



## EVALUATION OF THE EFFICACY OF TOPICAL FERACRYLUM SOLUTION (1%) AS A HAEMOSTATIC AGENT DURING MAJOR HEAD AND NECK SURGERY – A RANDOMIZED CONTROLLED STUDY.

### Clinical Research

**Dr. Vani Mehrotra** Post Graduate Student, Dept. of Oral & Maxillofacial Surgery, M.G.M Dental College and Hospital.

**Dr. Srivalli Natarajan\*** Professor & HOD, Dept. of Oral & Maxillofacial Surgery, M.G.M Dental College and Hospital. \*Corresponding Author

### ABSTRACT

**Background:** Limiting blood loss presents a challenge to the surgeon. An external, hemostatic agent – Feracrylum can be a good companion in major head and neck surgeries.

**Methods:** Total Sample size was 30 patients undergoing major head and neck surgery. These patients were randomly assigned to either group A (Feracrylum group, n = 15) or group B (normal saline group, n = 15).

**Results:** The mean difference in Haemoglobin values of group A and B were compared and greater drop were seen in group B as compared to group A on postoperative day 2 and 5 (p = 0.229), and more number of patients had greater loss (>2gm %) in group B. The mean values of drain collection were always more in group B when compared to group A.

**Conclusion:** It was observed in this study that 1% Feracrylum solution led to decrease in blood loss from surgical wounds, though the results were not statistically significant. It was found to be safe with no adverse effects on hepatic or renal parameters.

### KEYWORDS

1% Feracrylum Solution, Feracrylum Solution, Local Hemostatic Agent, Hemolok, Feracrylum.

### INTRODUCTION

One of the most common problems during major surgery is bleeding. The amount of blood loss during surgery varies with each patient for a given surgical procedure, which limits standardization of perioperative blood orders. Management of hemostasis during surgery has many key components that start, first and foremost, with good surgical technique and anaesthetic support. Postoperatively, blood continues to ooze from the cut ends of bone, the open intra-medullary canal and the raw, dissected soft tissue causing significant bleeding. Surgeons have an array of options to control bleeding, including mechanical and thermal techniques and devices as well as pharmacotherapies and topical agent.<sup>i</sup> The use of effective pharmacological methods during surgery can be a useful option or an adjunct to other methods in these situations. The pharmacological methods seek to augment surgical hemostasis by enhancing the natural coagulative mechanisms.<sup>ii</sup> This may include the use of pharmacological agents, such as epinephrine, desmopressin, topical hemostatic agents, tissue sealants, and tissue adhesives<sup>iii,iv,v,vi</sup>. An external, chemical, hemostatic agent – Feracrylum – has become a good companion in surgery nowadays. It is a biocompatible and biodegradable polymer and is an incomplete ferrous salt (II, III) of polyacrylic acid containing 0.05 to 0.5% of iron, developed as sterile solution by Themis Medicare Limited. It has antimicrobial and hygroscopic properties. Its use has been evaluated in varied surgical and diagnostic procedures. When feracrylum comes in contact with tissue protein, it forms a whitish thin film which creates a physical barrier. This reduces oozing from wound site, thus exerting haemostatic action. The formation of this whitish thin film in the form of a barrier, gel like structure protects the wound from exogenous contamination. The unique inherent antimicrobial property of these synthetic polyacrylates simultaneously prevents Gram-positive and Gram-negative bacterial growth on and near the inflammation site. Thus the present study was planned to evaluate the efficacy of Feracrylum solution (1%) as a topical haemostatic agent in patients undergoing major head and neck surgery of duration >45 minutes as compared to a control group using normal saline.

### METHODS:

Total Sample size was 30 patients undergoing major head and neck surgery. These patients were randomly assigned using research randomizer software to either group A (study group using Feracrylum 1%, n = 15) or group B (control group using 0.9% normal saline, n = 15).

### INCLUSION CRITERIA:

- Patients undergoing any major surgeries of head and neck region for duration > 45 minutes.
- Patients requiring the insertion of at least one drain per operative site.

- Patients with hemoglobin more than 8 g/dl (Hb% > 8 g/dl).
- Patients irrespective of any gender.
- Patients between age group of 18 to 60 years.
- Patients who were willing to abide by the study requirements.

