# Use of Polyethylene Glycol Ester and Trilysine Amine Solution in the Closure of Anterior Skull Base Defects

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*The surgical approach of the skull base pathology is in a state of constant development. The advancement of the ablative techniques forced the development in the field of reconstructive surgery of the skull base as well. The goal of the reconstructive surgery of the postablative defect of the skull base is to create a stable, watertight limit between the endocranian and the sinusal cavities. New reconstructive materials and adhesives were developed. The purpose of this article is to critically analyze the use of the mixture between the polyethylene glycol ester and trilysine amine solution as a sealant and adhesive in the reconstructive surgery of the skull base.*

*Keywords: polyethylene glycol ester, trilysine amine solution, skull base, reconstructive surgery*

In the last 10 years, the surgery of the anterior skull base pathology has been a surgical field in a state of constant development(1). The surgical technologies, reconstructive materials and surgical adhesives were continuously developed(1). New surgical techniques were used in this surgical field. The minimal invasive endoscopic surgical techniques are in a state of constant expansion. The trend is for the endoscopic approach to become the golden standard in the surgery of the skull base pathology. In the author's opinion, for the malignant pathology that involves the skull base, the endoscopic techniques seem to have limited indication and the combined approach (external and endoscopic approach) is still the standard.

The endocranian and the sinusal cavities are two distinct compartments that have to be clearly and solidly, water tight separated after the removal of the pathological masses (2). In this manner, complications, such as meningitis or herniation of the cerebral tissue in the sinusal cavities, are avoided (3).

The skull base defects can be divided in bony defects without dural defect and no CSF leak and bony defects with dural defect and CSF leak.

The goal of the reconstructive step of the surgery is to repair the dura mater defect, to stop the CSF leak and to repair the bony defect as well (4).

The goal of this study is to analyze the efficacy of the polyethylene glycol ester and trilysine amine solution in obtaining a water tight separation between the endocranian and the sinusal cavities in the surgical reconstruction of the skull base.

Polyethylene glycol (PEG) is a biocompatible, non-toxic, soluble component.

The trilysine amine solution is a small amine molecule with reactive linkage that in contact with the PEG will combine almost instantaneously and will form an absorbable hydrogel.

The component will adhere to the tissue cervices providing an excellent tissue adherence (5). The commercial product that contains the combination between polyethylene glycol ester and trilysine amine solution has a blue color that guides the surgeon in the surgical field.

The cross linking molecule of PEG and trilysine amine solution is gradually degraded in an uniform fashion, just like the absorbable sutures. Renal absorption and secretion of the degraded molecule is done gradually.

## Experimental part

*Materials and methods*

We have included in our study 14 patients with skull base defects. In the reconstructive step of the surgery we used the multilayer technique to repair the defect. Both natural and synthetic materials were used as layers of the reconstruction procedure. The surgical approach was both purely endoscopic or a combined approach.

We studied and documented the healing process of the skull base defect, both endoscopically and imagistically.

In the skull base bony defect without CSF leak we used both the underlay and the overlay repairing techniques.

| | Number | Overlay | Underlay |
|---|---|---|---|
| Frontal acute sinusitis | 2 | X | X |
| Fungus Sphenoidal sinusitis | 1 | X | |
| During ESS surgery in nasal polyposis | 3 | XX | X |
| Nasosinusal malignant tumors | 2 | X | X |

**Table 1**
ETIOLOGY OF THE SKULL BASE DEFECT WITHOUT CSF LEAK AND THE RECONSTRUCTIVE TECHNIQUE USED

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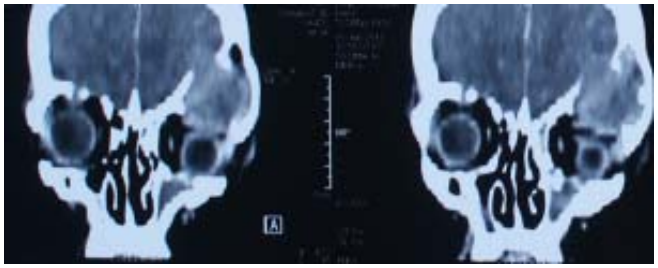

Fig. 1. Acute frontal sinusitis CT exam showing the destruction of the posterior wall of the left frontal sinus

Fig. 2. Bony defect of the skull base with denuded dura mater.

