PREVENTION OF WRAP DISRUPTION AFTER ANTIREFLUX SURGERY: AN EXPERIMENTAL STUDY

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ABSTRACT

Objective: *The worst complication after a fundoplication is the disruption of the fundic wrap which is the main cause of recurrent gastro-esophageal reflux. The purpose of this experimental study is to seek for an alternative technique to prevent wrap-breakdown.*

Material and Method: *The experiments were carried out on thirty canine subjects those were randomly allocated into 3 groups for performance of a Nissen procedure. Silk sutures were used for construction of the fundic wrap in Group I, silk sutures and fibrin glue were used in Group II and only fibrin glue was used in Group III for the same purpose. Operation durations were noted as minutes. The break-down force of the fundic wrap was measured and recorded. The results were recorded as kg and statistical examinations were performed by SPSS 13.0 statistical software program. The intergroup comparisons were performed with Kruskal-Wallis and Mann-Whitney U tests. p was significant at <0.05*

Results: *No post-operative complications were observed and all the animals survived until the post-operative 2nd month when they were euthanized and the wrap break-down forces were determined. The break-down force was 11.2 kg in Group I, 17.3 kg in Group II, and 11.5 kg in Group III. The difference between group I and II, with group III was statistically significant ($p<0.05$). But group I and III was not statistically significant ($p>0.05$). Operation times were 47.9 in Group I, 53.2 in Group II and 28.38 minutes in Group III. Operation times were significantly longer in Group II than in Group I and III ($p<0.05$), and significantly shorter in Group III than in Groups I and II ($p<0.05$).*

Conclusion: *We believe that, application of the fibrin glue together with the conventional suturing technique in construction of the fundoplication may prevent wrap-breakdown after the Nissen antireflux procedure.*

Keywords: *Fundoplication, wrap break-down, fibrin glue*
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ANTİREFLÜ AMELİYATI SONRASI YAKALIĞIN AYRILMASININ ENGELLENMESİ: DENEYSEL ÇALIŞMA

Özet

Giriş: Funduplikasyon ameliyatı sonrası yakalığın ayrılması en kötü komplikasyondur. Bu durum reflünün nüks etmesinin ana nedenidir. Çalışmada funduplikasyon yakalığının ayrılmasını engellemek için alternatif bir yöntemin deneysel olarak araştırılması amaçlandı.

Materyal ve Metod: Çalışmada 30 köpek kullanıldı. Denekler rastgele onarlı üç gruba ayrıldı. Her gruba farklı yöntemle Nissen Funduplikasyon uygulandı. Funduplikasyonun oluşturulmasında Grup I'de sadece ipek dikiş, Grup II'de ipek dikiş ve Fibrin Glue, Grup III'de ise sadece Fibrin Glue kullanıldı. Ameliyat süreleri kaydedildi. Denekler iki ay takip edildikten sonra sakrifiye edilerek yakalığın ayrılma kuvveti germe testi ile ölçüldü ve kg olarak kaydedildi. İstatistiksel analiz SPSS paket programı yardımı ile yapıldı. Gruplar arası karşılaştırma ise Kruskal-Wallis ve Mann-Whitney U testi ile yapıldı. $p<0,05$ anlamlı olarak değerlendirildi.

Bulgular: Deneklerde cerrahi komplikasyonla karşılaşılmadı. Yakalığın ayrılma kuvveti Grup I'de 11,2 kg, Grup II'de 17,3 kg Grup III'de 11,5 kg idi. Grup I ve Grup III ile Grup II arasındaki fark istitatistiksel olarak anlamlı idi ($p<0,05$). Grup I ile Grup III arasındaki fark ise anlamsızdı ($p>0,05$). Ameliyat süreleri Grup I'de 47,9, Grup II'de 53,2, Grup III'de 28,38 dakika idi. Ameliyat süresi Grup II'de Grup I ve III'den belirgin olarak uzundu ($p<0,05$). Grup III'de ise Grup I ve II'den belirgin olarak kısa idi ($p<0,05$).

