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Introduction of DMS irrigation to heal Endo–Perio lesions and Cysts

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Abstract

Introduction: This article discusses the introduction of DMS Irrigation Solution (Doxycycline, Metronidazole and Saline). It is an antibiotic solution, which can be pushed beyond the Periapical region to treat the Perio-Endo Lesions, Furcation, Fistula and even a big cyst of diameter 10 to 12 cm without causing any complications. *Material and Method*: The case study has been done in Sabya General Hospital, Jizan, Saudi Arabia in patients of the age group 18 to 55 after their proper consent. Only female cases were taken up for the study. *Observation*: Fifty cases were treated and followed up. Among them 20 cases had periodontitis and all of these had history of diabetes. During this procedure the DMS irrigation is used which directly flushes the microbes providing enough dilution, irrigation and initiates the process of healing, revascularization, regeneration and epithelialization of the wound. *Conclusion*: Delivery system seems to be an efficient system in treating the lesions; even of bigger diameters and DMS, as an irrigation seems to be the most appropriate additional irrigation besides the conventional ones used in dentistry.

Introduction

A clinician needs efficiency and proper knowledge of the defect prior to deciding any procedure. The latest evidences emphasize that an atraumatic procedure is always a better option and single or multiple visits should not be a reason to opt for the surgery. The relationship between the periodontium and the pulp was first discovered by Simring and Goldberg in 1964[(1)]. The sequel of events, their mixed anaerobic infections follow different pathways but lead to similar consequences: the abscess, the furcation, the sinus-tract, fistula, denudement of periodontal ligament and the bone destruction (periodontitis) and a more accentuated form - the cyst, which has other etiological factors too. A cyst is a challenge to treat non-surgically without enucleation. The pulpal and periodontal infections at times co-exist together in the form of combined lesions, showing different manifestations and following different patterns[(2)]. The periapical endodontic lesions increase in size and enlarge in a coronal direction, while at the same time a periodontal pocket progresses apically and the two lesions subsequently join. These teeth require both root canal therapy and aggressive periodontal treatment for their survival. Periodontitis is normally considered to be a chronic process. The micro-organisms associated with periodontitis may also be capable of producing necrosis of the pulp cells through the action of their metabolic products, destructive enzymes or other mechanics[(3)]. Porphyromonas and prevotella species induce the activation of macrophages which subsequently produces interleukin-1. This mediator may enhance bone resorption and perpetuation of the combined pulp-periodontal lesion. The larger the part of the lesion caused by root canal infection or plaque infection, the favorable prognosis is once the regeneration of attachment happens[(4)]. Root canal procedure seems to be the most appropriate treatment in draining the abscess produced by either of the two routes, Endo or Perio. The presence of A. actinomycetemcomitans is a major organism and the discovery that this organism penetrates the tissues offered new hope for therapeutic success, namely antibiotics. Currently an ideal such antibiotic does not exist, however a combination is necessary to eliminate all putative pathogens. The currently

used chemicals for irrigation include NaOCL, (Sodium Hypochlorite) CHX (Chlorhexidene), EDTA (Ethylenediaminetetraaceticacid) and MTAD (A mixture of doxycycline, citric acid and a detergent Tween80. None of these possess all the characteristics of an ideal irrigation. Hence the need to test the effectiveness of an easily prepared antibiotic solution for irrigation.

Material and Methods

Study Selection: The patients selected were only females between the age group of 18 and 55 years. They visited the OPD of Sabya General Hospital, Jizan, Kingdom of Saudi Arabia and were diagnosed with various lesions. The surgical procedures were decided but certain patients had preference for non-surgical procedures and some of the patients when given options opted for the atraumatic line of treatment. This whole procedure and follow up was done between May 2015 and January 2018.