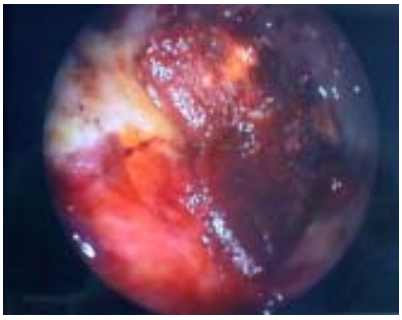

Fig. 3. Overlay gelaspone layer after an underlay layer of lyophilised dura

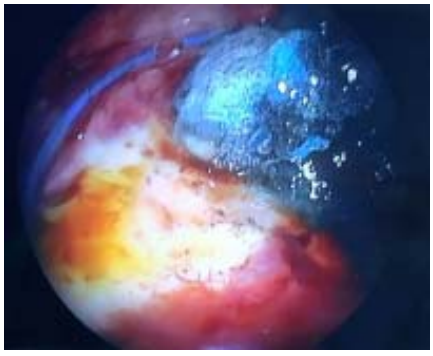

Fig. 4. Polyethylene glycol ester and trilysine amine mixture sealing the defect

| | Number | Overlay | Underlay |
|---|---|---|---|
| Persistence of Sternberg canal | 1 | X | |
| During ESS surgery in nasal polyposis | 2 | | XX |
| Nasosinusal malignant tumors | 3 | X | XX |

**Table 2**
ETIOLOGY OF THE SKULL BASE DEFECTS WITH CSF LEAKS AND THE RECONSTRUCTIVE TECHNIQUES USED

For the frontal acute sinusitis (fig. 1) that eroded the posterior bony wall of the frontal sinus we used a multilayer reconstructive technique, with an overlay placement of the grafts in one case, and an underlay placement for the other. The layers consisted of Gelaspone, lyophilized dura, nasal cartilage or bone, covered with polyethylene glycol ester and trilysine amine solution .

In one case of fungus sphenoidal sinusitis, where the posteroinferior bone of the sphenoid sinus was eroded, we used an overlay lyophilized dura glued with polyethylene glycol ester and trilysine amine solution.

In three cases of invasive recurrent nasal polyposis we encountered bony defects of the skull base. We reconstructed the defect in a overlay manner in two cases and in one case in a underlay manner, that were afterward glued with polyethylene glycol ester and trilysine amine solution. (figs. 2-4).

We also used polyethylene glycol ester and trilysine amine solution in the reconstruction of the skull base bony defects in the surgery of the nasosinusal malignant tumors that involve the skull base (6).

For the defects at the level of the skull base with CSF leaks we used the polyethylene glycol ester and trilysine amine solution as adhesive and sealant in one case of Sternberg canal persistence (overlay surgical multilayer reconstruction), two cases of skull base defects with CSF leaks encountered during invasive recurrent nasal polyposis surgery (underlay surgical multilayer) and three cases of nasosinusal malignant tumors (7) (1 case with overlay and 2 cases with underlay multilayer surgical reconstruction).

We did not use any lumbar drainage after the surgery that was performed for the closure of the skull base defects and the CSF leaks.

Polyethylene glycol ester and trilysine amine solution is available as a commercial product in two separated syringes. (1a,1b and 1c) (fig. 5). The surgeon has to mount the assemble that holds both syringes (1a and 1c) and provides the ability to apply and mix both substances over the skull base defect. The first step is to inject the substance from the 1a syringe in the 1b recipient. Then you shake the 1b recipient. The obtained mixture is put back in the 1a syringe. The second step is to mount the two syringes (1a and 1c) together using the surgical assemble (1d, 1g, 1f , 1e). The surgical assemble will provide the surgeon the ability to mix and apply simultaneously both the Polyethylene glycol ester and the trilysine amine solution over the defect. The component has to be applied quickly because the mixture will turn into gel in approximately 3 seconds.