Sonuç: Nissen antireflü amaliyatında klasik sütürlerle birlikte Fibrin Glue kullanılmasının yakalığın ayrılmasını engelleyebileceğini düşünüyoruz.

Anahtar Kelimeler: Funduplikasyon, yakalığın ayrılması, fibrin glue **Nobel Med 2015; 11(2): 49-53**

INTRODUCTION

Gastro-esophageal reflux disease (GERD) is the most common upper gastrointestinal disorder in the developed countries.[1,2] Every year millions of people are diagnosed to have GERD.[2,3] Surgical treatment for GERD is indicated in patients who are refractory to medical therapy, or in need of a lifelong medical treatment.[4,5] The most commonly used surgical procedure is a 360° fundoplication, which is named as the 'Nissen procedure'.[6,7] Although, the success rate of the operation can be as high as 90%, complications as wound infection, respiratory demise, dysphagia, hiccup, retching, dumping symptoms, and wrap disruption are not infrequent.[8-10] Despite the transient character of most of these symptoms, the wrap disruption is permanent and causes severe morbidity which is due to the recurrence of the GERD and subsequent reoperation(s).[8,11] Reoperation rates after the Nissen procedure has been shown to be as high as 6-25% in some studies and the most important reason for performing a reoperation is the wrap disruption.[10-12] Although technical errors were undoubtedly responsible for some of these disruptions others may simply reflect an inability of the fundoplication wraps to withstand disruptive forces, as physiological acute elevations of intra gastric pressure.[13]

The aim of this experimental study is search for an alternative way to prevent wrap breakdown after the Nissen procedure.

MATERIAL AND METHOD

The study was conducted by following the ethical standards laid by 'The Guide for the Care Use of Laboratory Animals' published by the U.S. National Institutes of Health (NIH publication No: 86-23, revised 1985) and approved by the Faculty Ethical Committee for the Experimental Research on the Animal Subjects.

The experiments were carried out on thirty young adult canine subjects weighting 15-20 kg. The animals were randomly allocated into 3 groups each consisting of 10 dogs.

Anesthesia was performed by ketamine hydrochloride 20 mg/kg and xylasine hydrocloride 2% 3,5 mg/kg intramuscularly and 1 gr Seftriakson disodyum was administered for infection prophylaxis to all animals preoperatively. All the operations were performed under aseptic conditions and the abdomen was entered by the median laparotomy.

The Nissen procedure was performed uniformly in all animals. First, the esophagus was fully detached from the hiatal margins. Several short gastric arteries were ligated and divided for facilitation of a full 360 degree fundoplication with undo tension and injury to the spleen. Sutures were placed through the anterior fundus and the wall of the esophagus, and the fundus was passed posterior to the esophagus. A 4 to 5 cm segment of the intraabdominal esophagus

was prepared and the wrap was constructed over the largest size esophageal dilator that safely fitted with in the lumen of the intraabdominal portion of the esophagus. The sutures were inserted at the tinea by the fundus in this manner. The wrap construction varied according to the study groups. Thus, only silk sutures were used in Group I (Figure A, B, C), silk sutures and fibrin glue (Tisseel®KIT 2.0 Immuno A.G Österreichisches, Institut für Haemoderivative G.M.B.H, Austria) were used together in Group II (Figure D, E) and only fibrin glue was used in Group III. In Group II and Group III, it was mandatory to wait for 10 minutes for stabilizing of the glue by the applied force attained by the Babcock clamps (Figure F, G). Three silk sutures (number 0) were used for diaphragmatic crural reapproximation in all groups and operations were terminated by closing the abdomen in anatomical layers (Figure A, B, C). All operation durations were noted and recorded as minutes.

On the post-operative 1st day a standard liquid diet via oral route was started and normal feedings were continued. All animals were re-operated at the end of the post-operative 2nd month, and 1/3 distal portion of the esophagus and stomach were resected together. While still anesthetized, the dogs were euthanized with lethal doses (120 mg/kg) of intraperitoneal pentobarbital sodium.

