Bubble Dynamics : Ultrasound Therapeutic Delivery And Monitoring (Sonoporation) A Review

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Abstract: Regularly a diagnostic aid, ultrasound, the emerging hopeful tool for administering drug to the patient in periodontal diseases and for the treatment of genetic disease. The ultrasonography releases bio-effects creating in production of heat to the tissues, force causes on the layers of the tissue, and formation of cavity in the organ, that has been useful for therapeutic purposes. Ultrasound cavitation, becomes better by sending micro bubbles. Many new drug delivery systems have come for intrapocket delivery of drugs i.e., injectable drug delivery systems, strips and compacts, Nano drug delivery systems, gene delivery using bubble liposomes for periodontal therapy. Sonoporation is a new advanced technique to release the drug from drug delivery systems in treating periodontal diseases.

Keywords: Ultrasound, Sonoporation, Gene therapy, Drug delivery.

I. INTRODUCTION

Conventional drug delivery systems, such as systemic administration via intravenous injection or oral administration, are often not enough for delivery of therapeutic compounds such as proteins and genes. A recent development in delivery systems for therapeutic compounds is ultrasound (US)-aided intracellular delivery(1). Ultrasound is a mechanical wave power produced as swing back pressure and with frequency more than 20 kHz. Ultrasonography produces bio-effects occurin production of heat in the tissues, shearing force and cavitation. The action of forming and rapid breakdown of gas bubbles are used for production of drugs and genes inside the cell(2). The determined use of Ultrasonography utilizes intensity between 5 and 500 W/cm². The surgical application uses intensity levels greater than 300 W/cm². The intensity used for the ultrasound therapeutic method is between 1 and 3 W/cm²(3). The side effect of ultrasound are produced from heat and non-heat properties(4). At low intensity it is used for non thermal property (5).

II. SONOPORATION

It is defined as intercourse of ultrasound with inaudible sound wave contrast agent that process of making the cell membrane for short period to time that allow to take different materials like strand of a chromosome and medications(6). It is used for producing remedial agents including gene products, amino acids and chemotherapeutic agents into the cell.

III. SONOPORATOR

Sonoporation is performed with a ultrasound device named sonoporator. Ultrasound sound waves play a vital role in sonoporation. The origin of them is a electroacoustic transducer which is filled with barium titanium. In the piezoelectric crystal the waves are produced by heat impulse, allowing the conversion of electrical energy into mechanical energy(7).

IV. MECHANISM

The machine produces us radiation form micro particles suspension. Cavitation bubbles are produced by ultrasound radiation, whereas these breakdown, transfers their power to the epidermis that forming pores in the dermis. So, this method engage the non thermal cavitation so that to increase production of bigger molecules, facilitates transmembrane carry of drugs into the cell(8).

- Advantages of Sonoporation
  1.) Drug perforation over diffusion.
  2.) Can have good control on transdermal penetration.
  3.) ULTS is for drug delivery.
  4.) Low risk of introducing infection to the skin.
  5.) Low pain and no anxiety to patient.
  6.) Greater patient satisfaction.
  7.) Not sensitizing immunologically.
  8.) Systemic absorption is of less risk than injection.

- Disadvantages
  1.) Time-taking to the operator.
  2.) Minor burning, itching, irritation will be observed.
  3.) Outermost layer of epidermis should be in contact for best drug penetration.

V. APPLICATIONS: GENE DELIVERY

It is a process in where the active genes are attain to substitute a faulty gene that the aim of the wanted cells, that to be changed, is obtained. “Hereditary vaccine” in opposition to influenza and malaria(10).
Its applications as follows:
(a). Osteoinduction: In bone healing bone morphogenic protein is involved and helps in regeneration. For Bonemorphogenic protein gene transfer is used.
(b). Initiation of dental follicle pro-cursor cells differentiation into odontoblasts: The main aim is to conserve teeth and extend the duration and life (Misako Nakashima (2003), observed that genetic therapy has the ability to succeed in forming reparative dentine (11).

