COMPARING FIBRIN GLUE TO SUTURES FOR CONJUNCTIVAL CLOSURE IN PARS PLANA VITRECTOMY

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ABSTRACT

Purpose: To evaluate whether fibrin glue causes less postoperative pain, discomfort and work inaptitude in conjunctival closure following 20 gauge pars plana vitrectomy than sutures.
Design: Retrospective study
Methods: A questionnaire was sent in 2006 to 506 patients who underwent 20 gauge pars plana vitrectomy in 2004 at the University Hospital, Leuven, Belgium. Patients were asked about their postoperative pain and discomfort of the eye and the duration of their work inaptitude.
Results: Our results showed a shorter duration of the eye being reddish (p-value 0,0471), discomfort of the eye (p-value 0,0376) and using an ointment (p-value 0,0105) in the glue group. The glue group used less ointment (p-value 0,0038) and independent workers had a shorter work inaptitude after receiving glue (p-value 0,0292). If patient had vitrectomy without cerclage, they had less pain on the first postoperative day when having received glue (p-value 0,0340)
Conclusions: Fibrin glue causes less postoperative pain, discomfort and work inaptitude for closure of conjunctival wounds in 20 gauge pars plana vitrectomy than sutures. Fibrin glue appears in our hands to be a better alternative to sutures for closure of conjunctival wounds in 20 gauge pars plana vitrectomy.

RÉSUMÉ

But: Évaluation de l'usage de colle de fibrine comparé à des sutures conjonctivales, par rapport à la douleur postopératoire, l'inconfort oculaire, et l'incapacité de travail, après vitrectomie à 20 gauge par pars plana.
Méthodes: En 2006, un questionnaire sur la douleur et l'inconfort oculaire postopératoire et la durée de l'incapacité de travail a été envoyé à 506 patients ayant subi une vitrectomie à 20 gauge par pars plana en 2004 dans le service d'ophtalmologie des Hôpitaux Universitaires de Louvain, Belgique. Les patients étaient divisés rétrospectivement en 2 groupes, selon la fermeture conjonctivale par colle de fibrine ou par sutures.
Résultats: Le groupe de fermeture conjonctivale par colle de fibrine a démontré une durée plus courte d'œil rouge (valeur de p 0,0471), d'inconfort oculaire (valeur de p 0,0376) et d'utilisation de pommade (valeur de p 0,0105). En plus, ce groupe a appliqué moins de pommade (valeur de p 0,0038) et ceux ayant un emploi indépendant ont eu une durée d'incapacité de travail plus courte (valeur de p 0,0292). Après une vitrectomie sans cerclage, la douleur postopératoire du premier jour dans le groupe de fermeture conjonctivale par colle de fibrine était inférieure à celle du groupe de fermeture par. sutures (valeur de p 0,0340).
Conclusion: La colle de fibrine entraîne une diminution de douleur et d'inconfort oculaire et un raccourcissement de la durée d'incapacité de travail par rapport aux sutures pour la fermeture conjonctivale après une vitrectomie à 20 gauge par pars plana.
A notre avis, la colle de fibrine semble être une alternative supérieure aux sutures quant à la fermeture conjonctivale après cette intervention.

KEY WORDS

Fibrin glue - Tissucol - conjunctival closure - vitrectomy - patient comfort - sickleave

MOTS-CLÉS

Colle de fibrine - Tissucol - fermeture conjonctivale - vitrectomie - confort du patient - incapacité de travail

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INTRODUCTION

Already since the early beginning of the twentieth century, people have been familiar with using human blood for hemostasis and wound-healing.
In 1909, surgeons reported the hemostatic properties of fibrin powder used in the surgical field. In the 1940s, combinations of fibrinogen and thrombin were first utilized. Most of the early attempts did not yield good results because the fibrinogen could not be prepared in a high concentration. Growing knowledge on the coagulation cascade and the fibrinolytic system led to the development of fibrin sealants in the 1970s. As the use of early fibrin sealants became more and more successful, this led to the industrial development of 'Tissucol Fibrin Sealant' (Baxter, Vienna, Austria), also commercialized in some countries as Tisseel (18).