A simple puller system was constructed to measure the maximal breaking capacity of the wrap. Stomach was tied at incisura angularis and the esophagus was tied at 10 cm far from the cardia. Esophageal end was fixed to a fulcrum point, and the maximal power needed to detach the wrap was measured and noted as kg, by traction with different weights applied to stomach side. The data were expressed as mean±standard deviation. Kruskal Wallis and Mann Whitney U tests were used for statistical evaluation and p was significant at 0.05.

RESULT

The weights of the subjects were 19.06±1.65 kg, and all the groups were comparable according to the weights (Table). No evidence of systemic toxicity was observed during the operations and on the post-operative period. Besides, no post-operative complications occurred. All the animals survived and started regular feedings by the end of the post-operative 24th hour, and bowel movements and defecations started on the post-operative 2nd day.

When relaparotomy was performed on the post-operative 2nd month, all the wraps were found to be surrounded with omentum and small intestinal segments but there was no proximal intestinal dilatation which was a sign of adhesive intestinal obstruction. Clear intraabdominal fluid was present in all animals.

Table: Statistical analyses of the subject weights (kg), fundic wrap break-down forces (kg) and operative time (min.) according to the study groups.

	Group I (Silk sutures)	Group II (Silk sutures and fibrin glue)	Group III (Fibrin glue only)	p
Weight (kg)	19.05±1.69	19.00±1.54	19.15±1.87	>0.05
Wrap break-down force (kg)	11.2±0.97$^{\mu}$	17.3±0.67$^{\mu,\alpha}$	11.05±0.59$^{\alpha}$	<0.05*
Operative time (min.)	47.9±3.43$^{\mu,\alpha}$	53.2±6.90$^{\alpha,\Psi}$	38.80±1.76$^{\mu,\Psi}$	<0.05*

*: p<0.05, Kruskal Wallis test, **μ, α, Ψ , :** p<0.05, Mann Whitney U test

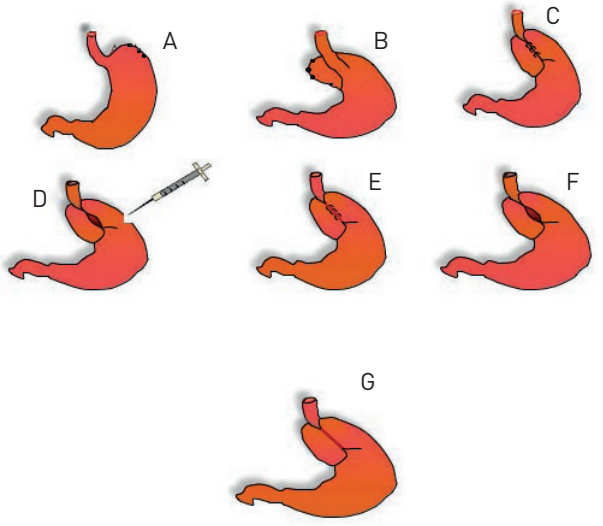

Figure: Fundoplication with A-B-C: Sutures only, D-E: Fibrin glue with silk sutures, F-G: Only fibrin glue

The mean wrap disruption values were 11.2±0.97 kg in Group I, 17.3±0.67 kg in Group II and 11.05±0.59 kg in Group III. Statistical evaluation of the mean maximal forces to disrupt the fundic wrap showed that Groups I and III were comparable (p>0.05), and Group II was significantly higher than Groups I and III (p<0.05) (Table).

The mean operation durations in Group I was 47.9±3.43 minutes, Group II was 53.2±6.90 minutes and in Group III was 28.38±1.76 minutes. Group II had a significantly longer operative time than Groups I and III (p<0.05), whereas Group III was significantly shorter than Groups I and II (p<0.05) (Table).

DISCUSSION

There has been a 2-fold increase in the annual rate of fundoplications after the introduction of laparoscopy in antireflux surgery. Similarly, the increases on the surveillances of some congenital anomalies as congenital diaphragmatic hernia and esophageal atresia, caused an increase in the number of antireflux surgeries performed in children.[9,10,14-16] Fundoplication is an essential technique for controlling severe and life-threatening GERD particularly in children with congenital trachea-esophageal and diaphragmatic anomalies.

