Adeoti, A.G., K.J. Vega, E.Z. Dajani, B.W. Trotman and P.C. Kloser, 1998. Idiopathic esophageal ulceration in acquired immunodeficiency syndrome: Successful treatment with misoprostol and viscous lidocaine. *Am. J. Gastroenterol.*, 93: 2069-2074.

Andriani, E., T. Bugli, M. Aalders, S. Castelli and G. De Luigi *et al.*, 2000. The effectiveness and acceptance of a medical device for the treatment of aphthous stomatitis. *Clinical observation in pediatric age. Minerva Pediatr.*, 52: 15-20.

Barrons, R.W., 2001. Treatment strategies for recurrent oral aphthous ulcers. *Am. J. Health Syst. Pharm.*, 58: 41-50; quiz 51-53.

Blanke, W. and B.V. Hallern, 2003. Sharp wound debridement in local anaesthesia using EMLA cream: 6 years' experience in 1084 patients. *Eur. J. Emerg. Med.*, 10: 229-231.

Burruano, F. and S. Tortorici, 2000. Major aphthous stomatitis (Sutton's disease): Etiopathogenesis, histological and clinical aspects *Minerva Stomatol.*, 49: 41-50.

Collier, P.M., S.M. Neill and P.W. Copeman, 1992. Topical 5-aminosalicylic acid: A treatment for aphthous ulcers. *Br. J. Dermatol.*, 126: 185-188.

De Cree, J., H. Verhaegen, W. De Cock and F. Verbruggen, 1978. A randomized double-blind trial of levamisole in the therapy of recurrent aphthous stomatitis. *Oral. Surg. Oral. Med. Oral. Pathol.*, 45: 378-384.

Drinnan, A.J. and S.L. Fischman, 1978. Randomized, double-blind study of levamisole in recurrent aphthous stomatitis. *J. Oral. Pathol.*, 7: 414-417.

Edres, M.A., C. Scully and M. Gelbier, 1997. Use of proprietary agents to relieve recurrent aphthous stomatitis. *Br. Dent. J.*, 182: 144-146.

Fontes, V., L. Machet, B. Huttenberger, G. Lorette and L. Vaillant, 2002. Recurrent aphthous stomatitis: Treatment with colchicine. An open trial of 54 Cases. *Ann. Dermatol. Venereol.*, 129: 1365-1369.

Gonzalez-Moles, M.A., P. Morales, A. Rodriguez-Archilla, I.R. Isabel and S. Gonzalez-Moles, 2002. Treatment of severe chronic oral erosive lesions with clobetasol propionate in aqueous solution. *Oral. Surg. Oral. Med. Oral. Pathol. Oral. Radiol. Endod.*, 93: 264-270.

Graykowski, E.A. and A. Kingman, 1978. Double-blind trial of tetracycline in recurrent aphthous ulceration. *J. Oral. Pathol.*, 7: 376-382.

Henricsson, V. and T. Axell, 1985. Treatment of recurrent aphthous ulcers with Aureomycin mouth rinse or Zendium dentifrice. *Acta Odontol. Scand*, 43: 47-52.

Holm, J., B. Andren and K. Grafford, 1990. Pain control in the surgical debridement of leg ulcers by the use of a topical lidocaine-prilocaine cream, EMLA. *Acta Dermatol. Venereol.*, 70: 132-136.

Jacobson, J.M., J.S. Greenspan, J. Spritzler, N. Ketter and J.L. Fahey, 1997. Thalidomide for the treatment of oral aphthous ulcers in patients with human immunodeficiency virus infection. National Institute of Allergy and Infectious Diseases AIDS Clinical Trials Group. *N Eng. J. Med.*, 336: 1487-1493.

Katz, J., P. Langevitz, J. Shemer, S. Barak and A. Livneh, 1994. Prevention of recurrent aphthous stomatitis with colchicine: An open trial. *J. Am. Acad. Dermatol.*, 31(3 Pt 1): 459-461.