Tissucol Fibrin Sealant consists of two components: one is fibrinogen mixed with factor XIII and aprotinin, the other is a thrombin-$CaCl_2$ solution. Both components are prepared from banked and well controlled human blood. Individual plasma donations undergo standard serological testing for HIV, HBV and HCV. In addition, plasma is tested by PCR for the presence of the viruses HIV, HAV, HBV, HCV and B19V. Additional margins of safety are provided by a dedicated virus inactivation step, vapor heating, where moisture-adjusted bulk product is heat treated for at least 10 hours at 60 °C. Other process steps further contribute to the overall virus clearance capacity of the manufacturing process. Tisseel has been used for the last 28 years in over 10 millions of applications in 50 countries worldwide and no single viral transmission related to the product has been reported as of today. By mixing the two components, natural fibrin formation occurs, consolidating the fibrin sealant and adhering to the site of application. The fibrin clot also stimulates the healing of the wound by allowing fibroblasts to proliferate in the clot and start repairing tissue.
This fibrin glue is a biological, nonirritating substance which is absorbed within a few days. Thrombin concentration can be varied to regulate the speed of coagulation: low thrombin concentrations (4 IU/ml) cause slow clotting while high thrombin concentrations (500 IU/ml) are beneficial where almost instantaneous clotting is desired. (6,7,18)

Tissucol Fibrin Sealant is being used in neurosurgery, plastic surgery, thoracic and abdominal surgery (5-7,14). In ocular surgery it is also being used successfully for sealing perforations in the lens capsule, adapting free skin transplant in lid surgery, repairing injured lid canaliculi, sealing postoperative bleb leaks in trabeculectomy and attaching conjunctival transplants in pterygium surgery (3,10,12,14 -17). Several reports of the application of fibrin glue in closing conjunctival wounds in ophthalmic surgery were published. These studies describe its use for wound closure in glaucoma surgery (1,15), strabismus surgery (2, 4,13) and following intraocular lens implantation (11,12). One study investigated 130 procedures with conjunctival wounds of which 20 pars plana vitrectomies (8). All of these studies concluded that fibrin glue offers a valuable or even better alternative to sutures, causing significantly less postoperative pain and discomfort and shortening surgery time (6-8, 10-12,17).
Several publications already showed that in contrast to glue the presence of sutures causes significantly more postoperative pain and postoperative foreign body sensation (7). This may be caused by an upregulated inflammatory process around the sutures during degradation. Whereas there is always some reparative inflammation following surgery, the glue components form pure human fibrin, which does not give rise to additional inflammation. The tensile strength of a clot formed with fibrin sealant was found to be approximately 17 kPA. The clotting procedure is also very fast, leading to firm adhesion after a few seconds. Thus wound closure by fibrin glue is fast and very efficient (6,7). In earlier studies no adverse effects of the applied fibrin glue could be detected (6,7,12). The excellent biocompatibility of this adhesive was expected, since Buschmann had used fibrin intraocularly to close traumatic defects of the lens capsule without any side effects due to the glue (3,8). None of the publications showed postoperative adverse or allergic reactions, bacterial infections, inflammation or delayed healing (6-8,10, 11,12,17).

With the surgical procedure 'pars plana vitrectomy', a variety of diseases of the posterior segment are treated nowadays. A 20 gauge vitrectomy starts with a conjunctival peritomy over 270 or 360 degrees. After the procedure is finished, closing of the conjunctival wounds can be performed by using either sutures or fibrin glue.

The present retrospective study is aimed at finding out whether fibrin glue causes less postoperative pain, discomfort and sickleave in conjunctival closure following pars plana vitrectomy than sutures.

