



Original article

The Effect of Topical 5-Fluorouracil Application on Preventing Nasal Adhesions after Endoscopic Partial Inferior Turbinectomy Combined with Submucous Resection of the Nasal Septum

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Abstract:

Aim and background: In this research, we aimed to compare the nasal adhesion prevention after combined endoscopic partial inferior turbinectomy and submucous resection of the nasal septum between 5-fluorouracil and silastic. **Patients and methods:** 50 individuals with persistent nasal obstruction brought on by hypertrophy of the inferior turbinates and a deviated nasal septum who had not responded to medical therapy were the subject of this investigation. With a mean age of 25, they ranged in age from 16 to 56. 26 patients were men and 24 were women. 25 of these patients were placed in

group A (the fluorouracil group), and 25 were placed in group B. (silastic group). **Results:** Regarding preoperative data, there was no statistically significant difference between the two groups. **Conclusion:** Our data and statistical analysis revealed that 5-FU application during endoscopic partial inferior turbinectomy combined with submucous resection of the nasal septum is an easy, effective, and safe method in reducing and preventing formation of adhesions as silastic sheet with a significantly lower postoperative pain, headache, and nasal obstruction than silastic in the first week postoperative.

1. Introduction:

By eliminating nasal obstructions, enhancing nasal airflow, treating diseases, and allowing sinus drainage, nasal operations strive to improve nasal breathing with the least amount of tissue damage possible. Direct tissue injury during surgery or indirect aberrant healing, such as adhesion development after surgery, may both cause tissue damage [1]. The preferred course of therapy for chronic sinus illness is endoscopic sinus surgery (ESS). This is primarily because this method efficiently eliminates the disease while preserving the sinus mucosa and allowing sinus airflow and drainage through the natural openings [2]. In

the last 20 years, the effectiveness of ESS has been thoroughly characterized; nonetheless, postoperative narrowing and adhesion development are the primary causes of surgical failure [3]. The most frequent ESS complication, with an incidence rate of 11% to 36%, is postoperative adhesion in the middle meatus. As a result, the natural sinuses mucociliary drainage channel is blocked, and the condition returns [3]. According to Ulualp (2008), the incidence of adhesions following ESS is generally between 11 and 36 percent, and the incidence of adhesions necessitating surgical intervention is between 1-2 percent. Spacers,

nasal packing containing absorbent material, such as antiadhesion pack containing hyaluronate sodium or carboxymethylcellulose, and anatomical barriers are now utilized to prevent or minimize adhesions following ESS. However, these techniques were only somewhat effective in avoidance of adhesions [4]. Numerous methods, including nasal packing in the middle meatus, suture medialization, and partial resection of the middle turbinate, have been utilized to halt the development of postoperative synechiae [5]. Numerous medical disciplines have employed 5-fluorouracil (5-FU) to reduce various adhesions and problems associated with epithelium development. It is used safely in dermatology to treat actinic keratosis and in ophthalmology to prolong trabeculectomy survival [6, 7]. An antineoplastic antimetabolite pyrimidine analogue, 5-fluorouracil. By blocking the enzyme thymidylate synthetase, it prevents the conversion of deoxy uridylic acid to thymidylic acid, which interferes with DNA synthesis [8].

2. Patients and Methods:

This was a randomized study performed in Beni-Suef university hospital during the period from February 2018 till January 2019 and involving 50 cases.

2.1 Inclusion criteria:

1. Patients having a deviated nasal septum and bilaterally hypertrophied inferior turbinates.
2. Patients aged 16 years or more.
3. Sex: both genders.
4. Hemoglobin > 10 gm /dl.
5. Normal coagulation profile, liver function and kidney function test.

Exclusion criteria:

1. Patients with uncontrolled systemic illnesses such as DM and hypertension.
2. Patients known to be allergic to 5-fluorouracil.
3. Pre-existing septal perforation.

