Novel Bone Adhesives in Fracture Fixation & its Possible Significance in Midfacial Surgery – A Review

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Abstract:- One of the most frequent medical conditions requiring inpatient hospitalization is fractures. In order to maximize the possibility of the fracture surfaces to join and fuse, surgical treatment of fractures typically begins with a reduction of the fracture, which places the bone fragments in their original location and close proximity to one another. Then, they are either externally cast-stabilized or implanted with screws, plates, and wires, among other implants. Medical and surgical management techniques have advanced significantly as a result of the incredible improvement in technology. Recently, the use of bone adhesives/bone glue in the treatment of fractures has been suggested. The idea behind "bone adhesives" is to fix simple and comminuted fractures as well as secure orthopedic implants and devices like plates and screws. In this article, we will give an overview on existing bone adhesive and its types, conventional internal fixation, its disadvantages and how bone adhesives can possibly overcome the drawbacks of other fixation techniques.

Keywords:- *Fracture, Bone Adhesives, Bone Glue, Internal Fixation.*

I. INTRODUCTION

This Any injury to the face or jaw brought on by physical force, foreign objects, animal or human bites, or burns is referred to as maxillofacial trauma. [1] It is classified into injuries involving the lower, middle and upper thirds of the face. Motor vehicle collisions, interpersonal violence, falls, and sports-related incidents are the most frequent causes of face fractures. Their relative frequency varies geographically. The most significant mechanism on a global scale is motor vehicle collision. [2] The most prevalent fractures are nasal, followed by dentoalveolar, mandibular, midface, and orbital floor fractures, and finally frontal sinus fractures. [3]

Management of such injuries, which can range from simple fracture to severe facial communition, can be quite difficult. The presence of the upper airway and the close proximity to the cranial and cervical structures that may be concurrently implicated aggravate injuries to this highly vascular zone. It can be life threatening and cause long term complications including damage to vital sensory structures. [4] Through a complex interplay between the facial skeleton and its soft tissue envelope, the surgical treatment of cranio-maxillofacial injuries entails the restoration of both form and function. [5] Management is done by following the sequence: Reduction, fixation/immobilization, and preventing infection. Widely used method of fixation for managing maxillofacial fractures is internal fixation which involves fixation of bone fragments in their anatomical location with the help of plated and associated screws until bone healing is accomplished. [6] Though it is the conventional technique followed, it still has disadvantages like plate fractures, patient discomfort and is also technique sensitive. With the tremendous technological advancement, medical and surgical management strategies has been greatly evolved. The use of bone adhesives has been proposed for last few years in management of fractures. In terms of not having produced adhesives that meet the various requirements of a successful product, this is still in its relatively early phases. Although there are many bone cements and bone void fillers available, none of them make the claim to have adhesive characteristics. PMMA bone cement is likely the most popular of these items. [7]

The aim of this article is to review on the current state of the art of bone adhesives in order to understand how close to surgical fixation of facial fractures, bone adhesive might be and in comparison with the conventional technique.

II. WHAT IS INTERNAL FIXATION ?

Internal fixation is the most crucial form of treatment for maxillofacial fractures in order to regain form and function. The basic principles for internal fixation is formulated by AO in 1958. [6]

Anatomic reduction: Reduction and fixation of fracture to regain normal anatomy

Stable fixation: Depending on the type of Fracture fixation with relative or absolute stability may be necessary.

Preservation of blood supply: By careful reduction, handling and preservation of vascularity of the bone and soft tissues

Early and active mobilization: early and safe mobilization for the purpose of treating the injured part

Internal fixation employs usage of systems like trans osseous wiring, compression plates, non-compression miniplate, lag screws, reconstruction plates etc.,

III. DISADVANTAGES OF CURRENT INTERNAL FIXATION

Before Internal rigid fixation techniques have a number of potential side effects, including as infection, nonunion, visible or painful hardware, and the frequently ignored problem of misalignment of the fracture pieces during reduction. Plate palpability was shown to be the most frequent cause of hardware removal at a major university centre (University of Michigan Medical Center) in a study by J S Orringer et al, followed by discomfort, hardware loosening, and plate exposure. [8] Greater exposure and soft tissue manipulation were needed to avoid insufficient or inappropriate fracture reduction and to guarantee proper plate fixation. Thereafter, concerns about potential rises in infection rates emerged. [9]