METHODS

In this retrospective study we sent a questionnaire to 506 patients who underwent pars plana vitrectomy in 2004 at the University Hospital, Leuven, Belgium. If patients had vitrectomy of both eyes during this period, only one eye, chosen at random, was included. If patients had several vitrectomies during this period, only one vitrectomy, also chosen randomly, was included.
In 2004 there was a gradual transition from using sutures (n= 254) to using glue (n= 252) for the closing of conjunctival wounds in pars plana vitrectomy in our hospital.
A questionnaire was developed and sent to these patients in February 2006 and we received answers until April 2006.
Eventually data could be obtained for 142 patients managed with glue (glue group) and for 131 patients managed with sutures (sutures group).

The following questionnaire was sent to the patients:

1. What is your profession? Retired/ Housework/ Employee or Independent
2. During the first night after your operation, did you sleep less because of pain of your eye? Yes/No
3. During the first week after your operation, did you sleep less because of pain of your eye? Yes/No
4. During the first night after your operation, did you wake up at night because of pain of your eye? Yes/No
5. During the first week after your operation, did you wake up at night because of pain of your eye? Yes/No
6. During the first night after your operation, did you take any pain medication because of pain of your eye? Yes/No
7. During the first week after your operation, did you take any pain medication because of pain of your eye? Yes/No
8. Did you use any ointment for your eye after the operation because of pain or discomfort? Yes/No
9. If so, for how many weeks did you use this ointment?
10. For how many weeks after the operation did you feel a discomfort of the eye?
11. For how many weeks after the operation did your eye look reddish?
12. For how many weeks after the operation did you have a sickleave?

We compared the answers of both the sutures and the glue group.
For the answers we received to the questions about the first night after the operation (sleeping less, waking up or taking pain medication because of pain during the first night after the operation), both the glue group and sutures group were divided in two subcategories: patients who underwent vitrectomy with cerclage, and patients who underwent vitrectomy without cerclage.
For the answers we received to the questions about the duration of the sickleave, the glue group and sutures group were each divided in two subcategories: patients who are employees, and patients who are independent workers.

All pars plana vitrectomies carried out in 2004 were performed by the same surgeon (PS) using the 20 gauge technique. The vitrectomies were performed for several different indications including retinal detachment, macular hole and many others. Some were performed under general anesthesia while other were performed under local anesthesia. The procedure began with a conjunctival peritomy using curved scissors. Two radial incisions were made in the conjunctiva at three and nine o'clock, after which the conjunctiva was dissected from the sclera and a 270 or 360 degrees conjunctival limbal incision was made. After that the sclerotomies were