Composition of DMS: DMS irrigating solution is used in the ratio of 1:5:5. One capsule of Doxycycline 100 mg, 5 ml of metronidazole and 5 ml of normal saline. The concentration of the drug used in this research is 5ml from 500ml of metronidazole which contains 500 mgs. This means the concentration used here is minimal i.e. 5 mg of metronidazole and 100 mg of doxycycline with 5 ml of normal saline. This combination has the least toxic complications and provides significant results. DMS is used on weekly basis for first month and then tapered in the second month. Local delivery: The use of local delivery method to administer antibiotics offers a novel approach to localized periodontal infections but in perio-endo lesions, all endo-irrigations have their limitations. Recently MTAD (a mixture of tetracycline isomer, acid and detergent) has been introduced which is a formulation of doxycycline, tween-80, and citric acid. Its effectiveness is attributed to its anti-collagenase activity, low pH & ability to be gradually released over time, however MTAD cannot be pushed beyond the canals in the periapical region to treat the furcation or a cyst[5]. DMS solution follows the process of osmosis and works against concentration gradient thereby reducing the acidic pH of the abscess at the site and relieving the pain immediately. The RCT (Root Canal Treatment) is an initial step done to relieve the pressure by providing the drainage. Tetracycline as a mouth wash was used on these patients initially and the hygiene was taken care of thoroughly. The mouthwash was not mandatory for other cases.

Pictures 1-4 from left to right shows infusion of Metronidazole 500mg, Cap Doxycycline 100mg, Normal saline, disposable syringe and loaded syringe of DMS Irrigant.

Observation:

All the patients responded without any complication except one patient aged 45, who developed sensitivity to doxycycline even after doing all her blood investigations. She felt pain while injecting it through the access cavity prepared in 41. She had a huge lesion, so after RCT apicectomy was considered the best treatment. From the various studies done so far it has been seen that there is a strong correlation between the periodontitis and diabetes. Any significant medication in treating the periodontitis in diabetic patients can become a motivational local delivery drug combination to treat the lesion. Meenavat et al[6] studied the effect of periodontal therapy in diabetics and found that there was reduction in HbA1c in patients who underwent periodontal therapy with systemic doxycycline and chlorhexidine rinse. Diabetic patients, their compromised bone structure and the excellent prognosis with Doxycycline helped me launch the concept of DMS in treating the lesions. The use of antibiotic in perio-endo lesion was first reported in 1951 by Grossman[7] which

was known as poly-antibiotic paste and was a mixture of penicillin, bacitracin, streptomycin and caprylate-sodium. The potency and efficacy of medicaments used in DMS have been separately been advocated by Jarmillo and Herrara[8]. They stated that antibiotic therapy should be taken into account in abscess formation. The antimicrobial property of calcium hydroxide and tetracycline has found a significant effect on enterococci[9]. In 2012 the mixture of metronidazole, ciprofloxacin and minocycline was added with macrogol propylene glycol and was a powdered mix in a ratio of 1:3:3[10]. Ledermix was used as a therapeutic intracanal medicament. It had two active components, triamicinolone a steroid (1 percent) and broad spectrum antibiotic di-methylchlortetracycline 3:2 and 1 percent democycline[11]. The discoloration occurred due to minocycline packed for 2 weeks. Metronidazole was used as a 1% solution or, more frequently, as a 0.75% or 0.80% gel. Two reported adverse effects were skin irritation and a burning sensation. In a study by Barker and Lockett it was found ineffective in eliminating streptococcus viridans in root canal of dogs[12]. Dogs were administered metronidazole orally at doses of 0, 25 and 50 mg/kg for a period of one month. They showed no physical or biological alteration and no tissue modification[13]. From the previous researches, it has been seen that the peak concentrations of metronidazole in plasma and saliva were in the same range, 8.7-13.8 micrograms/mL, and similar concentrations were found in the gingival fluid samples. It is concluded that metronidazole taken orally has similar pharmacokinetics in both saliva and plasma, and that a single oral dose of 750 mg metronidazole leads to a concentration of the drug in the gingival crevice fluid that exceeds the minimal inhibitory concentration for most anaerobic oral micro-organisms[14]. Generally, topical metronidazole was reported to result in a reduction or eradication of wound odor, decrease in wound drainage, improvement in wound appearance, decrease in surrounding cellulitis, halting of tissue necrosis, and decrease in pain. Although nurses report success with sprinkling crushed metronidazole pills on wounds, no published reports of this method of topical application are available. Topical metronidazole may be considered as an option for the management of malodorous wounds. In all these years antibiotics were used in the form of powder and mixtures but never as an irrigation.