Miniplates can have negative effects that necessitate removal, including as plate prominence and palpability, infection, plate migration, exposure, and temperature intolerance. The most frequent reasons for craniofacial plate removal of the midface are prominence and discomfort, while infection and exposure are the most frequent reasons for plate removal linked with maxillo-mandibular fracture patterns. [10]

In their collection of cases involving severe craniofacial injuries, Francel et al [11] reported a 7% infection rate, and O'Sullivan [12] et al reported a 4% infection incidence. Ewers and Harle reported infection rates of 1.1% and osteomyelitis of 2.2% in a series of 590 face fractures. [13] In their series of 74 patients who underwent elective midface craniofacial surgery, traumatic craniofacial injury treatment, and cranial vault reconstruction, Beals and Munro reported no infections. [14]

The microplate systems were created as a modification of current systems created for maxillary and mandibular fracture treatment because thin, brittle bones require accurate three-dimensional orientation. Schortinghuis et al [15] reported a clinical series of 44 patients who sustained craniofacial trauma repaired by open reduction and internal fixation with microplates. No plate-related infections, palpability, or malunion were reported. However, three patients required reoperation for complaints of pain. Only one patient's complaints were attributed to the microsystem as a loosened screw was noted, whereas the other two patients had persistent pain after plate removal. From 0% to 2% of patients who underwent microplate fixation reported having pain among the articles reviewed by Böker KO et al. [16]

IV. BONE ADHESIVES & ITS CHARACTERISTICS

The creation of bone adhesives that can bind bone surfaces together, bear stresses at fracture gaps, and permit biological components of bone healing to take place while gradually degrading to make way for bone ingrowth has attracted a lot of interest. [17] Bone adhesive is defined as, synthetic, self-curing organic or inorganic material used to fill up a cavity or to create a mechanical fixation (IUPAC). In the 1940s, PMMA was utilized for the first time in a clinical setting in plastic surgery to repair gaps in the skull. [18]

A consistent areal distribution of the physical forces could be achieved by the adhesive acting across the entire surface from a mechanical standpoint. It could also address some of the drawbacks of metallic implants, which are related to their relative high stiffness and rigidity as compared to bone material (e.g., physical stress and tissue damage in the area of bone fracture repair). [16]

Broken fragments might theoretically be put together quickly and directly, as well as the adhesive could eventually be replaced by the regrowing bone. [19] Because of this, the need for increased healthcare system expenses and secondary interventions would both be avoided. Since the production capacity and material costs are mostly unknown, it is difficult to determine the expenses of such a bone adhesive system at this time. And also less complications such as infections, problems with wound healing, thrombosis, embolisms, allergies, and intolerances might be anticipated as a result of shorter surgical procedures and the use of materials with better potential for designing biocompatibility. [16]

The following are the characteristics for a successful bone adhesive, [20]

- High degree of adherence to bone, frequently with impurities such lipids and proteins
- Bonds to moist surfaces and maintains binding strength in a humid environment.
- Mechanical resistance to tension, compression, and shear.
- Simple and simple to produce and use in operating room circumstances.
- Adequate working time and rapid setting time
- Biocompatible & non toxic
- Sterilizable
- Allow adequate fracture healing
- Cost effective
- Adequate shelf life

V. TYPES OF BONE ADHESIVES

Traditional bone cements might be made of synthetic or biologically inspired substances. Researchers used dental knowledge to employ methacrylate resins in bone surgery in the 1940s and 1950s. The primary study areas on bone adhesives are under the categories of synthetic, biomimetic, and biobased approaches: [16]

- **Synthetic adhesives**: The most often investigated type of bone adhesives are fully synthetic formulations, such as polyacrylic acid [19,21,22] or polyester [23], because of their capacity to customize adhesive properties, cross-linking intensity, functional groups, and viscosity. Recent investigations have shown that polyurethanes [24], which have long been regarded as biocompatible, function quite well. Methacrylates and cyanoacrylates are believed to have a strong potential for attaching to bone because they are members of the adhesive class. Cyanoacrylates are very promising for joining bones because of their characteristics and also they have been further developed to obtain micro tensile and shear bond strengths between 1 and 2 MPa; the latter for N-butyl cyanoacrylate is much higher than a plate and screw standard. [25, 26] Yet, the mechanical requirements have not been met by synthetic adhesives and also has insufficient biocompatibility. [27] Biomimetic approaches have been suggested as a solution to these problems.