### EXCLUSION CRITERIA:

- Terminally ill patients.
- Patient with uncontrolled diabetes i.e. fasting Blood level  $\geq$  200 mg % at baseline.
- Patients with uncontrolled hypertension.
- Patients suffering from severe peripheral vascular disease or suffering from bleeding disorder.
- Patients presenting with malnutrition, anemia (Hb < 8 gm%) and immunocompromised states.
- Patients with severe cardiac, hepatic, gastrointestinal, renal, pulmonary and skin diseases.
- Patients with deranged Liver and Renal function test.
- Patients with known hypersensitivity to any of the ingredients of the test formulation.
- Pregnant and lactating patients.

### Evaluation parameters:

- Measuring total weight of mops used (gms)
- Suction collection (ml)
- Post operative drainage collection (mL)
- Pre-operative and post-operative blood values (gm%)
- Duration of drain in situ (days)
- Hematoma formation.
- Blood transfusion.

**Human rights:** It has been approved by the Institutional Ethic Board. During the conduct of study, all human ethical principles as per the WMA-Declaration of Helsinki and the guidelines of GCP (ICMR) were observed.

**Informed consent:** The patients were informed about the study and necessary consent was taken from the concerned personnel.

### Methodology:

This study was carried out between December 2015 and August 2017. A standard proforma was used to collect necessary information regarding each case. All necessary preoperative, intraoperative and postoperative records were maintained for the patient.

Patients were divided into two groups, in Group A patients, the investigational product Feracrylum solution (1%) (Figure 1) was used as topical therapy in soaked mops and in patients in Group B, sterile normal saline (0.9%) was used as topical therapy during major surgeries from the time incision was given till the time when last suture

was placed. The investigational product was used for the control of bleeding due to capillary oozing. For the control of bleeding from



**FIGURE 1:** 1% Feracrylum solution used intraoperatively to achieve hemostasis at surgical site.

blood vessels, electrocautery was used or if possible vessels were ligated. A 25 x 40 cm Bipson mop was soaked wet in the study solution in group A and in control solution in group B and squeezed. Mops were weighed in digital weighing machine before use in both the groups. These mops were used to aid in control of bleeding due to capillary oozing and not for arterial or venous bleed. Every time Feracrylum soaked gauze was used, it was kept at place for 2-3 minutes and maximum 3-4 minutes, (Figure 2) and if oozing did not stop, electrocautery was used to achieve hemostasis.



**FIGURE 2:** Application of Feracrylum soaked mop at surgical site to achieve hemostasis.



**FIGURE 3:** Digital weighing machine measuring weight of blood soaked mops.

These mops could be used multiple times. Every time before the blood soaked mops were discarded, they were weighed in digital weighing machine in both the groups. (Figure 3) Blood loss intraoperatively was determined by measuring the difference in weight of mops pre use and post use, which was converted into blood loss and also by subtracting the irrigation volume from collection volume in suction bottles in both the groups. The mean weight of all the mops was divided by the weight of 1 mop for every patient in each group which gave the number of mops used. The blood loss through soakage was calculated by multiplying the number of mops used with the standard absorption capacity of abdominal mop i.e. 80 ml.

| For Feracrylum group,                                                     | For Saline group,                                                         |
|---------------------------------------------------------------------------|---------------------------------------------------------------------------|
| $\text{Blood loss} = \frac{(\text{Total weight of mops})}{71} \times 80.$ | $\text{Blood loss} = \frac{(\text{Total weight of mops})}{45} \times 80.$ |

For irrigation during the surgery, 0.9% sterile normal saline was used in both the cases. Before closure the drains were inserted 1 per operative site. The drains were kept in place postoperatively till the time, drain collection reduced to 20-25 ml (Figure 4).

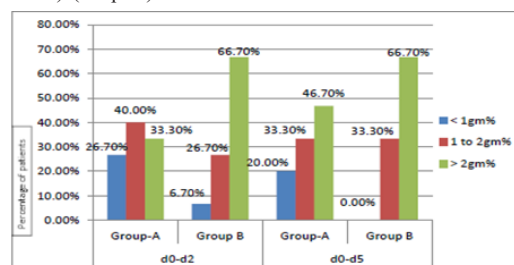


**FIGURE 4:** Measuring drain collection every 24 hours.

Patients in both the groups were otherwise continued to receive the standard pre, peri and post operative treatment available at the trial site for surgery. Blood transfusions were given to those patients, in whom the postoperative hemoglobin value was less than 8 mg/dl. All the operative procedures were carried out by the same surgeon.