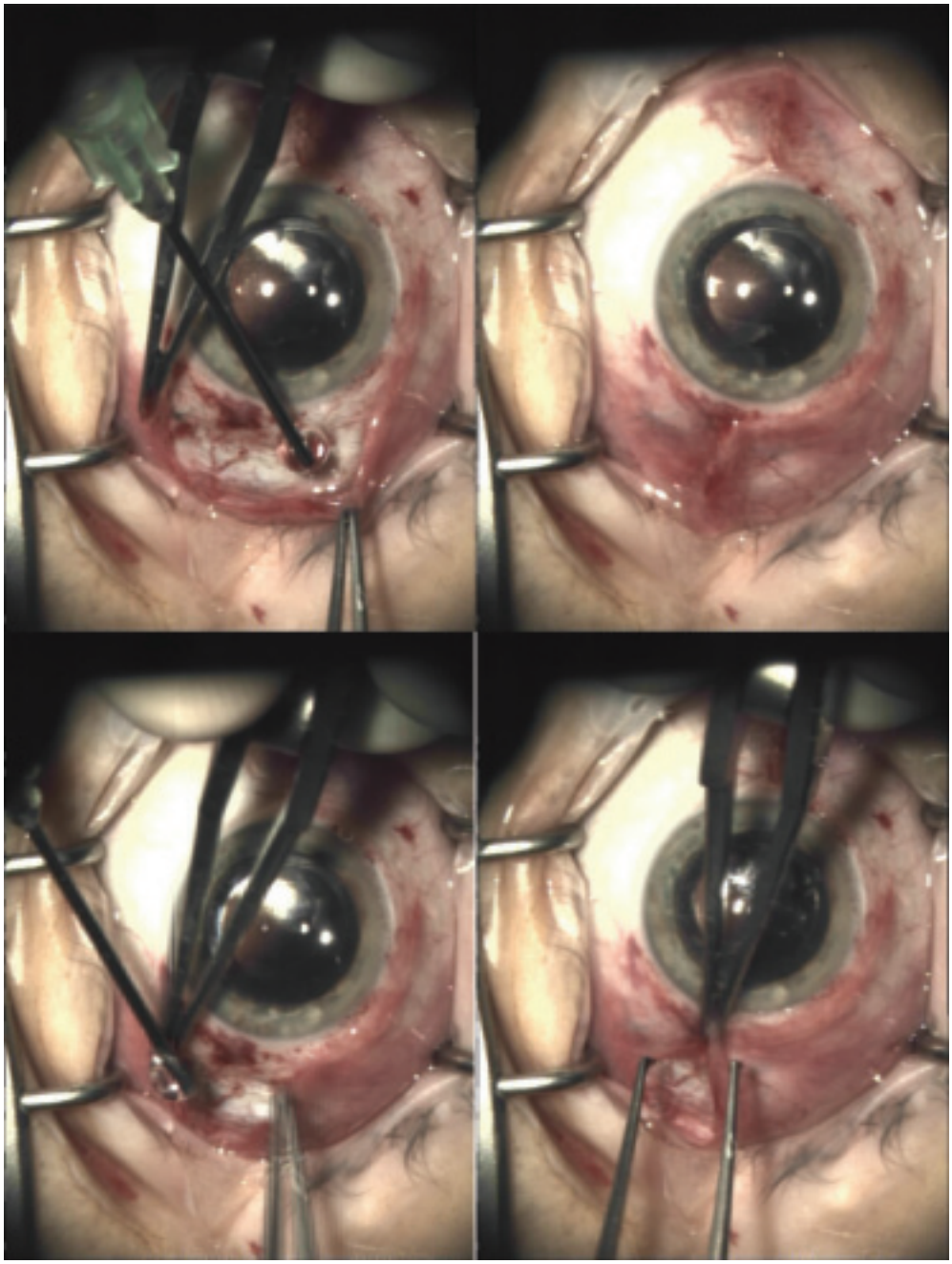

Figure 1: Technique of closure of the conjunctiva after vitrectomy using fibrin glue.

Top left: While lifting the conjunctiva from the sclera, a droplet of the first component of the fibrin glue is applied on the sclera.
Top right: a droplet of the second component is applied similarly.
Bottom left: Using two forceps, the conjuctiva is spread edge-to-edge on the sclera.
Bottom right: end result: the conjuncival wound is closed. No bare sclera is visible.