Following an anti-reflux surgery, the initial satisfactory outcome may be complicated by recurrent reflux symptoms in a minority of patients, which simply means the failure of the operation. This condition may be due to inappropriate patient and technique selection, poor surgical skills or wrap disruption. In a recent series, recurrent GERD after the Nissen procedure was found in 12 of 52 patients, which was due to the wrap disruption and the disorder was corrected in 7 of the patients with performing reoperations.[17,18] Similarly, it was shown that partial or total disruption of the fundic wrap occurred in 20-25% of patients in long term follow-up.[19- 21]

Some reasons may merely reflect an inability of fundoplication wraps to resist against disruptive forces as physiological acute elevations of intra gastric pressure that causes sutures to pull out of the fundic wrap.[11,13,22] Alternatively, chronic elevations of intra gastric pressure, secondary to impaired gastric emptying, could cause late post-operative wrap disruption.[13,20,21] The patients with chronic lung diseases, congenital diaphragmatic hernias and abdominal wall defects as omphaloceles and gastroschisis, and neurological impairments are at risk of wrap disrupture due to elevation of intraabdominal pressures because of their underlying disorders.[11,13] Radiologic investigations and reoperations in these patients often show that the wrap disruption is to be the main reason for failure of the operation. For similar reasons, wrap fundoplication should not be performed in children with a short intraabdominal esophagus as in an esophageal atresia unless the intraabdominal esophagus is liberated from the hiatal margins and elongated.[9,15,24]

Cyanoacrylate derived tissue glues, those are of an interesting area of investigation in abdominal surgery, were already used in constructing, sealing and enforcing high-risk intestinal anastomoses.[25] Similarly, fibrin glue has been found to be successful in sealing bowel anastomoses with the extra advantage of lacking local and systemic toxicity.[26] Additionally, it was utilized in cardiothoracic surgery to control bleeding and sealing tracheal anastomoses. The efficacy of fibrin glue, which is a mixture of fibrinogen and thrombin, is based on the transformation of fibrinogen and fibrin resulting in an insoluble fibrin polymer with high mechanic stability. Early fibroblast growth and formation of a dense granulation tissue are the major late effects of fibrin sealing.[19,27]

When we performed re-laparotomy, we observed that all the fundic wraps were surrounded with omentum and intestinal segments possibly because of the aforementioned effect of the fibrin glue. Although, we did not observe any proximal intestinal dilatation which was a sign of adhesive small bowel obstruction in none of the animals, we can not comment on late onset adhesive small bowel obstruction as our results reflect only post-operative second month period.

Use of fibrin glue in wrap construction in Nissen antireflux procedure prompted an equal power as attained by the silk sutures. Not surprisingly, enforcement of the wrap with the fibrin glue propelled nearly a 1.5 fold increase in the mean resistive force of the wrap. It can be assumed that the tissue stabilization was increased by using the fibrin glue together with the silk sutures. For this reason, we may speculate that intra thoracic herniation of the wrap may also be prevented if a similar application is used for the diaphragmatic crural approximation.[19,27]

Operation durations were inevitably longer in the suture groups, which was due to the time consuming nature of the suturing work. But, we can not recommend merely application of the fibrin glue in construction of the fundic wrap in order to shorten the operation time, as fibrin glue itself did not gain enough strength as when it was used together with the sutures. Thus, unsuccessful results could be expected.

One weakness of our study is that it lacks the histopathological examinations and biochemical analyses of the fundic wraps, which could have shown the healing status of the specimens according to the study groups. But, we know that fibrin glue does not have a detrimental effect for the tissues. Additionally, abundant fibrosis might have not been demonstrated because of the 2 months of waiting time as this period suits the plato phase of the tissue healing which means that proliferation and decrement are in equilibrium.

As a conclusion, the present study supports the use of fibrin glue in conjunction with the conventional sutures in fundic wrap construction in the Nissen procedure in the experimental setting. The technique has not caused operative mortality and morbidity and seemed to be cost effective when re-operations due to wrap disruptures are taken into count. Besides, application of the fibrin glue may be feasible even in second look operations and laparoscopic fundoplications.

* The authors declare that there are no conflicts of interest.

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