The DMS Irrigating solution obeys the physical phenomenon of osmosis. It is of great importance in biological processes. The transport of solute molecules of doxycycline and metronidazole creates selective diffusion process driven by the internal energy of solvent molecules. This attains enough pressure for diluting the abscess incubated in the inaccessible furcation area, or even a cyst henceforth increasing, the pH from an acidic consistency of 6.7 to 7. The initial response is the relief in pain. Grahms and Ficks Law of Thermodynamics are profound in transportation and natural phenomenon. The drugs used in this research have specific modalities like tetracyclines. They were initially used as a mouthwash in the diabetic patients and finally got replaced by doxycycline in DMS due to their chemically modified nature. Jens Ove Andersen[15] in his studies showed that topically applied tetracycline solution doubled the chance of pulp re-vascularization. Tetracycline has some specific properties including low pH. Its acidic property causes it to function as calcium chelator and demineralize enamel and dentin. This mineralization is comparable by what is gained through citric acid. Furthermore, tetracycline has retention property absorbed by dentin and cementum and freed gradually. In high densities, tetracycline can have a bactericidal impact. Among other specific properties of tetracycline is its ability to decrease the root resorption by affecting the osteoclast activity and reducing collagenase; although tooth color is a harmful side-effect of this irrigant[16]. Doxycycline has higher availability in gingival crevice. It's more significant against A. actinomyetemcomitans and Enterobacter faecalis. It has host modulating properties: antimicrobial, anti-collagenase, anti-inflammatory, inhibition of bone resorption, and promotes re-attachment[17]. Collagenase and gelatinase are matrix metalloproteinases (MMPS) which play an important role in tissue destruction. Doxycycline inhibits MMPS and prevents tissue destruction independent of their anti-microbial activity. The molecular environment of chronic wounds like many other

chronic inflammatory diseases contains abnormally high levels of pro-inflammatory cytokines, tumor necrosis factor (TNF)-alpha and interleukin (IL-1beta) and MMPs which impair normal wound healing. The US Food and Drug Administration (USFDA) approved antibiotic appears to inhibit members of the MMP superfamily like MMPs and TNF-alpha converting enzyme (TACE). The use of topical doxycycline enhances healing of chronic wounds. The favorable clinical response may in part be due to inhibition of classical phagocytes, neutrophils and mesenchymal collagenase/MMP8 activities produced by doxycycline. This anti–collagenolytic doxycycline effect is mediated through inhibition of the enzyme. Doxycycline scavenges hypochlorous acid and superoxide radicals produced by phagocytes. Doxycycline increases the level of interleukin 34. It is a cytokine which promotes the proliferation, survival and differentiation of monocytes and macrophages. It promotes the release of pro-inflammatory chemokine and thereby plays an important role in regulation of osteoclast proliferation and bone resorption. Yagiela et al[18] explained the mechanism of doxycycline as it is primarily bacteriostatic, inhibits bacterial protein synthesis by binding to and interfering with ribosomes. This bacteriostatic action may be advantageous because in the absence of bacterial cell lysis, antigenic byproducts such as endotoxins are not released. The research concluded that doxycycline administered at sub-antimicrobial doses led to improvements in disease parameters with no apparent side effects and appears to have significant potential as an oral adjunctive therapy in the long term management of adult periodontitis[19]. Metronidazole is the drug of choice for treating Actinomycetemcomitans and is more effective when used in combination with other antibiotics. It's also effective against P. gingivalis and Prevotella intermedia. Metronidazole rapidly enters human gingival fibroblasts via simple diffusion. Metronidazole has a marked anti-inflammatory action and as such leads to early regression of pain and inflammatory edema and healing of ulcer[20]. The ultimate goal of periodontal therapy has been the regeneration of the supporting tissues lost as a consequence of inflammatory periodontal diseases, various modalities are available to treat the bone defects and achieve a goal in treating localized infra bony and class 2 furcation defects by using guided tissue regeneration GTR. Metronidazole which is an anti –microbial drug helps in the management of infrabony bone defects associated with periodontal defects, non–surgically when incorporated with the doxycycline as an irrigation to reach the inaccessible areas and to reduce the mobility[20] . Rao et al[21] used metronidazole and reported a significant increase in the epithelialization in the wound. Normal saline (isotonic solution of 0.9% sodium chloride) is used to flush wounds and is an effective endo-irrigant. It acts as a vehicle to transport the doxycycline and metronidazole granules, facilitating the reduction of pathogens and promoting the antibiotics to work efficiently. It can be used safely in periapical area when compared to 2.6 percent sodium hypochlorite which has its complications.

It leaves us no doubt that the DMS in the form of irrigation gains accessibility without causing any side effects. Lastly calcium hydroxide is packed in the canals. The hydroxyl group of calcium hydroxide is considered the most important component which provides an alkaline environment thereby encouraging repair and active calcification. It neutralizes the lactic acid from osteoclasts, arrests inflammatory root resorption and stimulates healing.