- **Biomimetic adhesives:** The foundation of TetraniteTM is O-phospho-L-serine, which is a constituent of numerous proteins found in natural secretions. It is bioresorbable, has an immediate adhesive strength, satisfies practically all criteria for a bone adhesive, and is presently undergoing FDA approval. [28, 29]

Pajari-Palmer [30] and colleagues described a "Novel Class Injectable Bioceramics" made similarly to TetraniteTM in association with the phosphoserine-based technique. However, α-Tricalciumphosphate and phosphoserine were used in place of tetracalciumphosphate, and they were able to cure in moist environments and demonstrated bond strengths that were up to 40 times stronger than those of commercial cyanoacrylates (0.1 MPa) and 100 times stronger than surgical fibrin adhesives (0.04 MPa). A brand-new mussel adhesive has been created. Using an enzyme from Methanocaldococcus jannaschii, pre-modified intestinal bacteria were used to create this. [31] Malkoch [32] and his group's work on allyl, methacrylamide, and thiol groups is another example of bio-inspired methods. About 0.3 MPa was the shear strength of the created adhesive.

- **Biobased adhesives:** In rabbits, a proteinogenic, autologous fibrin adhesive was effectively evaluated as a K-wire substitute. [33] In addition to proteinogenic adhesives, sugar-based ingredients can also be used to make bone adhesives. Studies on two-component chitosan and dextran bone adhesive hydrogels provided evidence to support this. [34, 35] Another instance of biobased approaches is the incorporation of calcium carbonate and hydroxyapatite in biocomposites that will be utilized as chitosan-based bone adhesives. [36] The most promising results were seen in a formulation with 4% calcium carbonate and hydroxyapatite, 2% chitosan, with strong adherence to the bone surface (0.27 MPa) and cohesion failure, that is, failure in the adhesive substance rather than at the surface-adhesive interface. [36]

VI. BONE ADHESIVES IN MIDFACIAL SURGERY

Use of adhesive systems for internal fixation were advocated in various in vitro and in vivo studies in last few years and concluded that they can be useful for bone bonding. [37, 38, 39, 40, 41]

P Maurer et al [37] performed a study Using two distinct adhesive methods (Clearfil New Bond and Histoacryl) and compared the tensile bond strengths reached between composite and bone and between bone and bone.

Amanrante et al. [38] investigated the viability of obtaining bone fixation of the upper face skeleton with n-butyl-2-cyanoacrylate and contrasted the fixation achieved with this adhesive to that achieved with plates and screws in an animal model.

Perry et al. [39] conducted a study to determine whether adhesive techniques could play a role in bone fixation in specific cases. They compared the current "Champy" miniplate system to bonded stainless steel using cyanoacrylate or dental composite cement in vitro, and found that the Champy system failed at a force (N) that was significantly higher than the adhesives.

M. A. Shermack et al [40] carried out a study to see if the healing and strength offered by plate and screw fixation could be achieved by cyanoacrylate fixation of the bone flap in a rabbit craniotomy model.

Fibrin glue (FG), also known as fibrin sealant, has been utilised in a variety of orthopaedic procedures to promote osteogenesis in human maxillary and mandibular bone, to fix osteochondral fractures, to fix osteochondral fragments, and to fix bone chips during spinal surgery. [42] Heiss et al. [44] described a recently created alkylene bis (dilactoyl)-methacrylate as a bone adhesive with some similarities to polymethylmethacrylate (PMMA), which has been widely utilised in dentistry [43] and orthopaedic surgery for anchoring prosthesis. PMMA is the most affordable, widely available, and biocompatible of these polymers, enabling instant fixation to cancellous bone (which is not usually the case for the other materials). PMMA cement added to screws results in improved primary stability. [45, 46]

However not enough data is available for its application in the maxillofacial region. Endres, Kira et al. [47] described an innovative method using bone adhesive to attach thin cortical bone pieces to osteosynthesis plates. The plate is secured to thick cortical bone structures with standard screws, and adjacent or delicate bone pieces are connected to the plate with bone cement through the screw holes in the plate.