2.2 All patients were subjected to:

A. At the preoperative visit.

1– Subjective assessment:

Analysis of the patient complaint which was the nasal obstruction through:

- Onset, course, and duration of nasal obstruction.
- Side of nasal obstruction whether unilateral or bilateral.
- History of associated symptoms as snoring, headache, and disturbed smell sensation.
- History of associated allergic symptoms.
- Past history of using nasal decongestant drops or any other medical treatment and its results.

- History of previous nasal surgery.

2 – Objective assessment:

a) Anterior rhinoscopy: was performed to:

- Examine the inferior turbinate showing its color, surface and size and examine nasal septum showing septal abnormalities as septal deviation, dislocation, and spur.
- Detect the presence of any other causes of nasal obstruction such as nasal masses, polyposis or nasal synechia.

b) Nasal endoscopic examination:

To examine the nasal cavity and postnasal space by using the 2.7mm 0° nasal endoscope and with the use of nasal decongestants if needed "if initial trial of nasal endoscopy was difficult due to obstruction".

c) CT scan of nose and paranasal sinuses: to rule out concomitant anatomic abnormalities, sinus disease or polyps.

d) Routine laboratory investigations: including blood sugar, complete blood count, coagulation profile, liver, and kidney function tests.

B. At the follow-up visits.

- After 48 hours, the nasal pack was removed.
- After seven days, the silastic sheet in Group B was taken off.

- Oral antibiotics, analgesics, alkaline nasal washes, and nasal decongestants were given to all patients for a total of 7 days.

- Over a three-month period, all patients were followed up at the outpatient clinic as follows: (one week, two weeks, one month and three months).

- By evaluating the symptoms and doing a physical examination with a rigid endoscope, follow-up was done.

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Examining any nasal adhesions, crustations, or discharge has been the primary goal of the physical.

• **Statistical methodology**

The following data analysis was carried out using an IBM computer using SPSS, a statistical tool for social science. - The mean, SD, and range of quantitative values.

- Description of qualitative variables as number and percentage. $P < 0.05$ is considered significant.

3. Results:

The 50 patients in this randomized prospective comparative analysis had bilaterally enlarged inferior turbinates as well as a deviated nasal septum. Patients were divided into two groups at random. The 5-fluorouracil pack was applied to Group A's

(n=25) nasal cavity for 5 minutes on both sides, while Group B's (n=25) nasal septum received a 7-day silastic sheet application on both sides.

1) Demographic data:

Group A (5-Fluorouracil group): patients' ages ranged from 16 years to 45 years and

Group B (Silastic group): patients' ages ranged from 16 years to 56 years In fluorouracil group there were 10 (40%) males and 15(60%) females but in silastic group there were 16 (64%) males and 9 (36%) females Table (1).

Characteristics	Fluorouracil group	Silastic group	P-value
<u>Age</u>			
Mean ±SD	24.7±8.1	25±9.4	0.898
Range	16-45	16-56	
Median	23	24	
<u>Sex No (%)</u>			
Males	10(40)	16(64)	0.088
Females	15(60)	9(36)	

Table (1): Age and sex distribution among the study groups.

A) Preoperative assessment of both groups:

Regarding preoperative data, there was no statistically significant difference between the two groups Table (2).

Preoperative assessment	Fluorouracil group		Silastic group		P-value	Sig.
	Number (25)	Percent (100%)	Number (25)	Percent (100%)		
Nasal obstruction	25	100%	25	100%	1.000	NS
Headache	10	40%	12	48%	0.675	NS
Discharge	20	80%	18	72%	0.654	NS
Snoring	16	64%	17	68%	0.878	NS
Hyposmia	18	72%	16	64%	0.867	NS

Epistaxis	5	20%	4	16%	0.898	NS
Associated allergic symptoms	19	76%	20	80%	0.879	NS

Table (2): Comparison between both groups as regards preoperative data.

B) Postoperative assessment:

1) Postoperative nasal obstruction:

We assessed nasal obstruction in the 1st three months postoperative in both groups table (3).