**Local Drug Administration**
The minimally-invasive platform for targeted delivery of pharmaceuticals is by local delivery of therapeutic molecules by ultrasound.(12). Limiting toxicity for healthy tissues a required amount of drug concentration at the diseased site is achieved by local drug delivery(13). In this technique microbubbles are co-injected directly administered into the targeted superficial tissues(14).

**Tumor Cell Killing**
For cancer therapy, acute drug delivery system was given. The Iwanga et al(15). in 2007 in Japan studied in vitro and in vivo, the capability of Sonoporation regarding the growth interference of human gingival squamous carcinoma cells. In this study, a human gingival squamous carcinoma cell was used, Ca9-22. Sonoporation is for delivering bleomycin and transfect a cdtB in vitro and in vivo. The results showed that tumors nearly disappeared in Ca9-22 cell-implanted treated with bleomycin or cdtB-expressing plasmid during the 4-weeks experimental period.

**Induction of Apoptosis**
It is a systematic programmed death of a cell. Ashush et al., and Ando et al., ended that subjection of cells to ultrasonic cavitation induced cell which causes cell breakdown and necrotic disintegration(16).Cancerous cells can be killed in the future by this process and other cells of benign growths before malignant change takes place or reduction in size of the growth before surgeries.

**Gene Transduction**
Gene transduction gives details about gene function. It is an undisturbed and present advanced one which transduces genes into mesenchymal cells without any proper injury to target tissues. So to study the molecular function of morphogenesis, Sonoporation is effective for gene transduction.

**Recurrent Aphthous Stomatitis**
The less intensify ultrasound produces a healing profit by increasing the healing by a change in cell membrane permeability, increased angiogenesis aggravation of fibroblasts, and change of bacteria and other microorganisms.

**Ultrasonic Therapy in Myofascial Pain**
Ultrasound is used to cure those patients who is suffering from MPDS which is impulsed at a frequency of 1 MHz, a pulse repetition rate of 120 Hz, and intensity of 0.75-2 W/cm for 3-5 min which was performed by Esposito et al. Washout pain mediators will help in pain relief by increased blood flow and changes in nerve conduction, which finally reduces inflammation and pain.

- **Ultrasonic Therapy for TMD Joint Dysfunction**
  For TMD disorders, ultrasonic therapy is not effective alone but effective when compared with other treatment modalities, i.e., muscle exercises, splint therapy, and heat application. Kropman et al. stated that there is no much difference in comparison of different surgical and physical therapies, which included TU for TMD dysfunction.

- **US Guided Lithotripsy of Salivary Calculi**
  It is treatment to the therapy of calculi. For extracorporeal shock wave for the sialolith of the parotid and submandibular gland, lithotripsy with a specially designed lithotripter is used.

- **US Therapy in Bone Healing and Osseointegration**
  Ultrasound may be helpful in facilitating the bone regeneration by low intensity that has been pulsed to increase the bone healing. Successful technique is distraction osteogenesis to gain bone and soft tissue. After assessing the bone formation by different methods. Low intensity pulsed US is used to accelerate bone healing indicating that US may be used in facilitating the bone regeneration.

**VI. CONCLUSION**
As in the advanced dentistry, this new technique with old Ultrasound is likely to serve as a new avathar in the field of diagnosis and therapeutic dentistry. As there are many advantages it could stand as the top of the recent advanced techniques as it requires only minimal equipment which would emerge new form of sound energy will revolutionize.

**REFERENCES**


[4]. Jyothirmai Koneru, Ravikiran Alaparthi1, Samatha Yalamanchili1, Sudhakara Reddy R. Therapeutic ultrasound - The healing sound and its applications in


[10]. Anthony Delalande, Spiros Kotopoulis, Michiel Postema, Patrick Midoux, Chantal Pichon. Sonoporation: Mechanistic insights and ongoing challenges for gene transfer. GENE -38471; No. of pages:9; 4C.

[11]. Misako Nakashima, PhD, DDS, and Akifumi Akamine, PhD, DDS. The Application of Tissue Engineering to Regeneration of Pulp and Dentin in Endodontics. JOE — Volume 31, Number