made and the vitrectomy was initiated. At the end of the procedure sclerotomies were sutured using Biosorb 7/0 (Alcon Laboratories, Fort Worth, TX). After that conjunctival incisions were closed using sutures or fibrin glue.
When the conjunctiva was sutured, the same Biosorb 7/0 was used. This resorbable suture starts to disintegrate after about two weeks. Each of the two incisions was closed by one or two sutures. The loose ends of the knot were cut to a length of a few millimeters.
For closing the two conjunctival incisions with glue we used Tissucol Duo 500 0,5 ml. This consists of two deep-frozen solutions in separate prefilled syringes: 0,5 ml of Tissucol solution (fibrinogen mixed with factor XIII and aprotinin) and 0,5 ml of Thrombin-500 solution (thrombin with $CaCl_2$). The Thrombin-500 solution contains a high concentration of thrombin (500 IU/ml) which allows quick clotting. After defrosting, simply by taking the syringes out of the freezer at the beginning of the surgery, the solutions were ready to use. The two components were applied sequentially using the two syringes separately (figure 1). With a few seconds interval, a drop of both components was instilled on the sclera. Next, the conjunctiva was held against the sclera using a forceps for 5 to 10 seconds. This procedure was carried out for both conjunctival radiary incisions. Excess glue was removed with a forceps.
After the vitrectomy procedure was finished, a subconjunctival injection with Betamethasone and Clindamycin was given to each patient. An Atropine ointment was applied to the eye and the eye was covered during the first night. The patients received six drops of Prednisolone Acetate and two drops of Atropine 1% a day in the operated eye for two weeks.
When there were no complications, patients stayed in the hospital for two nights after the vitrectomy. When people had too much pain, they received oral pain medication (Paracetamol). In case of discomfort of the eye or the sensation of a foreign body in the eye, an ointment with antibiotics and corticosteroids was given to the patient. People could use this ointment until they were discharged from the hospital or they could continue it at home. If examination showed an excess of glue during the first postoperative examination, this was removed by using a pincet at the slitlamp. If the loose ends of the suture seemed to cause the discomfort, these were shortened by using scissors.
After about two weeks, patients came for a check-up at the hospital. If the sutures still caused much discomfort at that time, they were removed. At that time the Atropin drops were stopped and the Prednisolone Acetate drops were tapered (four drops a day during one week, three drops a day during the next week, two drops a day during the next week, one drop a day during the following week and then stopped).

The obtained data were tested statistically using the Chi-Squared Test and the Wilcoxon Rank Sum Test.

RESULTS

Table 1 shows the number of patients who answered positive to the questions about sleeping less, waking up or taking pain medication because of pain during the first night after the operation.
In summary, we found that in the group who underwent vitrectomy without cerclage, the glue group used statistically significant less pain-medication on the first day after the operation ($p=0.0340$).

Table 2 shows the number of patients who positively answered to the questions about sleeping less, waking up or taking pain medication because of pain during the first week after the operation or about using an ointment during the postoperative period.
In summary, we found a statistically significant smaller amount of patients using an ointment during the postoperative period in the glue group ($p=0.0038$).

Table 3 shows for how many weeks the patients had sickleave.
For employees, we found no significant difference in sickleave between the glue and sutures group whereas for independent workers we found that patients who received glue had statistically significant less weeks of sickleave ($p=0.0292$).

Table 4 shows the amount of weeks of the eye being reddish, of discomfort of the eye and of using an ointment

Table 1: *Pain postoperative day one in patients with sutures vs fibrin glue after pars plana vitrectomy*

	Glue + Cerclage	*Sutures + Cerclage*	*P-value (Chi-Squared Test)*	*Glue - Cerclage*	*Sutures - Cerclage*	*P-value (Chi-Squared Test)*
Number of patients sleeping less because of pain during the first day postoperative/ total answers	10/40	12/29	*0.1496*	35/102	41/102	*0.3849*
Number of patients waking up because of pain during the first day postoperative/ total answers	10/40	8/29	*0.8092*	27/101	35/102	*0.2410*
Number of patients taking pain medication during the first day postoperative/ total answers	17/40	10/29	*0.5006*	37/101	51/99	*0.0340*

Table 2: *Patient comfort after surgery in patients with sutures vs fibrin glue after pars plana vitrectomy*

	Glue group	*Sutures Group*	*P-value (Chi-Squared Test)*
Number of patients sleeping less because of pain during the first week postoperative/ total answers	25/142	33/131	*0.1258*
Number of patients waking up because of pain during the first week postoperative/ total answers	19/141	22/130	*0.4287*
Number of patients taking pain medication during the first week postoperative/ total answers	25/142	31/131	*0.2036*
Number of patients using an ointment in their eye during the postoperative period for pain or discomfort of the eye/ total answers	41/142	60/131	*0.0038*

Results show that the glue group had significant shorter duration of the eye looking reddish (p= 0.0471) and of discomfort of the eye (p=0.0376). The glue group also used an ointment for a shorter period of time (p= 0.0105).