For the clinical application of adhesively fixing osteosynthesis plates in midfacial surgery, a modified PMMA bone cement was developed by adding a photoinitiator to the PMMA powder component, which can be light-cured. Unlike typical PMMA bone cements, which can take up to 15 minutes to polymerize, it enables a surgeon to control the precise moment at which the polymerization starts. This saves the surgeon and his team valuable time when adhesively fixing an osteosynthesis plate during midfacial surgery. [47]

VII. BONE BONDING AGENT

Bone bonding agents, which are comparable in composition to dentin bonding agents that have been in clinical use for many years, may have the ability to resolve the problem of the bonding partners' incompatible wetting qualities. [41, 48, 49, 50] According to various investigations, using dentin adhesives proved to create a stronger bond strength to bone than that produced with the cyanoacrylate glue because the dentin bonding agents are amphiphilic in nature and can bond with both hydrophilic dentin and hydrophobic composites. [37,38,39,40]

ISSN No:-2456-2165

Monomers with hydrophilic and hydrophobic characteristics dominate the composition of amphiphilic bone bonding agents. It contains hydrophilic functional groups like hydroxy groups R-OH and carboxy groups R-COOH, where R is a stand-in for the organic remainder, as well as hydrophobic monomers like MMA molecules. The bone bonding agent will penetrate the surface of the bone after application, creating a hybrid layer. In order to maximize the wetting of hydrophilic bone, the hydrophilic monomers in the bone bonding agent are used. [47] (Fig. 1)

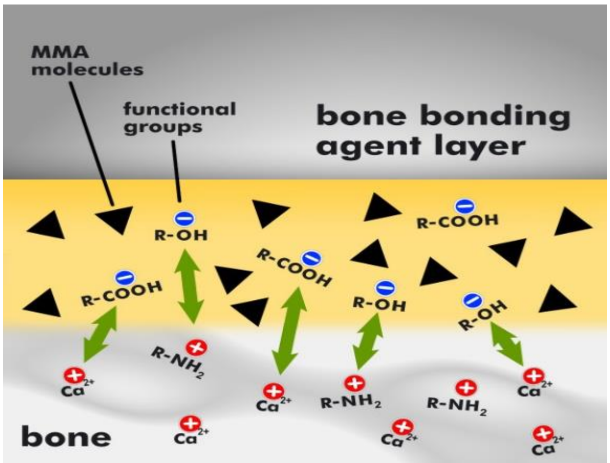

Fig. 1. Chemical bonding of the bone bonding agent to the bone. [47]

VIII. POSSIBLE CLINICAL SIGNIFICANCE OF BONE ADHESIVES

Based on several studies, it is apparent that there is a greater possibility of applying bone adhesives in future clinical practice. If applied in practice, the following are the possible clinical significance of bone adhesives over conventional fixation techniques. [16]

- Uniform areal distribution of physical forces
- Overcome disadvantages of metallic implants like physical stress and tissue damage
- Theoretically, adhesive uniting bone fragments could be gradually replaced by the regrowing bone
- Avoids the necessity for secondary interventions
- Reduced operating time
- Lesser possibility for infection, wound healing disorders and intolerances

IX. CHALLENGES

The surgical treatment for fractures would be revolutionized with the usage if bone adhesives for individualized bone restoration and repair. The major challenges for the adhesives to be faced are inadequate biocompatibility, adhesive strength, fixation techniques. So far there hasn't been a pure bone adhesive that is commercially accessible for use. The indicated mechanical criteria of 40 – 150 MPa have also not been met by synthetic adhesives [51]. Parallel to the advancement of these synthetic adhesives interest in biomimetic adhesives have grown. While biomimetic adhesives such as fibrin glues, mussel adhesive protein have been found to have high biocompatibility and biodegradability, they have proven to have week mechanical strength and little bone attachment. [52 53, 54]

X. CONCLUSION

Bone adhesive is a futuristic and researched possible treatment modality that would revolutionize the current status of the bone repair and restoration. Even with numerous studies to its name there is no adhesive that delivers all the desirable properties in a single commercial available product. The three main requirement of bone adhesive i.e biocompatibility, biodegradability and bond strength is a challenging factor that is one of the major cause for the failure for the adaptation of bone adhesive alone with the complex bone environment. In this review we have concluded that though there are multiple researches and studies conducted in the adaptation and production of bone adhesives they are mostly in vivo and in vitro studies. Bone adhesives in orthopedic fractures have less clinical studies to its name and even lesser studies when pertaining to midfacial fractures. Though the vision of a adhesive that could fix fractures remain attractive to surgeons it is a need that would remain unmet as it seems unlikely that conventional osteosynthesis would be replaced any time soon.

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