The clinical pictures and the radiographic presentations of few patients are depicted below showing the healing of lesions atraumatically and demonstrating the effects of DMS.

A patient aged 25 years with an old composite restoration and a pyogenic granuloma in the lingual sulcus in relation to 36 is shown in the picture below.

Iopa (Intra-oral peri-apical) X-ray reveals radiolucency in relation to tooth 36, mobility grade 2, vitality negative; Periodontal examination depicts the depth of 4-7mm and class 2 furcation involvement (measured with Naber’s probe).

Pictures 5-7 show from L-R the healing of a lingual granuloma at 36 at the time of presentation (Pic 1), after two weeks (Pic 2) and after four weeks (Pic 3). Note complete recession of the granuloma non-surgically.

Pictures 8-10 from L-R depict the x-rays showing the healing of furcation and efficient bone regeneration. No recurrence of lesion is even seen after 2 years follow up.

B)A 10-year-old patient with Swelling and pain is diagnosed a Fistula related to 41.

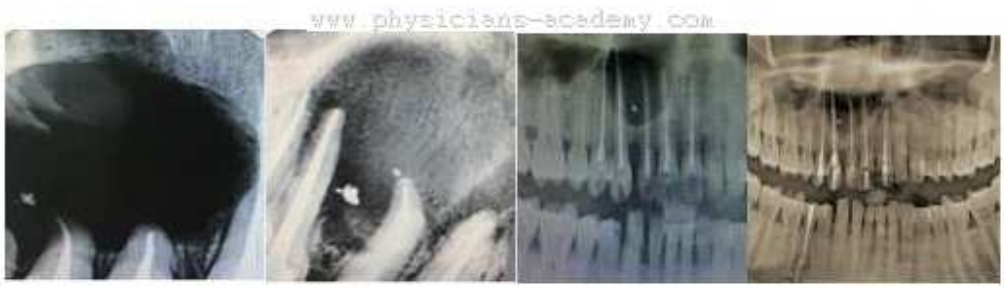
Pictures 11-14 from left to right shows the fistula and its stages of recession followed by complete healing without scaring with DMS irrigation.

Pictures 15-18 from L-R show the x-rays prior (Pic 15) and six months after treatment (Pics 16, 17) followed by an x-ray after two years (Pic 18).

C) Represents a 25 year old patient with radicular cyst based on clinical and radiological diagnosis. Differential diagnosis should include dentigerous cyst, ameloblastoma, odontogenic keratocyst, periapical cementoma and Pindborg tumor. The patient was treated on the same lines as the previous cases. Success was attained within 2 months of treatment and the patient was kept on follow up. It was a challenge to treat such a big radiolucency without enucleation. In the first two sessions the pain and the huge swelling was reduced. Slowly and gradually the huge radiolucency got replaced remarkably by bone and tissue epithelialization started filling up the empty space. There were many speculations regarding its recurrence, however the reduction of a cyst non-surgically was remarkable. The patient was kept on follow up and even after 8 months there was no recurrence.

Pictures 19-22 from L-R show the sequel of excellent healing of a large cyst of diameter 10 to 12 cm in diameter.

Pic 23-27 from left to right reveals the sequence of x-rays depicting the regeneration of bone and perfect epithelialization of wound atraumatically with DMS irrigation.



Pic 28-31 from left to right shows a comparison between the first visit where the patient has a huge radiolucency of palate indicating cyst and the healing.

Pic 32-33 show Surgical procedure vs Non-surgical procedure.

Age	Number	Diagnosis	Number of DMS Therapy	Outcome
18-25	10	Fistula	4;once per week	Excellent
26-35	25	Lingual granuloma	3;once per week	Excellent
36-45	5	Cyst	4; then tapered in next month two times a month.	Excellent
46-55	15	Periodontal abscess	4	Excellent

Table 1. Shows the details of the patients treated with DMS and their outcome.

Serial evaluations showed remarkable outcome and the irrigation varied as per the patient's lesion and its severity. Oral hygiene was one of the most important factor and a priority in treating these lesions.