DISCUSSION

The aim of this retrospective study was to find out whether the closure of conjunctival wounds in pars plana vitrectomy using fibrin glue causes less postoperative pain, discomfort and sickleave than sutures.
Our results showed that the glue group had a shorter duration of the eye being reddish, of discomfort of the eye and of using an ointment. The glue group used less ointment and independent workers had a shorter sickleave after receiving glue. Finally, if the patients underwent vitrectomy without cerclage, they had less pain on the first day postoperative when having received glue.

This study examines the result of vitrectomies performed in 2004. The patients did not receive the questionnaire until 2006. Obviously, it is more difficult to answer the questions after such a long time. However we think this does not have any influence on the results of our study since both the fibrin glue group and the suture group filled in the questionnaire equally late.

Concerning the answers to the questions about sleeping less, waking up or taking pain medication because of pain during the first night after the operation, we divided both the glue and sutures group in two subcategories: patients who underwent vitrectomy with cerclage and patients who underwent vitrectomy without cerclage. This was done because it is a general known fact that an additional encircling procedure during vitrectomy causes much more pain during the first postoperative day (9). This may explain why patients who received cerclage showed no difference in sleeping less, waking up or taking pain medication because of pain during the first night after the operation between the sutures and glue group.

Table 3: *Duration of sickleave in patients with sutures vs fibrin glue after pars plana vitrectomy*

	Glue-Employee (n=38)	*Sutures-Employee (n=32)*	*P-value (Wilcoxon Rank Sum Test)*	*Glue-Independent (n=13)*	*Sutures-Independent (n=11)*	*P-value (Wilcoxon Rank Sum Test)*
Mean number of weeks of sickleave	4,7105	5,4687	*0,8818*	0,7692	2,0000	*0,0292*

Table 4: *Eye-related discomfort in patients with sutures vs fibrin glue after pars plana vitrectomy*

	Glue group	*Sutures Group*	*P-value (Wilcoxon Rank Sum Test)*
Mean number of weeks of the eye looking reddish after the operation	2,3455	4,1637	*0.0471*
Mean number of weeks of discomfort of the eye after the operation	2,0080	2,6956	*0,0376*
Mean number of weeks of using an ointment of the eye for pain or discomfort of the eye after the operation	0,9142	1,4173	*0,0105*

For analyzing the answers to the questions on the duration of the sickleave both glue and sutures group were divided in two subcategories: employees and independent workers. This was done because it can be expected that people who work independently restart their working activities sooner. This was confirmed, since the results show no significant difference in sickleave in the employee category and a significant difference in the independent category.

Earlier publications already described many advantages of using Tissucol.

One disadvantage of using Tissucol for closing conjunctival wounds could be the extra cost for the patient. When using sutures, we used the same Biosorb 7/0 for closing both sclerectomies and conjunctival wounds. Therefore, sutures cause no extra cost for the patient. The use of Tissucol makes the surgery more costly (approximately Eur 60 in Belgium).

For certain indications, like duodeno-pancreatectomy, Tissucol is partially reimbursed to the patient by the Belgian health insurance. At this moment , the use of fibrin glue is not reimbursed in any ophthalmic procedure in Belgium.

At present, the sutureless 23 or 25 gauge techniques are being used more frequently. In these procedures the conjunctival wounds need no closure. Yet, a significant amount of the pars plana vitrectomies is still being carried out using the 20 gauge technique.

Looking at the many advantages of the use of fibrin glue already described in earlier studies, and based on our results, the fibrin glue appears a better alternative to sutures for closing of conjunctival wounds in pars plana vitrectomy.

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