Nasal obstruction	Fluorouracil group (n= 25)	Silastic group (n= 25)	P-value	Sig.
At one week follow up	0 (0%)	11 (44%)	0.001**	HS
At two weeks follow up	2 (8%)	1 (4%)	0.432	NS
At one month follow up	0 (0%)	1 (4%)	0.321	NS
At 3 months follow up	0 (0%)	0 (0%)	1.000	NS

Table (3): Comparison between both groups regarding postoperative nasal obstruction during the first 3 months postoperative.

2) Postoperative headache: figure (1)

All cases with headache at two weeks and one month postoperatively were due to sinusitis and relieved completely with medical treatment [for two weeks table (4).

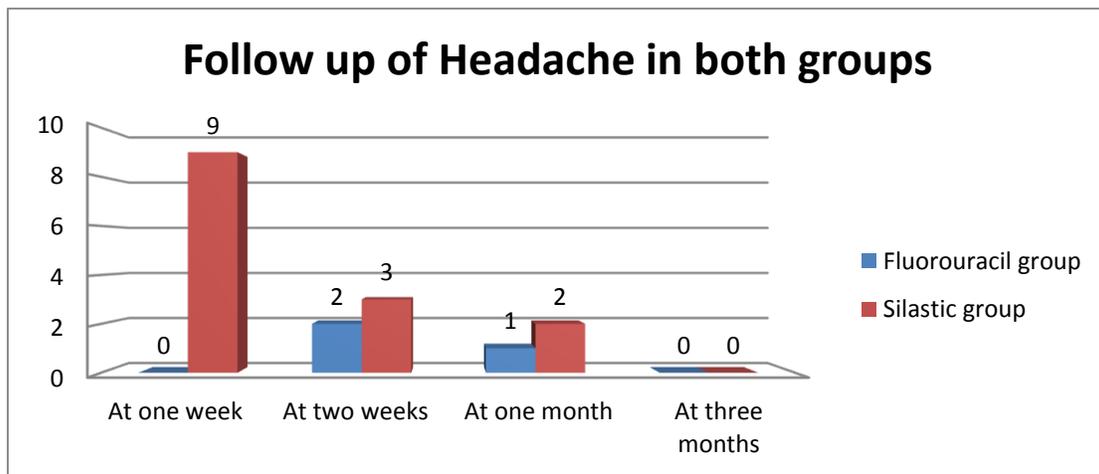


Figure (1): Headache among both groups

Headache	Fluorouracil group (n= 25)	Silastic group (n= 25)	P-value	Sig.
At one week follow up	0 (0%)	9 (36%)	0.001**	HS
At two weeks follow up	2 (8%)	3 (12%)	0.201	NS
At one month follow up	1 (4%)	2 (8%)	0.432	NS
At 3 months follow up	0 (0%)	0 (0%)	1.000	NS

Table (4): Comparison between both groups regarding postoperative headache during the first 3 months postoperative.

3) Postoperative nasal discharge: table (5).

Discharge	Fluorouracil group (n= 25)	Silastic group (n= 25)	P-value	Sig.
At one week follow up	0 (0%)	0 (0%)	1.000	NS
At two weeks follow up	2 (8%)	3 (12%)	0.201	NS
At one month follow up	1 (4%)	2 (8%)	0.432	NS
At 3 months follow up	0 (0%)	0 (0%)	1.000	NS

Table (5): Comparison between both groups regarding postoperative discharge during the first 3 months postoperative.

5) Postoperative pain:

We assessed pain 7 days postoperative.

The fluorouracil group had only 3 cases (12%) with postoperative pain while silastic group had 17 cases (68%) with postoperative pain during application of silastic and relieved after removal of it with figure (2).