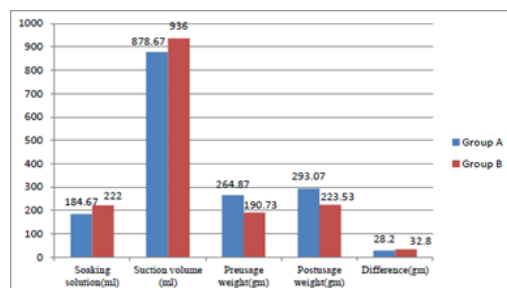
## RESULTS:

In study group, patients ranged from 35 years to 60 years of age, with mean age of 50.9 years, out of which 8 patients were female and 7 patients were male. The average duration of surgery was 6 hour and 30 minutes. In control group, age of the patients ranged from 36 years to 60 years, with mean age of 53.06 years, out of which 11 patients were male and 4 patients were female and the average duration of surgery was 6 hours and 30 minutes. The mean difference in Hb values of group A and group B were compared and greater drop in Hb values were seen in group B as compared to group A on postoperative day 2 ( $p=0.229$ ) and 5 ( $p=0.432$ ). More number of patients had greater loss ( $>2\text{gm}\%$ ) in group B as compared to group A on postoperative day 2 and 5 ( $p=0.145$ ). (Graph 1)



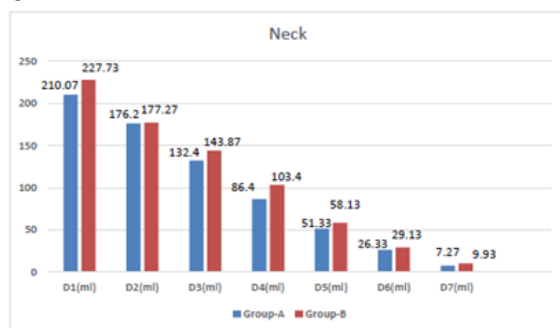
**GRAPH 1:** Graph depicting categorization of patients according to change in Hb values.

The difference in weight of mops was found to be less in group A as compared to group B ( $p=0.302$ ). The weight of mops both preoperatively and postoperatively was more in group A as compared to group B, but the difference was found to be less in group A as compared to group B. The weight of mops were converted into blood loss in mL and the mean correlated blood loss was 330.21 ml in group A and was 397.38ml in group B. In this study, the blood loss through suction collection was found to be 220.48 ml in Feracrylum group and 249.33 ml in control group. (Graph 2)



**GRAPH 2:** Graph comparing the solution used, suction volume collected, weight of mops and difference in weight of mops of group A and group B.

The mean values of drain collection were compared for every consecutive day and the drain collection was always more in group B when compared to group A for neck. (Graph 3) Though the numbers of days were same in both the groups. For everyday p value was found to be greater than 0.05.



**GRAPH 3:** Graph depicting the drain collection values from D1 to D7 for neck.

### DISCUSSION:

Severe bleeding can progress into haemorrhagic shock in a flash rather than a gradual decent. There are several conventional haemostatic techniques to minimize blood loss. Mechanical means include manual pressure, ligation and the application of a tourniquet, which can be labour intensive and add time to the operative procedure.<sup>vii</sup> Sealing of bleeding vessels can also be achieved by thermal methods such as electro cauterization or laser cauterization, but these create areas of char and necrotic tissue, increasing the likelihood of infection and damaging wound edges. This may lead to impaired and delayed healing.<sup>viii</sup> Conventional methods are also less effective in controlling bleeding from complex injuries and inaccessible areas. Topical haemostatic agents may be particularly useful in such situations. Several topical haemostatic agents are currently available and are different in their mode of action. Appropriate selection of hemostatic agent for any case, is of utmost importance to achieve hemostasis instantly. Factors affecting the selection of topical haemostatics include the type of procedure, cost, severity of bleeding, and the personal experience and preference of the surgeons.<sup>ix</sup> Feracrylum solution has a unique mechanism of action as it acts by activation of thrombin, which subsequently causes conversion of fibrinogen to fibrin and thus clot formation. In addition, on coming in contact with serum proteins, it forms a thin film, thus acting as a mechanical barrier sealing off capillary oozing. Since blood is a good culture media, it aids in increasing microbial count. By achieving hemostasis, Feracrylum does not contribute in raising microbial count. The hemostatic action of Feracrylum was evaluated by measuring intraoperative blood loss through soakage (which was calculated by measuring the total weight of mops used and converting them to blood loss), suction collection, preoperative and postoperative blood values, drain collection, hematoma formation and need for blood transfusion. Lahoti et al in 2010, studied the hemostatic activity of Feracrylum solution in hypospadiac surgeries and they found that the average number of blood soaked gauge pieces was 3.56 per patient, correlating with average intraoperative blood loss of 17.8 ml and in controls, average blood soaked gauge pieces were 6.2 per patient corresponding to an average blood loss of 31 ml.<sup>x</sup> In this study, we compared the mean differences in the weight of mops used intraoperatively before and after soakage of blood of both the groups. It was found on comparison that the mean difference in the weight of the mops and the mean blood loss was less in Feracrylum group as compared to Saline group, which indicates that either the soakage in Saline group was more or the more number of mops were used intraoperatively in saline group, which correlates with the hemostatic activity of Feracrylum. On application, it reacts with free plasma proteins mainly albumin, it forms an insoluble polycomplex and converts soluble fibrinogen to insoluble fibrin which then forms coagulum. This arrests bleeding and oozing from highly vascularised tissues.<sup>xi</sup> Because of the different mechanism of action, Feracrylum alone or along with other hemostatic agents can be used in patients who are under antithrombotic medication. Since Feracrylum does not act on coagulation factors and it does not affect coagulation cascade, it acts externally and has low chances of any undue risk. Laddha et al in 2015, compared Feracrylum and adrenaline as topical hemostatic agent, and found there was less blood loss in Feracrylum group than controls ( $P < 0.0001$ ). The average duration of surgery in study group was 79 min while the same in controls was 94

