

**Clinical effect of topical use of 5-fluorouracil in the management of discharging post-mastoidectomy cavity**

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**Abstract: Background:** Discharging post-mastoidectomy cavity, is one of the most common complications that occurs due to many factors during or after the operation, and many trials to control the discharge were studied for many times. **Objective:** was to clarify the clinical efficacy of the commercially used 5-fluorouracil (5-FU) topical cream. **Patients & Methods:** After cleaning the debris within the cavity under microscopic examination, 2-3 ml of 5% 5-FU topical cream was applied on the discharging post-mastoidectomy cavities of 20 patients for five times with the interval of 2 weeks, and on the other 20 patients of control group cream containing antibiotic, antifungal and corticosteroid were applied by the same manner. Clinical efficacy was evaluated 3, 4 and 6 months after initiation of treatment. **Results:** Ninety percent of cases were evaluated with high success rate of good and fair results after 3 and 4 months and success rate after 6 months was 85%, as regard to the first group. **Conclusion:** Five-fluorouracil topical cream appeared effective and safe for the treatment of discharging post-mastoidectomy cavities. [Samer Badee Kamel. **Clinical effect of topical use of 5-fluorouracil in the management of discharging post-mastoidectomy cavity.** *Life Sci J* 2013;10(2):1238-1240] (ISSN:1097-8135). <http://www.lifesciencesite.com>. 171

**Keywords:** 5-fluorouracil; post-mastoidectomy cavity; discharge

**1. Introduction**

A cholesteatoma is a lesion of the temporal bone that is lined with keratinizing squamous epithelium, or it may follow preformed pathways to invade the mastoid, middle ear, or petrous apex .(1)

Cholesteatoma may be acquired (most common) or congenital in origin. (2)

The medical management of cholesteatoma includes in-office debridement and treatment of acute inflammatory changes. Dry ear precautions (e.g., with cotton ball and petroleum jelly) are mandatory. Otological antibiotics with steroids are used to reduce secondary infection. Systemic antibiotic therapy can also be used for concomitant infection. However, definitive treatment of cholesteatoma requires surgical intervention. (3)

The options for management of cholesteatoma include canal wall-up or canal wall-down mastoidectomy but the later procedure is considered the gold standard for treatment of cholesteatoma . (4)

Discharging post-mastoidectomy cavity is one of the most common complications after surgical management of cholesteatoma, the presence of mechanical factors which influence the dryness of the open mastoidectomy cavity include the size of the cavity, the height of the facial ridge, the adequacy of the meatal opening and the presence of air in the tympanic cavity. (5)

Secondary infection of the open mastoidectomy cavity occurs either through the Eustachian tube from upper respiratory tract infection, or through the external meatus as a result of entrance of micro-organisms with water. (6)

Five-fluorouracil (5-FU) is one of the oldest chemotherapy drugs and has been around and in use for decades. It is an active drug against many cancers. 5 FU is a clear and colourless liquid and is given by intravenous route. It is also available in cream form for treatment of skin cancers. 5 FU has become accepted because of its efficacy, economic price and relative absence of side effects. (7)

This preliminary study reports the clinical efficacy of 5-FU topical cream on discharging post-mastoidectomy cavities after canal wall down procedure due to persistent granulation tissue.

**2. Patients and Methods**

The study included 40 patients attending the outpatient clinic of Benha University Hospital in the period between 9/2011 and 7/2012. They represented cases treated surgically at the department of otorhinolaryngology, Benha hospital by radical mastoidectomy operation (canal wall-down procedure). All patients suffered from intermittent or continuous discharge from mastoid cavity (the discharge purulent or may be bloody) of a period that ranged up to 6 months from the date of their operation with good meatoplasty. Patient's ages ranged from 20 to 35 years.

All the participants in the study were assessed with history, general examination, local examination including otoscopic and otomicroscopic examination of the operated ear that showed persistent granulation tissue in the cavity and pure-tone audiometry before and after the end of the protocol of treatment for each patient.

The patients were randomly divided into 2 groups (A & B) as regard the line of management, each group included 20 patients.

- Patients of group A undergone treatment with 5-fluorouracil cream.
- Patients of group B (control group) undergone treatment with cream containing antibiotic, antifungal and corticosteroid.

The study was approved by the Local Ethics Committee and informed consents were obtained from each participant in the study after providing sufficient explanations and informations.

All other treatment modalities (systemic and local antibiotics, steroidal or nonsteroidal anti-inflammatory medications) were stopped except 5-FU cream. After cleaning the debris, pus and wax within the external canal and cavity as much as possible under microscopic examination, 2-3ml of 5% 5-FU topical cream was applied 5 times with an interval of 2 weeks, before each application, the pack was removed and ear was cleaned under microscopic examination in the same manner.

Clinical efficacy 3,4 & 6 months after initiation of this treatment was evaluated according to the criteria that described by Takahashi *et al.* 2005 . (8) as follows :

**Good:** granulations and discharge disappeared and remained for longer than a month.

**Fair:** granulations and debris decreased.

**Poor:** granulations and debris not decreased.

#### Statistical analysis

Data obtained were statistically analyzed using The Statistical Package for Social Sciences (SPSS, Chicago, USA) software version 15.0 for Windows. Results were expressed as numbers and percentages. Proportions were compared using the chi-square test. A p value of less than 0.05 was considered statistically significant.