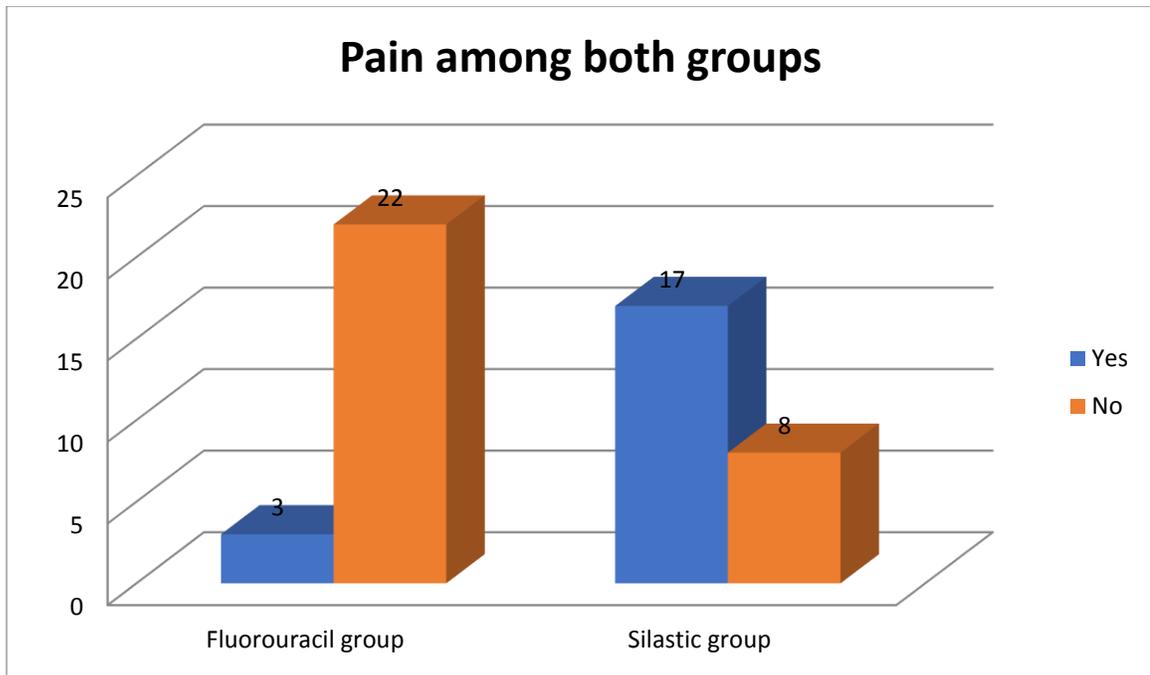


Figure (2): post-operative pain among both groups

6) Postoperative smell affection:

Fluorouracil group had 2 cases (8%) with hyposmia while silastic group had 1 case (4%) with hyposmia 3 months postoperatively table (6).

Smell affection	Fluorouracil group (n= 25)	Silastic group (n= 25)	P-value	Sig.
Hyposmia	2 (8%)	1 (4%)	0.552	NS
No hyposmia	23 (92%)	24 (96%)		

Table (6): Comparison between both groups regarding postoperative smell affection

7) Postoperative nasal dryness:

We assessed for postoperative nasal dryness and these cases with dryness were due to mucosal loss during turbinectomy and treated with daily application of panthenol cream in nasal cavity and relieved with treatment table (7).

Nasal dryness	Fluorouracil group (n= 25)	Silastic group (n= 25)	P-value	Sig.
At one week follow up	0 (0%)	0 (0%)	1.000	NS
At two weeks follow up	0 (0%)	0 (0%)	1.000	NS
At one month follow up	1 (4%)	1 (4%)	1.000	NS
At 3 months follow up	1 (4%)	0 (0%)	0.321	NS

Table (7): Comparison between both groups regarding postoperative nasal dryness during the first 3 months postoperatively.

8) postoperative adhesions:

All cases with adhesions treated with removal of adhesions by scissor or dissector under local anaesthesia and all cases relieved from adhesions Table (8).