min. The two-tailed P value was 0.0006, which was considered as extremely significant.<sup>xii</sup> This decrease in duration of surgery was attributed to better haemostasis caused by 1% Feracrylum citrate, which improves visibility of surgical field and hence speed of surgery. The blood loss through suction volume was calculated by quantifying the total collection in suction bottles minus the amount of irrigation used. The resultant value gave the amount of blood loss. Mean blood loss was calculated and compared in both the groups. In this study, the resultant value was found to be less in Feracrylum group as compared to control group, which indirectly reflected the action of Feracrylum on capillary oozing and reducing the blood loss. Shah et al in 2013, calculated the total amount of blood loss in 150 knee joint replacement surgery. Amongst the various parameters, decrease in the level of haemoglobin values was one of them. They concluded that the mean reduction in hemoglobin level was 1.6 gm/dL.<sup>xiii</sup> The mean difference in the hemoglobin values in the similar studies done by Yamaski et al was 1.7 gm/dl and by Camarasa et al was 2.5 gm/dL.<sup>xiv</sup> The difference in haemoglobin values in this study in Feracrylum group on day 2 was 1.88gm/dl and on day 5 was 2.08gm/dl. In Saline group, it was 2.53gm/dl on day 2 and 2.42gm/dl on day 5. The drop in the level of the haemoglobin from preoperative to postoperative value in both the groups was the direct indicator of blood loss in this study. The results of this study showed that the blood loss was less in Feracrylum group on day 2 ( $p = 0.145$ ) and day 5 ( $p = 0.171$ ). The difference of drop in the haemoglobin values was noticeable, but not statistically significant. This might be because of small study sample size. In this study, the two groups were compared on the basis of the mean number of days the drain was in situ at each operated site, and by comparing the mean drain collection on every consecutive days from day 1 to the number of days the drain was in situ. Although the number of days the drain was in situ were equal in both the groups i.e. 6.27days for neck and 3.33days for chest, but the mean drain collection on every consecutive day was less in Feracrylum group. The consistent low drain values indicate the long lasting effect of layer formed by Feracrylum at the site of application intraoperatively. Lahoti et al in 2010 observed postoperative hematoma in only 8% patients in study group while, it was seen among 18% of patients in controls, indicating a significant reduction in hematoma formation postoperatively ( $P < 0.01$ ).<sup>xv</sup> Laddha et al in 2015 compared Feracrylum and adrenaline as topical hemostatic agent and they found that the postoperative haematoma (irrespective of size) was seen in 3.33% of the controls while none of the patient in Feracrylum group had this complication.<sup>xvi</sup> However in this study, the total number of patients with hematoma formation in both the groups was 2, which showed no difference. Shah et al in 2013 used Feracrylum as a part of strategy to decrease blood loss in 150 total knee replacement cases. He had preset the criteria for blood transfusion as postoperative haemoglobin of less than 8 gm/dL. The results of this study showed that equivalent numbers of patients i.e. 3patients were given blood transfusion in both the groups.

**CONCLUSION:** It was observed in this study that 1% Feracrylum solution when used topically led to decrease in blood loss from surgical wounds, though the results were not statistically significant. It did not show any superior efficacy as an antiseptic agent in wound healing when topically applied, it was found to be safe with no adverse effects on hepatic or renal parameters.

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**Declaration of interest:** None.

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