- Kerr, A.R., C.A. Drexel and A.I. Spielman, 2003. The efficacy and safety of 50 mg penicillin G potassium troches for recurrent aphthous ulcers. *Oral. Surg. Oral. Med. Oral. Pathol. Oral. Radiol. Endod.*, 96: 685-694.
- Kutcher, M., 2001. Evaluating the efficacy of 2-octyl cyanoacrylate bioadhesive for treatment of oral ulcerations. *Compend. Contin. Educ. Dent. Suppl.*, pp: 12-16.
- Kutcher, M.J., J.B. Ludlow, A.D. Samuelson, T. Campbell and S.N. Pusek, 2001. Evaluation of a bioadhesive device for the management of aphthous ulcers. *J. Am. Dent Assoc.*, 132: 368-376.
- Matthews, R.W., C.M. Scully, B.G. Levers and W.S. Hislop, 1987. Clinical evaluation of benzydamine, chlorhexidine and placebo mouthwashes in the management of recurrent aphthous stomatitis. *Oral. Surg. Oral. Med. Oral. Pathol.*, 63: 189-191.
- Matsuda, T., S. Ohno, S. Hirohata, Y. Miyanaga and H. Ujihara *et al.*, 2003. Efficacy of rebamipide as adjunctive therapy in the treatment of recurrent oral aphthous ulcers in patients with Behcet's disease: A randomised, double-blind, placebo-controlled study. *Drugs R.D.*, 4: 19-28.
- McBride, D.R., 2001. Management of aphthous ulcers. *Am. Fam Physician*, 64: 737.
- Muzio, L.L., A. della Valle, M.D. Mignogna, G. Pannone and P. Bucci *et al.*, 2001. The treatment of oral aphthous ulceration or erosive lichen planus with topical clobetasol propionate in three preparations: A clinical and pilot study on 54 patients. *J. Oral. Pathol. Med.*, 30: 611-617.
- Narang, U., 2001. Cyanoacrylate medical adhesives--a new era Colgate ORABASE Soothe. N. Seal Liquid Protectant for canker sore relief. *Compend Contin. Educ. Dent. Suppl.*, 32: 7-11.
- Natah, S.S., Y.T. Kontinen, N.S. Enattah, N. Ashammakhi, K.A. Sharkey and R. Hayrinen-Immonen, 2004. Recurrent aphthous ulcers today: A review of the growing knowledge. *Int. J. Oral. Maxillofac Surg.*, 33: 221-234.
- Olson, J.A. and S. Jr. Silverman, 1978. Double-blind study of levamisole therapy in recurrent aphthous stomatitis. *J. Oral. Pathol.*, 7: 393-399.
- Paulo Filho, W., J.E. Ribeiro and D.S. Pinto, 2000. Safety and efficacy of Eupatorium laevigatum paste as therapy for buccal aphthae: Randomized, double-blind comparison with triamcinolone 0.1% orabase. *Adv. Ther.*, 17: 272-281.
- Petersen, M.J. and R.A. Baughman, 1996. Recurrent aphthous stomatitis: Primary care management. Recurrent aphthous stomatitis: Primary care management. *Nurse Pract.*, 21: 36-40, 42, 47.
- Rees, T.D. and W.H. Binnie, 1996. Recurrent aphthous stomatitis. *Dermatol. Clinics*. 14: 243-256
- Rhodus, N.L. and J. Bereuter, 1998. An evaluation of a chemical cautery agent and an anti-inflammatory ointment for the treatment of recurrent aphthous stomatitis: A pilot study. *Quintessence Int.*, 29: 769-773.
- Rosenthal, D., F. Murphy, R. Gottschalk, M. Baxter, B. Lycka and K. Nevin, 2001. Using a topical anaesthetic cream to pain during sharp debridement of chronic leg ulcer. *J. Wound Care*, 10: 503-505.
- Saxen, M.A., W.T. Ambrosius, Rehemtula al-KF, A.L. Russell and G.J. Eckert, 1997. Sustained relief of oral aphthous ulcer pain from topical diclofenac in hyaluronan: A randomized, double-blind clinical trial. *Oral. Surg. Oral. Med. Oral. Pathol. Oral. Radiol. Endod.*, 84: 356-361.
- Shashy, R.G. and M.B. Ridley, 2000. Aphthous ulcers: A difficult clinical entity. *Am. J. Otolaryngol.*, 21: 389-393.
- Ship, J.A., E.M. Chavez, P.A. Doerr, B.S. Henson and M. Sarmadi, 2000. Recurrent aphthous stomatitis. *Quintessence Int.*, 31: 95-112.
- Viguiet, M., S. Fouere, F. Pascal and P. Morel, 2000. Herpetiform ulceration: 5 cases *Ann. Dermatol. Venereol.*, 127: 707-710.
- Vincent, S.D. and G.E. Lilly, 1992. Clinical, historic and therapeutic features of aphthous stomatitis. Literature review and open clinical trial employing steroids. *Oral. Surg. Oral. Med. Oral. Pathol.*, 74: 79-86.
- Ylikontiola, L., T. Sorsa, R. Hayrinen-Immonen and T. Salo, 1997. Doxymycine-cyanoacrylate treatment of recurrent aphthous ulcers. *Oral. Surg. Oral. Med. Oral. Pathol. Oral. Radiol. Endod.*, 83: 329-333.
- Zunt, S.L., 2003. Recurrent aphthous stomatitis. *Dermatol. Clin.*, 21: 33-39.