Adhesions	Fluorouracil group (n= 25)	Silastic group (n= 25)	P-value	Sig.
At one week follow up	0 (0%)	0 (0%)	1.000	NS
At two weeks follow up	5 (20%)	4 (16%)	0.713	NS
At one month follow	3 (12%)	3 (12%)	1.000	NS
At 3 months follow up	0 (0%)	0 (0%)	1.000	NS

Table (8): Comparison between both groups regarding postoperative adhesions during the first 3 months postoperative.

9): postoperative crustations:

All cases with crustations treated with removal of crusts in out-patient clinic using Tilley Dressing Forceps and nasal irrigation with alkaline nasal douches at home Table (9).

Crustations	Fluorouracil group (n= 25)	Silastic group (n= 25)	P-value	Sig.
At one week follow up	25 (100%)	20 (80%)	0.018*	S
At two weeks follow up	10 (40%)	6 (24%)	0.225	NS
At one month follow	0 (0%)	0 (0%)	1.000	NS
At 3 months follow up	0 (0%)	0 (0%)	1.000	NS

Table (9): Comparison between both groups regarding postoperative crustations during the first 3 months postoperative.

4. Discussion:

The purpose of nasal operations is to improve nasal breathing by eliminating nasal obstructions, increasing nasal airflow, treating diseases, and enabling sinus drainage, while they may also cause minor tissue damage. Indirect aberrant healing, such as adhesion development after surgery, or direct tissue injury during surgery are also possible forms of tissue damage [8]. The most frequent reasons of failed ESS are anatomic blockage and recurrent mucosal illness. 56 percent of patients having revision ESS had adhesions, 27 percent had stenosis of the maxillary sinus ostium, and 25 percent had stenosis of the frontal sinus ostium [9]. With an incidence rate of 1-36 percent, adhesion development and ostial stenosis are frequent ESS consequences. It arises mostly from contact between

untreated mucosal surfaces as a lesion heals [9]. During surgery, various surgical techniques, systemic medications, and site-specific barriers have been employed to minimize inflammation and damage in order to lower the chance of synechiae development [4]. Numerous medical disciplines have employed 5-fluorouracil (5-FU) to reduce various adhesions and problems associated with epithelium development. To enhance the survival of trabeculectomy, it is used safely in ophthalmology [6]. and is used to treat actinic keratosis in dermatology [7]. 50 individuals with persistent nasal obstruction brought on by hypertrophy of the inferior turbinates and a deviated nasal septum who had not responded to medical therapy were the subject of this investigation. They were

between the ages of 16 and 56 years, with a mean age of 25. There were 24 female patients and 26 male patients. 25 of these patients were placed in group A (the fluorouracil group), and 25 were placed in group B. (silastic group). Regarding preoperative data, there was no statistically significant difference between the two groups.

In group B, silastic sheets were applied to both sides of the nasal septum, and all subjects underwent surgical intervention in the form of an endoscopic partial inferior turbinectomy combined with submucous resection of the nasal septum and in group A 5-fluorouracil application in both sides of the nasal cavity. After combined endoscopic partial inferior turbinectomy and submucous resection of the nasal septum, our research was created to assess and compare the effectiveness of 5-fluorouracil against silastic sheets in avoiding nasal adhesions. The majority of postoperative data, such as nasal obstruction, headache, discharge, dryness, discomfort, odor sensitivity, adhesions, and crustations, were compared. Regarding postoperative nasal obstruction, there were no instances of it in the fluorouracil group at one week after surgery, but there were 11 cases (44 percent) of it in the silastic group during the application of silastic sheets and they were eased once they

were removed. At two weeks after surgery, there were two instances (8%) of nasal obstructions in the fluorouracil group and one case (4%) in the silastic group as a result of severe nasal crustations that were treated by scraping the crusts out in an outpatient clinic and using alkaline nasal douches at home. One month after surgery, the fluorouracil group had no instances of nasal obstruction, whereas the silastic group had one case (4%) of nasal obstruction brought on by nasal adhesions that had been surgically removed under local anesthesia. Neither the fluorouracil nor the silastic groups had any incidences of nasal blockage three months after surgery. Due to the use of silastic sheets during surgery, our study found that postoperative nasal obstruction was significantly higher in the silastic group than in the fluorouracil group at the first postoperative week. However, at two weeks, one month, and three months after surgery, there was no statistically significant difference between the two groups.