### 3. Results

This study was conducted on 40 patients all had done radical mastoidectomy and having discharging mastoid cavity with age ranging from 15 to 35 years.

**Group A:** included 20 patients: 9 males (45%) and 11 females (55%).

**Group B:** included 20 patients: 10 males (50%) and 10 females (50%).

There was no statistically significant difference between gender distribution in study and control groups (chi-square = 0.1, p = 0.75 )

**Table (1)** shows the results after 3 months from start of treatment in 5-FU group compared to the control group with significantly more good response patients in the 5-FU group.

**Table (2)** shows the results after 4 months from start of treatment in 5-FU group compared to the control group with significantly more good response patients in the 5-FU group.

**Table (3)** shows the results after 6 months from start of treatment in 5-FU group compared to the control group with significantly more good response patients in the 5-FU group.

There was no serious side effect observed. No patient suffered from hearing loss or tinnitus during or after this treatment. None of the patients showed skin erosion of external auditory canal.

### 4. Discussion

The blocking effect on DNA synthesis is deemed primarily responsible for the therapeutic effect of 5-FU which is one of the oldest chemotherapeutic drugs.

In this clinical study, 5-FU cream was applied on discharging post-mastoidectomy cavities of canal wall down procedures to record its clinical effect.

**Table (1) Results after 3 months from initiation of treatment:**

	5 Flourouracil group		Control group		Total		X2 test	P Value
	No	%	No	%	No	%		
After 3 m							7.506	0.0234*
Good effect	15	75.0	7	35.0	22	55.0		
Fair Effect	3	15.0	4	20.0	7	17.5		
Poor effect	2	10.0	9	45.0	11	27.5		
Total	20	100.0	20	100.0	40	100.0		

\* Significant

**Table (2) Results after 4 months from initiation of treatment:**

	5 Flourouracil group		Control group		Total		X2 test	P Value
	No	%	No	%	No	%		
After 4 m							8.24	0.016*
Good effect	15	75.0	7	35.0	22	55.0		
Fair Effect	3	15.0	3	15.5	6	15.0		
Poor effect	2	10.0	10	50.0	12	30.0		
Total	20	100.0	20	100.0	40	100.0		

\* Significant

**Table (3) Results after 6 months from initiation of treatment:**

	5 Flououracil group		Control group		Total		X2 test	P Value
	No	%	No	%	No	%		
After 6 m							9.1	0.011*
Good effect	13	65.0	5	25.0	18	45.0		
Fair Effect	4	20.0	3	15.5	7	17.5		
Poor effect	3	15.0	12	60.0	15	37.5		
Total	20	100.0	20	100.0	40	100.0		

\* Significant

The clinical efficacy of topical use of 5-FU were recorded for all cases of the study after 3 months, 4 months and 6 months from initiation of treatment and results after 3 & 4 months are similar to each other as 15 patients showed good effect, 3 patients showed fair effect and 2 patients showed poor effect, on the other hand results after 6 months from start of treatment were 13 patients with good effect, 4 patients with fair effect, and 3 patients had poor effect respectively.

The results of the present study agree with the results of Takahashi *et al.*, 2005 (8) in their study who demonstrated that even, the pathogenesis of granulation tissue formation and recurrent cholesteatoma is limited, but an important pathological process in this entity is active proliferation of epithelial cells, which is thought to be stimulated by various growth factors.

Among the latter, they focused in their study on the keratinocyte growth factor (KGF) which was abundantly located in the granulation tissue underneath the epithelium of the cholesteatoma, which is rich in keratinocyte growth factor receptors (GKGR), indicating that cell proliferation is facilitated by chronic inflammation underneath the cholesteatoma epithelium.

By comparison of the previous data with the antiproliferative effect of 5-FU that arises from inhibition of thymidylate synthetase, which converts ribonucleotides to deoxyribonucleotides, thus inhibiting DNA synthesis and granulation tissue cell proliferation.

From study of the previous mechanism of action of 5-FU it is concomitant with the high success rate in the present study as good and fair ratio after 3,4 and 6 months were 90 % , 90% and 85% respectively, as previous canal wall down procedure with good meatoplasty allow more contact between surface of inflammation and the applied 5-FU cream.

These results agree with Takahashi *et al.*, 2005 (8) results between attic type cholesteatoma and recurrent type one which were 77 % and 93 %

respectively after 6 months from initiation of the treatment.

The failed cases were due to recurrent infection during or after treatment or fungal infection as demonstrated by Takahashi results.

By analysis of data of the present study topical use of 5-FU cream had no serious side effects as preliminary and post treatment audiogram showed no deterioration of hearing loss, no tinnitus, no skin ulceration and no vertigo.

### Conclusion

In conclusion, 5-FU topical cream appeared effective and safe for treating discharging post-mastoidectomy cavities and with further studies on cholesteatoma patients, it may be one of the options in the treatment of cholesteatoma at least, when patients refuse or cannot have surgery for various reasons such as serious underlying diseases and old age.

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