DISCUSSION

Infections are associated with the usual symptoms but if they are related to a tooth they are encased inside a closed structure thereby exaggerating all those symptoms resulting in severe intolerable pain. In all kinds of infections of any origin, antibiotics are prescribed systemically. These antibiotics reach a peak level and start combating all manifestations of the disease. In case of a tooth these antibiotics play a major role too but to relieve the pressure build up inside the tooth we adopt RCT for drainage and use irrigating solutions. The infection in the tooth leads to lesions which can be seen as radiolucency of various diameter on x-rays. The radiolucency in the perio-endo lesions are difficult to treat due to inaccessible position e.g the furcation, aggregate of microbes. Seven bacterial species can be found in oral cavity leading to various perio-endo lesions and destruction of tissue. Collagenase and gelatinase are matrix metalloproteinases (MMPS) which play an important role in tissue destruction. During all these years, surgical procedures are being done on the lesions of various types. They are invasive procedures done every now and then It takes time for bone regeneration and epithelialization of wounds, but when we think of non-surgical techniques they seem difficult and time consuming. In other words we can opt for these techniques only if the patients are co-operative and we have profound knowledge of the procedures we are doing. The best achievement is when both the techniques provide the same results non-invasively without scarring or suturing. In both these techniques we use irrigations. During surgery we use normal saline and while opting for non-surgical techniques we opt for RCT and use various irrigating solutions. Since 1920 Sodium hypochlorite has been used and is one of the most frequently used endo-irrigation to treat the lesions. Its bactericidal and proteolytic efficacy is quite known but NaOCL causes haemolysis and necrosis if injected beyond peri-apical region[22].

Many studies in the literature indicate that combined periodontal and endodontic therapy is essential for successful healing of a periodontal-endodontic lesion. It has been said that either endodontic or periodontic treatment alone would not lead to a satisfactory prognosis, if both disease entities are present and that both must be considered together. Hiatt and Amen[23] claimed that persistent periodontal disease may clear up only after definitive periodontal therapy is followed by successful endodontic treatment. Simring and Goldberg[1] postulated that endodontic therapy is indicated in the treatment of terminal periodontal disease that does not respond to periodontal therapy. The localized nature of the periodontal infection and the easy access of the teeth, has prompted the development of delivery systems which release the antimicrobial agent directly into the periodontal pocket. The first of these delivery systems that is commercially available is a tetracycline impregnated cord which can be wrapped around the tooth below gingival margin. The cord releases over 100 µg of tetracycline per ml of gingival crevicular fluid during the entire period that it is *in situ*[24]. In this manner, patient compliance is assured and the plaque microbes are constantly exposed to therapeutic levels of the agent. The double-blind metronidazole studies indicate that EOP (Early onset periodontitis) and AP (Adult periodontitis) respond to treatment as if they were anaerobic infections and would seem to presage the more frequent usage of anti-anaerobic agents, such as metronidazole[25]. In the future treatment of periodontal disease, further developments of delivery systems which release antimicrobials directly into the periodontal pocket should assure that most periodontal infections will be medically managed[26].

Directly infusing antibiotics into the infected area maintains a high local concentration level while minimizing systemic toxicity. Work has been done no doubt in orthopedic implant surgery, however it also suggests that this method avoids the potential for growth of antibiotic resistant strains of bacteria. Locally applied antibiotics concentration is 1000 times higher and causes major reduction in infection, therefore it can be applied in the peri-apical lesions too[27].

The local drug delivery devices, which have been approved for the treatment of periodontal diseases, are Perio chip®, Jerusalem, Israel (2.5 mg chlorhexidine gluconate, thin solid chip system), Atridox®,(Atridox is a FDA approved 10% doxycycline in 1 a gel system using a syringeFort) Collins, Colo, USA (10% doxycycline hyclate, flowable polymer syringe), Actisite®, Palo Alto CA, USA (25% tetracycline fibers) and Arestin®, Warminster, Pennsylvania (1 mg minocycline hydrochloride, microspheres syringe)[28]. Metronidazole: Elyzol is a topical medication containing an oil-based metronidazole 25% dental gel , applied in viscous 1 consistency to the pocket[29]. USFDA has approved these drugs and are being used individually but if these drugs are combined their efficacy becomes better and that is what has been attained with DMS irrigation.

CONCLUSION

We recommend that DMS can be used as an ideal irrigation in the treatment of endo-perio lesions. We know that at a junction the two maladies (endo or perio) lead to the same sequence of destruction. If endodontically we acquire a hermetic seal in the canals, the elimination of microbes, epithelialization of tissues and healing of lesions can be easily attained by the combination of anti-microbial agents like DMS. However, the delivery system should be advanced and the irrigation should be made in the refined and modern manner.

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