In terms of postoperative headache, nine instances (or 36% of the total) of headache in the silastic group at one week after surgery were eased once the silastic sheet was removed. In contrast, there were no cases of headache in the fluorouracil group at this time. Two weeks after surgery, there were two cases (8%) of headache in the

fluorouracil group and three (12%) in the silastic group. At one month after surgery, there were two cases (8%) of headache in the silastic group and one case (4%) in the fluorouracil group. Neither the fluorouracil nor the silastic groups had any incidences of headache three months after surgery. All instances of postoperative headache at two weeks and one month were caused by sinusitis, which was totally resolved with medical care for two weeks (nasal decongestants, antibiotics, analgesics, and mucolytics).

In the first week after surgery, our research found that postoperative headache was much more common in the silastic group than in the fluorouracil group, but at two weeks, one month, and three months after surgery, there was no significant difference between the two groups. After the first week of follow-up, there was no statistically significant difference between the two groups in terms of nasal obstruction, headache, discharge, smell change, dryness, and crustations (after removal of silastic sheets). This is consistent with the findings of the study by [11], which evaluated the impact of 5-FU on postoperative complications following endoscopic inferior turbinoplasty combined with one or more other nasal surgeries. They found no significant differences between the 5-fluorouracil and saline treatment groups

for nasal obstruction, headache, discharge, smell change, and crustations.

No statistically significant difference existed between the two groups in terms of postoperative adhesions (p-value=0.933) (table 9). At one week after surgery, neither the fluorouracil nor the silastic groups had any instances of adhesions. Adhesions were seen in 5 instances (20%) in the fluorouracil group and 4 cases (16%) in the silastic group at two weeks postoperatively. Adhesions were seen in 3 instances (12%) in the fluorouracil group and 3 cases (12%) in the silastic group at one month postoperatively. At three months after surgery, neither the fluorouracil nor the silastic groups had any occurrences of adhesions. All patients with adhesions are addressed by having them surgically removed using scissors or dissector surgery while under local anesthesia. In previous research revealed that there was statistically significant difference between fluorouracil side and saline side regarding postoperative adhesions [11]. Adhesions were seen in 24 patients (35%) within the first week after surgery, 6 patients (9%) bilaterally, and 18 patients (26%) unilaterally (only 3 (4%) in the 5-FU sides and 15 (22%) in the saline sides). Adhesions were discovered in 21 patients (36%) at the eighth follow-up week, with bilateral adhesions in 2 patients (3%)

and unilateral adhesions in 19 patients (33%) (only 4 patients (7%) had 5-FU sides and 15 patients (26%) had saline sides).

Pain after surgery was significantly different between the two groups: the 5-fluorouracil group had it in only three instances (12 percent), whereas the silastic group experienced it in seventeen cases (68 percent), all of which were resolved after the silastic was removed.

This is consistent with the findings of [12], who conducted a retrospective investigation on sixty patients who received septoplasty without any further nose surgery. Sixty adults were divided at random into two groups: those who received silastic sheets and those who did not. All patients did not have their noses packed. According to the results of this research, removing silastic sheets a week after surgery dramatically enhanced postoperative pain and nasal discomfort.

5. Conclusion and Recommendations:

Our data and statistical analysis showed that the application of 5-FU during endoscopic partial inferior turbinectomy combined with submucous resection of the nasal septum is a simple, effective, and safe method of reducing and preventing the formation of adhesions as silastic sheet, resulting in

significantly less postoperative pain, headache, and nasal obstruction than silastic in the first week after surgery. The use of 5-fluorouracil is novel, and we strongly encourage other surgeons to learn from our experience.

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