The mixture between Polyethylene glycol ester and trilysine amine solution will be absorbed gradually during the next 4-8 weeks. PEG will be cleared from the body through the kidneys.

All patients were monitored endoscopically and imagistically. The endoscopic examination was performed every 2 days in the first 3 weeks after surgery, then once a week for 8 weeks after surgery. The imagistic computer tomography examination was performed 3 and 6 weeks after surgery. Additionally, for the malignant sinonasal tumors, we performed in the first year an endoscopic examination every two months and the imagistic examination was recommended once a year afterwards.

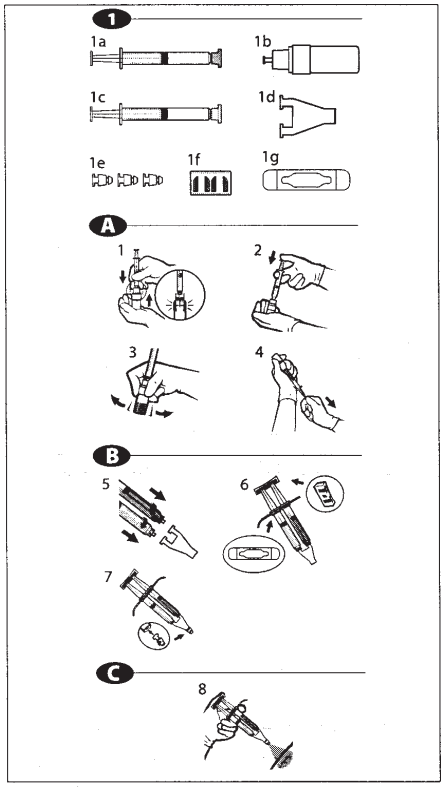

Fig. 5. Polyethylene glycol ester and trilysine amine solution surgical assemble

## Results and discussions

We have never encountered a secondary CSF leak after using polyethylene glycol ester and trilysine amine solution mixture, even for the patients that underwent early radiotherapy (1 month after surgery).

The qualities of the component are: strong tissue adherence, high cohesive strength and elasticity, the abbility to withstand elevated CSF pressures and to prevent CSF leaks.

The unwanted material can be resected and removed if it blocks the natural sinusal ostium and/or the choana.

We never encountered any adverse events after using polyethylene glycol ester and trilysine amine mixture, but in the literature there are reported some adverse events that occur in less than 1% of the cases, such as: arrhythmia, bleeding, cerebral edema, the development of a pseudomeningocele, dermatologic events, dizziness, electrolyte imbalance, postoperative fever, headache, hydrocephalus, meningitis, neurological symptoms, stroke, urinary difficulty, wound inflammation. A direct link between these conditions and the use of Polyethylene glycol ester and trilysine amine solution mixture in the reconstructive surgery of the skull base was not demonstrated

Besides the adhesive quality of the Polyethylene glycol ester and trilysine amine solution mixture, we have to underline the sealant property of the component that provides water tight reconstruction even in the cases of CSF leaks with pressure. These qualities recommend the Polyethylene glycol ester and trilysine amine solution mixture as the best adhesive and the only sealant solution in the reconstructive surgery of the skull base.

## Conclusions

The most frequent indication for using polyethylene glycol ester and trilysine amine solution mixture is in the skull base defects with CSF leaks. We used this mixture in skull base defects without CSF leaks when we wanted to seal the endocranian cavity from the sinusal cavity. In those cases we consider that the sealant quality of the mixture will act as a barrier in front of the puss and germs from the sinusal cavity.

Because of the adhesive and sealant qualities, good tolerance and good wound healing process, easiness in applying the mixture, gradually dissolving and absorbing properties, we consider that the polyethylene glycol ester and trilysine amine solution is one of the best adhesive and sealant options available in the reconstructive surgery of the skull base.

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